Specialty Topics in Pediatric Neuropsychology

Michael J. Boivin
Bruno Giordani *Editors*

Neuropsychology of Children in Africa

Perspectives on Risk and Resilience

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Preface

The Purpose of This Book

Children in Africa face an astounding array of risk factors in their development, stemming from grinding poverty and from the myriad public health and educational challenges afflicting most of the continent. Because the developmental milieu for African children can vary so dramatically, this population provides fertile ground for the study of how brain/behavior development reflects both vulnerability and resilience in the face of impoverishment, war and displacement, and disease. Therefore, cross-cultural neuropsychology as applied to brain/behavior development in African children provides an excellent opportunity to further the frontiers of neurocognitive science in understanding how the human brain copes with pervasive developmental deprivation and stress within an ecosystem. This is the principal reason for this book.

This book is also very much needed for humanitarian reasons. It is only with advances in the field of cross-cultural neuropsychology with African children that biomedical science can discover evidence-based, effective, and sustainable ways of better protecting these children from significant brain/behavior injury. Cross-cultural neuropsychology will also provide the foundation for effective rehabilitation when such injury does occur. Of course, such advances will benefit not only African children but also children everywhere.

The Professional Pilgrimage Leading to the Inception of This Book

Working as a graduate student "rat-runner" in a behavioral biopsychology laboratory in 1976, I (mjb) would never have anticipated a career someday as a fulltime researcher with African children in the public health domain. That pilgrimage began that same year when I met my future wife, Grace, who was living in the USA and had planned to return to Africa with the Peace Corps after finishing university. Grace had grown up in the DR Congo where her father served for 35 years as a medical missionary and her mother as a school teacher. Through our courtship and marriage, Grace's upbringing in the Congo was an intriguing part of her past, but not relevant to my scientific and professional career goals at that time. Her Peace Corps volunteer plans evaporated as we married and began a family and as I settled into a career as a university psychology professor.

Ten years into our marriage and four children later, Grace's Africa past suddenly came to the forefront of our family life. She wanted to return as a family to Africa so that we could see her childhood "home" and the legacy of her parent's lifelong service before they retired from the mission field that following year. I did not want to travel to the DR Congo with our four young children, fearing for our health and safety. However, because of the support of a small overseas research grant from my university, and the generosity of Grace's parents, we were able to travel as a family to the Congo for a month-long stay at a small remote medical mission where Grace's parents lived, several hundred kilometers east of Kinshasa.

That month at this remote medical mission changed my life. My wife and I and our four small children spent that month with her parents at the medical mission of Moanza on the Inzia River in Bandundu Province, Zaire. While traveling that month to public health outposts with Grace's father and to villages with clean water due to the efforts of a newfound Peace Corps volunteer friend, David Anderson, I saw and felt a level of human need and suffering that I could never have imagined. It was then that I proposed to use whatever tools or skills I had to offer in brain/behavior science, to trying to make a difference in addressing that need.

It challenged me to find a way to make my scientific passion relevant to the needs of these children and led to my returning to the DR Congo a year later on a Fulbright research award to investigate the neuropsychological outcomes of various public health risk factors and interventions in the northern Bandundu Province. That year at the small medical mission of Kikongo in northern Bandundu Province solidified my commitment to finding ways to making neuropsychological science relevant to the public health needs of African children in low-resource settings. At the end of that Fulbright research year in August 1991, we left the country only weeks before Mobutu's army units began widespread looting in major cities, eventual anarchy and civil war, an invasion from Rwanda, and the ultimate collapse of the government of Sese Seko Mobutu.

This was the first of two Fulbright fellowships to Africa (Zaire 1990; Uganda 2003), a West African Research Association Fellowship (Senegal 1997), and as a PI on 6 NIH-sponsored research grants to Uganda. These activities eventually positioned Bruno Giordani and me to consider a book that could provide an overview of the research taking place on the neurodevelopment and neuropsychology of African children in low-resource settings.

Influences Shaping the Public Health Emphasis in the Neuropsychology of African Children

Following my Fulbright year in the DR Congo, I pursued a master's degree in public health at the University of Michigan while continuing to teach fulltime in psychology at my home university. The plan was to return to Africa and to pursue a fulltime vocation in public health work with African children. As I pursued my M.P.H. degree following my Fulbright year in the DR Congo, my training and passion for brain/behavior science shifted fully towards a global health emphasis. My thesis topic was on the neuromotor disease called konzo, a disease in the DR Congo for insufficiently processed toxic cassava (Boivin 1997). In September 2011, I returned to the DR Congo after 20 years to begin a neuropsychological investigation of konzo, with the support of an NIH grant to Dr. Tshala-Katumbay, a neurologist from the DRC who is now at Oregon Health and Sciences University (see https://vimeo.com/42317386 for a video overview of this study).

Working with my mentor in neuropsychology, Dr. Bruno Giordani, we evidenced this newfound professional trajectory with publications from my summer research experience in the DR Congo in 1989 (Boivin 1991) and from the year-long Fulbright award the following year (1990–1991) (Boivin and Giordani 1993; Boivin et al. 1993, 1995a, b, 1996; Giordani et al. 1996).

Following my MPH degree, I consulted with Penny Holding on her Kenyan-based study on the neuropsychology of cerebral malaria (Holding et al. 1999), and I returned to Africa for 2 months for a neuropsychology of cerebral malaria in Senegal in 1997 (as a West African Research Association fellow) (Boivin 2002, 2006). Dr. Holding has a chapter in this book on cerebral malaria, as does one of her former students (Dr. Abubakar) on malnutrition. Then in 2003, I received my second Fulbright research award, which allowed me to complete a year-long study on the neuropsychology and immunopathogenesis of cerebral malaria at Makerere Medical School/Mulago Hospital in Kampala, Uganda.

During that year, a partnership was formed among a core team of Ugandan and American researchers. This collaboration has been sustained to this day with the support of NIH grants. I acknowledge the dedication and support of Dr. Chandy John at the University of Minnesota; Drs. Paul Bangirana, Robert Opika Opoka, Noeline Nakasujja, and Justus Byarugaba at Makerere University; and Ms. Esther Ssebyala at Global Health Uganda. Without their dedication and support, my second Fulbright year could never have succeeded, and our research program today could never have been realized. It is because of their friendship and support that my colleague and friend, Bruno Giordani, was able to be directly involved as a coinvestigator in our NIH-sponsored work in Uganda and that the dream for this book could be realized. Our Fulbright experience as a family in 2003–2004 in Uganda is available on the Fulbright website at http://www.cies.org/stories/s_mboivin.htm.

Paul Bangirana, who was my first research assistant during that Fulbright year in Uganda, eventually went on to earn his Ph.D. in neuropsychology (Uganda's first) and has a chapter in this book as well. Thanks to a recent NIH D43 training grant embedded within our malaria research program at Makerere/Mulago, we now have support for the Ph.D. training in neuropsychology for two more Ugandans, and this book will be one of the resources for their training.

Because of this Fulbright research award (Uganda, 2003–2004) as well as an NIH/Fogarty R21 grant (PI: John), we were able to publish pioneering research in the neuropsychology and immunopathogenesis of cerebral malaria (Boivin et al. 2007; John et al. 2008a, b). The role these colleagues played in eventually making possible this book is also evidenced by the cerebral malaria publications of our research group in leading journals and our presentations at many international and national meetings (Bangirana et al. 2009; Bangirana et al. 2006; Boivin et al. 2007, 2008; John et al. 2006, 2008a, b, c).

Student Collaborators and the Further Formation of This Book

Since my coming to Michigan State University in 2006, Bruno Giordani and I have had the opportunity to bring graduate and medical students from our respective universities to Uganda for summer research internships. The Ugandan-based research efforts of those students in our NIMH-sponsored pediatric HIV research programs have blossomed into several chapters in this book (Chaps. 5 and 6 by Dr. Rachelle Busman; Chap. 7 by Erin Lorencz). Other significant presentations and publications have come out of their work (Boivin et al. 2008; Boivin et al. 2010a, b). Her doctoral dissertation work with HIV orphans in Malawi is represented in Kim Ferguson's chapter, and other chapters represent joint authorship and collaboration between senior scholars and their students (e.g., Chaps. 3, 8, 10, and 15). This volume represents an excellent balance among more established senior investigators who pioneered neurodevelopmental research in African children (e.g., Dr. Jane Kvalsvig) and some of the best and brightest of a new generation of African child development scholars and researchers who have taken the lead in their own chapter contributions (e.g., Drs. Abubakar, Kihara, Bangirana, and Ferguson).

Because of the pandemic of HIV disease and severe malaria across the sub-Sahara of Africa, neuropsychological studies of affected children have multiplied over the past two decades especially. The scientific literature related to the developmental effects of these and other tropical diseases has blossomed to the point where a book is very much needed to organize and interpret the state of the science. This book fills this gap in the scientific literature by providing a review of the neuropsychological research literature in African children as affected by major diseases such as HIV and severe malaria, malnutrition, sickle-cell disease, and other pervasive medical and social risk factors. Our book provides a hopeful dimension by providing evidence of the neuropsychological benefit of public health therapeutic interventions that have occurred in response to these developmental threats.

Biocultural Co-constructivism as the Organizing Framework for This Book

As we interpret the various chapters related to the neuropsychological effects of disease and deprivation on brain/behavior development of African children, we will use the "co-constructive" paradigm (Li 2003). This paradigmatic approach was applied to a review of portions of the pediatric neuropsychology literature related to HIV and to severe malaria in a recent chapter by Boivin and Giordani (2009). This chapter provides the framework for the present book proposal. Cross-level dynamic biocultural co-constructivism is a holistic multidimensional approach that emphasizes reciprocal biocultural influences across the life span. It also emphasizes the reciprocal interaction of culture and the genome in shaping brain/mind at multiple levels: neurobiological, cognitive, behavioral, and sociocultural (Li 2003). The successive chapters and sections of our book address each of these levels in practical and innovative ways.

The concept of neuroplasticity in human development is central to the dynamic biocultural co-constructivist paradigm, and this concept will drive our understanding of how risk, resilience, and rehabilitation occur for African children. These constructs are particularly relevant when considering the array of ecological stressors of pervasive disease and deprivation encompassed within this book. The book addresses how cross-cultural neuropsychology in healthy and diseased brains, brain imaging technologies, and genomic research can triangulate the manner in which a universal brain/behavior omnibus drives plasticity across the life span. As such, the further scientific characterization of the brain/behavior development of African children can provide a vital lynchpin between biology and culture in Li's co-constructive paradigm. Ultimately, this has the potential of revolutionizing our understanding of neurocognitive development and culture.

This volume was inspired by a conceptual overview of our African-based neuropsychological assessment work in severe malaria and in HIV (Boivin and Giordani 2009). The chapter was entitled "Neuropsychological Assessment of African Children: Evidence for a Universal Brain/Behavior Omnibus Within a Co-constructivist Paradigm." It was published in an edited volume of *Progress in Brain Research* dedicated to the theme of cross-cultural cognitive neuroscience (J.Y. Chiao, Ed.). Our chapter was the only one that focused on African children.

At that point, we decided that a book was needed that would compile and organize a sample of the immense wealth of neurodevelopmental/neuropsychological research emerging from this continent. This book is the first of its kind, providing an integrated conceptual overview and interpretation of what we consider to be some of the best of what this emerging field has to offer, contributed by an all-star cast of its leading scientists and scholars. Dr. Elaine Fletcher-Janzen, the editor for the Springer Publishers Series in cross-cultural neuropsychology, believes that this book will be a "seminal" work for developmental brain/behavior science in general. We agree with this assessment, not because of our efforts but because of the outstanding contributions from the chapter authors who represent the leading scientists and scholars in the field of the neurodevelopment of African children. They present their work with clarity, rigor, innovation, and humanitarian concern for the well-being of African children.

The foundational premise of this book is that neuropsychology has the tools to provide a sensitive, sensible, and consistent methodology for characterizing patterns of risk and resilience in the brain/behavior development of African children. This premise is borne out evidentially in successive chapters as neurodevelopmental and neurocognitive performance is evaluated for children at risk from HIV, malaria, malnutrition, sickle-cell disease, and other public health risk factors. These brain–behavior disease processes are also modified in a consistent manner cross-culturally by quality of developmental milieu and caregiving. Later chapters present findings from the pioneering use of computerized cognitive rehabilitation therapy (CCRT) with Ugandan children surviving CM and with HIV. This neuropsychological evidence that CCRT enhances positive brain plasticity in a consistent manner across cultures supports the "co-constructive" paradigm (Li 2003), since plasticity across the life span is the hallmark of this approach.

In the final chapter, we summarize and interpret the principal scientific and theoretical contributions of the chapters using the concept of a brain/behavior omnibus. This metaphor is proposed as a way to conceptually interface foundational neuropsychological functions consistent across cultures, with cognitive tendencies and abilities more readily shaped by ecological necessity and cultural experience. We also believe that future cross-cultural neuropsychological research will describe and substantiate the explanatory power of the construct of a universal brain/behavior omnibus.

In conclusion, we posit that it is critical that any neuropsychological assessments applied across cultures be based on the latest cognitive neuroscience and neuroimaging research. This is because the cross-cultural application of neuropsychology assessments has provided a means of methodologically triangulating the omnibus. It does so by using more dynamic assessments across various cultural groups, along with neuroimaging and genomic technologies in both impoverished and resource-rich settings. Cross-cultural neuropsychology, brain imaging, and genomic technologies together can elucidate a brain/behavior omnibus foundational to human plasticity across the life span. The integration of these approaches can provide a powerful new paradigm in understanding the relationship between the developing brain, culture, and cognitive ability. Such a paradigm can help us better understand how, across the life span, ecological necessity sculpts culturally specific cognitive ability profiles, doing so upon a universal brain/behavior omnibus.

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Acknowledgments

Bruno Giordani

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Bedell, Steven B. Manuck, and, my closest and longest mentor and friend, Stanley Berent. I also thank my colleague, David Potter, who has emphasized the importance of an international, historical perspective in research and life and, of course, my collaborator and friend all these years, Michael Boivin. Finally, I would like to thank my family for their long patience and support with my work and travels—my wife, Anne; my children, Helen and James; my mother-in-law Elizabeth Burroughs; and my father and mother, Papa Bruno and Nonna Johanna.

Michael J. Boivin

> Some men see things as they are and ask why. Others dream things that never were and ask why not.
>
> George Bernard Shaw

My collaboration with Dr. Bruno Giordani and my other colleagues and my work in Africa, let alone this book, would never have happened had it not been for my wife Grace and her missionary parents, Dr. Norman and Jean Abell. Now, as I write these words, Dr. Abell is in hospice care as he continues to weaken day by day from lung and other infections related to chronic bronchial infections and other complications from post-polio syndrome. His affliction is borne out of compassionate humanitarian service to afflicted children in Africa. Our book is dedicated, in part, to that sacrifice.

Norman Abell arrived in what was then the Belgian Congo in 1956, the only surgeon in a missionary hospital serving a region of 50,000 people. His career as a surgeon ended in 1961 after, although vaccinated with the Salk vaccine, he contracted polio from treating a Congolese infant with the disease. Following a long and difficult recovery that left him without the use of his left arm and with general weakness in his legs, he completed an MPH at Johns Hopkins School of Public Health. He then spent the next 18 years in public health administration and as a general practitioner in the western part of Zaire.

It was not just seeing the need firsthand that changed my life during my first trip to the DR Congo in June 1989; it was also seeing how he poured himself into meeting that need in compassionate, skillful, and creative ways despite the physical obstacles stemming from post-polio syndrome. This is why I (mjb) dedicate my efforts in this book to Dr. Norman Abell, Mrs. Jean Abell his wife who has worked side by side with him during almost 65 years of marriage, and to their daughter and my wife of 34 years, Grace (Abell) Boivin. Finally, I dedicate these efforts to Grace and my four children: Monique, Daniel, Josiah, and Matthew. They all had to endure being uprooted and carried off to Africa for extended periods of time during our Fulbright years. Monique herself is now pursuing a career in global public health, perhaps in part because of these experiences. Hopefully this book will be relevant to her work.

I also must acknowledge my mentors along the way and those who helped make this book possible. Dr. John Allen was my first mentor as my principal psychology professor during my undergraduate years. I have shared in more detail how he mentored me in an article I published after his unexpected passing (Boivin 1988). During a sabbatical year at the University of Michigan in 1987, I began my transition from rat-runner to human neuropsychology research under the tutelage of Dr. Bruno Giordani (coeditor of this volume) and Dr. Stanley Berent. I will always be grateful to them for the opportunity to learn in their program and continue my involvement to this day as an adjunct associate professor in the University of Michigan medical school.

This expertise, along with my MPH in public health and my close relationships with a number of international and national colleagues, were a good complement to the global neurology research expertise already represented in Dr. Gretchen Birbeck's International Neurologic and Psychiatric Epidemiology Program (INPEP). It was this marriage of neuropsychology and neurology within INPEP's Africa-based and global health vision which brought me to Michigan State University in May 2006. Without the support of Drs. Jed Magen (MSU Psychiatry Chair), David Kaufman (MSU Neurology Chair), and Gretchen Birbeck (MSU INPEP Director), I would never have had the opportunity to become engaged full-time in this field of research.

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Finally, we must acknowledge the various students who have worked beside us since we began this work over 20 years ago. We are committed to an educational model that moves students into a mentoring relationship with professional persons who can bring them alongside and model the profession with integrity, virtue, and human ethical concern. Just communicating disciplinary content is not enough. For transformative learning to occur, students must "do." As they begin to see their mentors model the pursuit of the discipline or profession with virtue and integrity, students begin to realize the substance of what that university has to offer.

Our graduate and medical students that have worked with us in Africa have consistently challenged us to embody the commitment and excellence to which we ask them to aspire. They have made us better persons and scientists. Some have chapters in this book (Rachelle Busman, Erin Lorencz, Paul Bangirana, Hailey Wouters, Karen Dobias). Others have published and presented work with us that has been foundational to our research represented in this volume (Sujal Parikh, who died in Uganda from a tragic accident), Raina Vachhani, and Elizabeth Schut). Others have very recently worked beside us in Uganda and helped sustain our research program efforts in very practical ways (Esther van der Lugt, Kim Walhof, Sarah Murray).

These students have served to remind us,

> "… that the effective teacher is not a pleader, a performer, or huckster, 'but a confident, exuberant guide on expeditions of shared responsibility—perhaps most like a mountaineering guide…'. We must never lose sight of the magic and majesty of the learning experience: nor should we forget that good teaching is a self-eradicating process. Teaching must be a highly active and interactive task of shared responsibilities and risks." (Butman 1993, p. 255)

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Chapter 1
An Introduction to the Neuropsychology of African Children Within a Co-constructivist Paradigm

Michael J. Boivin, Hailey Wouters, and Bruno Giordani

1.1 The Neurodevelopment of African Children: A Strategic Vantage Point

The neurodevelopmental and neuropsychological (ND/NP) assessment of African children is a strategic vantage point from which to advance a scientific approach to child development. Such a process is vital to providing an evidence-based approach to public health interventions for at-risk children, particularly in a resource-poor setting. The humanitarian need for these scientific tools is great, because no other continent has a greater proportion of children at risk from infectious disease (malaria, HIV, diarrheal disease, and a host of other CNS infections), malnutrition, and genetically based chronic disease [e.g., sickle-cell disease (SCD)]. At the same time, no other continent faces greater challenges in addressing these risk factors with effective, accessible, and sufficient programmatic resources to enhance brain–behavior development in the face of these overwhelming public health issues.

The purpose of this book is to provide methodological and theoretical resources for the use of ND/NP assessment in developing evidence-based interventions to

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address the developmental needs of African children in the public health context. We believe that this is the first such book and that it comes at a critical time in this field of work.

1.1.1 Three Areas of Emphasis for Each Chapter

All of the chapters in this book contribute to the field of child development in three ways, by providing the following: (1) methodological tools for ND/NP research in low-resource settings in Sub-Sahara Africa, (2) scientific contributions related to an understanding of the developmental brain/behavior effects of the public health risk factors studied for African children, and (3) theoretical contributions as to how risk factors and resilience come into play in child development universally. Although all of the chapters in this book address all three areas, they vary as to the relative emphasis placed on each. In this introductory overview, we briefly characterize the areas of emphasis for each chapter.

1.1.2 Cross-Level Dynamic Biocultural Co-constructivism

Li (2003) uses this phrase to describe a framework for understanding the biocultural orchestration of developmental plasticity in brain/behavior development (Li 2003). We believe that this is a useful framework when considering the ND/NP assessment of African children in terms of risk and resilience because it is comprehensive, multilevel, interactive, and dynamic in its approach to brain/behavior development in children. The basic elements of Li's co-constructivist approach are not novel considerations within the history of the nature-nurture and mind–brain debate. However, Li's approach is comprehensive and contemporary in terms of how it frames these enduring issues. This makes Li's dynamic biocultural co-constructivism a useful paradigm for organizing the chapter topics, research findings, and predominant themes in this book.

1.1.3 Principal Emphases of Li's Biocultural Co-constructivism

A more detailed presentation of Li's co-constructivist approach is found in the original review article (Li 2003). Some of the most essential features are as follows: (1) a definition of culture that lends itself to biological interactions; (2) a multilevel mutually interactive emphasis between biology, culture, and social evolution; (3) a core emphasis on brain/behavior plasticity; (4) a core emphasis on dynamic

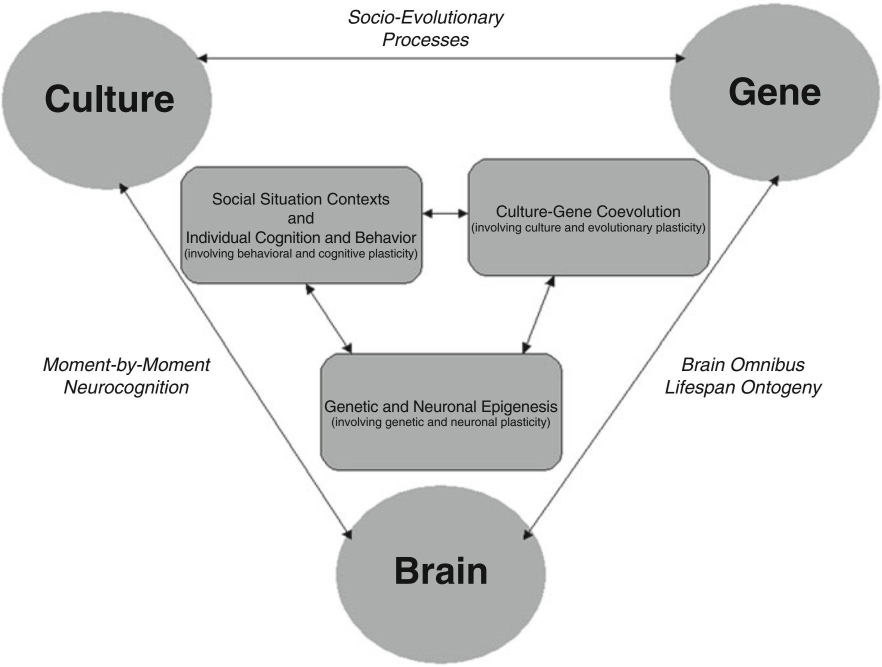

Fig. 1.1 This schematic is adapted from Li (2003) to depict the principal levels of interaction for dynamic biocultural co-constructivism. The mutually interactive levels are culture, genes, and brain. These three levels interact in terms of culture–gene socio-evolutionary processes, culture–brain moment-by-moment neurocognition, and gene–brain universal brain/behavior omnibus processes across the life span (see Chap. 16). The foundational principal for this multilevel interaction is brain plasticity, which occurs at the evolutionary, cultural, individual, and neuronal/microgenesis levels

brain/behavior processes across time (moment-by-moment, across the life span, or in human evolutionary processes over epochs); and (5) the integration of behavioral genetics and cognitive neuroscience in child development theory.

Within Li's co-constructivist paradigm are three levels of interactive processes. The highest level involves socio-evolutionary processes between culture and gene, whereby culture modifies natural selection to shape biological evolution (human phylogeny) (see Fig. 1.1). The next level involves interactions between gene and brain during the lifetime of the individual (brain/behavior omnibus). At this level, genes shape behavioral and cognitive development during the lifetime of the individual (life span ontogeny). The third level is that of culture–immediate individual context, where culture shapes and directs moment-by-moment neurocognition. The interactions among these three levels are dynamic and bidirectional (top–downward and bottom–upward) (Fig. 1.1).

1.1.4 Framework for Introductory Overview of Successive Chapters

For the following chapter overviews, we note the predominant emphasis for each: methodological, scientific, or theoretical. We will also note each chapter's principal contributions in terms of specific interactive processes (culture–brain, culture–gene, gene–brain).

1.2 Approaches to Assessment of Very Young Children in Africa in the Context of HIV (Kammerer, Isquith, and Lundy)

In spite of substantial progress in HIV/AIDS prevention and treatment, the overall encumbrance of the HIV epidemic remains highest in sub-Saharan Africa. In this area, children living with the disease and developmentally at risk because of the effects of HIV on their households and caregiving, are faced with grim challenges each day. Given the numerous risk factors, it is imperative to follow the development of these children to determine the true extent of the human burden of HIV disease. This chapter primarily emphasizes methodological considerations in the developmental assessment of very young African children affected by HIV.

Identifying the effects of HIV disease and the various biological factors associated with the disease is a necessary process in order to maximize the efficacy of interventions. While assessment methodologies to measure the impact of risks in HIV/AIDS are well developed in industrialized countries, these methodologies do not necessarily translate directly within African culture or languages. This chapter focuses on the current status of assessment of African children for arriving at valid and sensitive measures of the impact of HIV disease.

Existing tests that have been adapted for use in Africa are examined and compared with data from other studies in other cultures and diseases. Various fundamental assessment issues are reviewed, such as whether to rely on direct or indirect assessment methods, inclusive measures, or domain-specific measures.

This chapter also defines the features of African culture within a complex web of poverty that informs how best to interpret the developmental outcomes of HIV disease. As such, it contributes to the first area of emphasis in Li's co-constructivist paradigm (culture–brain). It does so by making comparisons across studies within different cultural contexts in the study of pediatric HIV. In doing so, this chapter fosters a co-constructive approach toward understanding brain–behavior relationships in very young children at risk from this disease.

1.3 Acknowledging Methodological Complexity in Assessing Children in HIV-Affected Communities (Kvalsvig, Taylor, Kauchali, and Chhagan)

Progress toward improving the circumstances of children living in poverty in resource-poor settings where HIV is prevalent is often complicated by social and economic repercussions from this disease in communities and households. For example, many children living in sub-Saharan Africa already experience poor nutrition and a lack of quality health and education services because they live amid social and political disruption. These pervasive risk factors are significantly aggravated by HIV.

The principal thrust of this chapter is to sensitize the reader to the methodological complexities of assessing developmental outcomes in children with HIV within this cultural context. The authors also caution that any recommendations related to potential interventions for children must recognize the multifaceted and dynamic roots of developmental lag associated with HIV.

Most of the ND/NP data available to guide intervention for children with HIV are mainly from research conducted in developed nations, where the risk factors are less severe and support services are more accessible for children. This chapter focuses on the circumstances of children living in poverty in resource-poor KwaZulu-Natal, South Africa, where HIV infections are widespread. It illustrates how best to define the impact of culture on child development by incorporating the biological impact of pediatric HIV disease on brain/behavior development. Consistent with this, the chapter proposes methodological approaches for research in KwaZulu-Natal as an example of how to optimize the development of children living in a communities affected by poverty, HIV, and a limitation of resources. In so doing, this chapter emphasizes the complex interactions between culture and brain as children develop in impoverished communities affected by HIV.

1.4 Cognitive, Motor, and Behavioral Development of Orphans of HIV/AIDS in Institutional Contexts (Ferguson and Lee)

Each year, millions of children in sub-Saharan Africa lose one or both parents to HIV/AIDS. As orphan populations in Africa rise, reliance on infant orphanages increases. With 650,000 children orphaned by HIV/AIDS, Malawi is one of the countries most profoundly impacted by this crisis. Due to the increasing number of infants being institutionalized in Malawi, as well as across sub-Saharan Africa, an assessment of infants' developmental functioning within these orphanages and of the quality of care provided is drastically needed.

This chapter describes a methodology for the cognitive, motor, and behavioral assessment of infants living in institutional settings, using as an example a study of sixty 2- to 35-month-old orphaned children in Malawi. This chapter's emphasis on evaluative approaches complements the focus in the previous two chapters on assessment methodology for very young African children living with HIV in resource-poor settings.

The results of the research program described in this chapter demonstrate that orphaned Malawian children's cognitive and motor development appear to be less optimal than in US samples, while their behavioral development is more optimal. These findings are compared with other studies evaluating both institutionalized and noninstitutionalized children and related to an evaluation of quality of caregiving and learning enrichment in such settings. Specific evidence-based recommendations for interventions to improve Malawian infant's developmental functioning and the quality of physical and social environment within these institutions also are summarized. Evaluative results from such programs are desperately needed to inform African policy makers and orphan caretakers.

Throughout this chapter, the authors use a cross-cultural approach to emphasize a mutually interactive dynamic between culture and brain development for institutionalized children affected by HIV in Malawi. Because of this emphasis, the theoretical model used by Ferguson and her colleagues in the interpretation of their study findings are grounded within a co-constructivist culture–gene and gene–brain approach.

1.5 Factors Contributing to the Psychosocial Adjustment of Ugandan Preschool Children with HIV/AIDS (Busman, Page, Oka, Giordani, and Boivin)

This chapter addresses the psychosocial, motor, and cognitive development delays faced by rural Ugandan children with HIV/AIDS. Original research findings for preschool Ugandan children with HIV are used as a model for fostering a better scientific understanding of the developmental effects of pediatric HIV.

Data on psychosocial outcomes presented in this chapter are centered on internalizing (emotional well-being), externalizing (behavior toward others), and total psychosocial adjustment for younger children with HIV in the rural African context. These variables are studied according to an ecological model of stress and coping consistent with the co-constructivist approach proposed by Li (2003). The results from this study show a dynamic relationship between the child's living environment (demographic, health, and caregiving variables, along with child psychosocial development) and caregiver emotional well-being (e.g., anxiety and depression). For example, children's internalizing (emotional) and total behavior symptoms are impacted by the quality of the relationship between the caregiver and the child, as modified by the mother's own level of depression and/or anxiety. These findings support a co-constructivist emphasis on risk and resilience (plasticity).

It does so by interpreting these findings in terms of dynamic interrelationships between HIV disease and its impact on the family and caregiving quality. The authors then go on to interpret these risk and resilience factors in terms of life span brain/behavior development, both from the direct biological and the secondary psychosocial effects of the disease on the child. This dynamic approach, therefore, emphasizes co-constructivist interactions at both the culture–brain and gene–brain levels.

1.6 Examining the Psychosocial Adjustment and School Performance of Ugandan Children with HIV/AIDs (Busman, Oka, Giordani, and Boivin)

HIV/AIDS imposes a heavy burden on children and their families in sub-Saharan Africa. In particular, this epidemic has a widespread impact on the children of Uganda, where over 100,000 children are infected with HIV/AIDS. Because the AIDS epidemic has received global attention, medical treatment has improved recently; consequently, the life span of HIV/AIDS children is increasing. However, research examining the quality of life of these children is limited. Because having HIV/AIDS is associated with a plethora of negative outcomes, it is important to study the protective factors that promote resiliency. Research is needed to better comprehend the protective factors associated with psychosocial adjustment and educational success, because conclusions from such work can inform the development of interventions to endorse resilience and promote a better quality of life for Ugandan children with HIV/AIDS.

This chapter presents data from a study of 60 Ugandan children with vertically transmitted HIV. The study evaluates the psychosocial adjustment of children with chronic disease and its relationship to school performance, based on the stress and coping model of resilience. The model is similar to the one used by these authors in their previous chapter to evaluate the effects of HIV in very younger Ugandan children. However, the present chapter focuses on middle childhood in emphasizing the importance of child illness parameters and the caregiving context in planning for intervention for HIV/AIDS children in resource-poor settings in rural Africa.

The results of the research findings shared in this chapter have a clear theoretical focus. The findings emphasize the importance of cultural context in understanding the neuropsychological effects of HIV. As in the previous chapter, this chapter emphasizes a dynamic biocultural approach as vital for developing evidence-based interventions to combat the brain/behavior development risks through the school-age years for children affected by HIV disease in impoverished, low-resource African settings.

1.7 Screening for Neurodisability in Low-Resource Settings Using the Ten Questions Questionnaire (Lorencz and Boivin)

Although many tools used to evaluate child development in Europe and North America exist, western-specific assessment measures cannot be readily applied to all populations due to cultural differences and limited resources. This chapter focuses on assessment methodology and specifically the ten questions questionnaire (TQQ). The TQQ is a screening tool for childhood neurodisabilities widely used in low- and middle-income countries because of the ease with which it can be applied with little prerequisite training for administration and cost for this tool.

This chapter's theoretical contribution centers on a discussion of the utility and appropriateness of clinically validated screening tools to track the epidemiology of developmental risk in populations of children across time at all three levels (culture–brain, culture–gene, gene–brain). The validation of the epidemiological utility of the TQQ as a screening tool in ND/NP research with African children is consistent with Li's co-constructivist emphasis from a practical methodological standpoint. This is because the use of such tools with populations of African children can prove sensitive, practical, and sustainable in monitoring dynamic brain/behavior processes in children over time, whether moment-by-moment, across the life span, or intergenerationally within communities and across cultures.

1.8 Language Development in Sub-Saharan Africa (Alcock and Alibhai)

Studying children's language is an integral part of the study of child development, with early spoken language abilities being prognostic of future educational success. Language development is sensitive to causes of brain injury and dysfunction commonly faced by children in sub-Saharan Africa, such as HIV infection, cerebral malaria, meningitis. This chapter emphasizes the theoretical foundations of the neuropsychology of language, as applied across cultural contexts experienced by children in sub-Saharan African.

The chapter integrates its theoretical emphasis on language development with a methodological one in terms of assessment practices. This is because it is essential to develop culturally appropriate tools to study children's language in addition to attention placed on grammatical and lexical differences between languages. This chapter presents an outline of language research in sub-Saharan Africa, including lexical and language development in middle infancy, syntactic development, and language socialization.

To date, most studies of language development in this region have been motivated by linguistic theory. However, it is necessary to extend research findings to applied outcomes from programmatic interventions for children developmentally at risk in the African context. To illustrate, this chapter includes a practical emphasis by reviewing speech and language therapist capacity in East Africa and how to best incorporate results of scientific research findings into these types of language-specific interventions.

Alcock and Alibhai's review on the neuropsychology of language in African children illustrates a dynamic approach across the life span and across generations in the course of human social evolution of linguistic processes. At the same time, it illustrates how foundational language development is in studying co-constructivist interactions (top–downward and bottom–upward). The neuropsychology of language is foundational in assessing risk and resilience in the public health context in African children at the culture–brain, culture–gene, and gene–brain levels.

1.9 Psychosocial Aspects of Malnutrition Among African Children: Antecedents, Consequences, and Interventions (Abubakar)

Childhood malnutrition is a major public health problem worldwide. Malnutrition, which can be in the form of either undernutrition or overnutrition, can further stress already vulnerable populations by increasing the risk of mortality, morbidity, cognitive, and behavioral problems. Malnutrition not only leads to various psychosocial consequences, but is associated with a wide range of psychosocial antecedents. These can include compromised caregiving through poor maternal physical and emotional health, as well as in terms of maternal unemployment and impoverishment within a subsistence agricultural setting in which food security depends on the mother. Over the long terms, this places a child at risk due to a poor developmental *milieu* for children in the home from a lack of nutritional, healthcare, emotional, social, and cognitive development resources. When considered in this context, the human burden of undernutrition in African communities is perhaps one of the greatest threats to the future of this continent.

This chapter integrates the current empirical evidence concerning malnutrition-related effects on neurodevelopment in African children. As it does so, it highlights research gaps and possible points of intervention. The approach is largely theoretical, although linked to a practical application of evidence-based interventions at a programmatic level. Malnutrition is presented within an agro-economic context and therefore socially derived with profound neuropsychological and social repercussions in child development across the life span of individuals and communities and within the social evolution of populations in Africa.

1.10 Assessing the Effects of Maternal Anemia on Child Development in Benin (Bodeau-Livinec, Cot, Koura, and Boivin)

Although undernutrition and micronutrient deficiencies go hand-in-hand and are critically important in brain/behavior development, they are typically not considered together in a public health context in child development research. That is why this chapter on maternal anemia and child development outcomes is an excellent complement to the previous chapter on malnutrition.

Despite a high prevalence of anemia among women of child-bearing age in sub-Saharan Africa, little research has been done on anemia during pregnancy and how it impacts cognitive outcomes in childhood. Over half of pregnant women in Africa develop moderate anemia, with about 5–10 % of these women developing severe anemia. Anemia among pregnant mothers in Benin is common and is likely the result of genetic, agro-economic, and social/nutritional factors. Anemia increases the risk of mortality and morbidity in mothers. However, maternal anemia in pregnancy and maternal iron deficiencies are also associated with adverse developmental outcomes in children.

This chapter presents a methodological strategy for assessing the cognitive function of children at risk from anemia during pregnancy. To do so, data are presented that follow a group of infants born after a randomized controlled trial of sporadic preventive treatment for malaria in women during pregnancy in Benin. Mothers were followed from the second trimester of pregnancy until delivery, and blood samples were drawn three times during pregnancy to assess for infections (malaria) and micronutrient deficiencies. Blood samples in infants are collected to assess hemoglobin (Hgb) concentration, malaria, iron deficiency, and lead in blood. Children born to these mothers are then assessed with the Mullen Scales of Early Learning (MSEL) at 12 months of age.

The impact of maternal anemia on gestational and infant brain–behavior development is significant, yet presents complex methodological issues. The authors suggest that it is as yet unclear whether interventions developed for anemia in mothers during pregnancy (e.g., malaria prevention, micronutrient supplements such as folic acid, vitamin A, and iron) clearly benefit the neuropsychological development of their very young children. A multilevel co-constructivist approach on the mutually interactive dynamic between culture, gene, and brain are needed in addressing this research problem. Such an approach will also be important in arriving at evidence-based points of intervention that are sustainable with a maternal and child health public health program in a low-resource setting like rural Benin.

1.11 The Assessment of Skill Learning in African Children (Adi-Japha)

Procedural learning refers to the long-term memory system that allows acquisition of skills and habits, relying on a system of brain structures that include corticostriatal circuitry. This memory system is involved in multiple key developmental domains, such as motor skills, language rules, and academic achievement. In spite of the essential role of the procedural memory system in development, tasks related to this system are not commonly studied as part of the assessment of cognitive development in young children from resource-limited settings, such as sub-Saharan Africa.

This chapter focuses on age-appropriate and culturally sensitive measures of skill learning that involve both computer-based and paper-and-pencil testing. As such, this chapter is largely methodological. However, it also supports its assessment strategies on the basis of recent theoretical and scientific advances in the study of brain/behavior development in children.

Impairment in procedural learning is strongly associated with both developmental disorders that are related to learning disabilities and with diseases that affect the brain, such as cerebral malaria, HIV, and SCD. The results of this chapter highlight the importance of including a skill learning assessment with more traditional neuropsychological-based assessments, emphasizing the important contributions such an approach can contribute to the study of neurodevelopment in African children. Because motor-skill learning is a foundational and universal dimension in child brain/behavior development from a gene–brain standpoint, its assessment is vitally important in the neuropsychology of African children in low-resource settings. However, the author's methodological emphasis in this chapter can be readily interpreted in terms of both co-constructivist culture–brain and gene–brain interactions. Interactions at both levels make motor-skill learning a highly sensitive index of neuropsychological integrity (both in terms of risk and resilience) in African children.

1.12 Neuropsychology of Severe Malaria in African Children (Holding and Boivin)

Malaria remains one of the most widespread infections in the world, yet the human burden of disease globally is primarily in sub-Saharan African children. Severe malaria from *P. falciparum* infection is the most common acute non-traumatic childhood encephalopathy in African children, accounting for most hospital admissions and deaths in many endemic malaria areas. This chapter reviews the neuropsychological effects of severe malaria in African children.

The authors of this chapter review use a cross-cultural approach in surveying the neuropsychological research literature pertaining to severe malaria in African children. Throughout their review, they emphasize the importance of culturally appropriate and sensitive assessment tools to gauge the neuropsychological effects of severe malaria in a valid manner. Therefore, the chapter focus is heavily methodological, in presenting principals for designing a neuropsychological assessment battery that is valid and appropriate within a given cultural context in African low-resource settings.

A theoretical conclusion that emerges from their survey of the literature is that the neuropsychological effects of malaria should be considered as part of a syndrome. This is because there are multiple mechanisms and models of immunopathogenic and neuropathogenic neuropsychological sequelae for this disease. These multiple mechanisms, in turn, lead to multiple pathways for brain/behavior risk and resilience.

Furthermore, the brain/behavior effects of severe malaria are embedded within a multifaceted web of poverty that can carry with it malnutrition, comorbid infections (e.g., HIV), and poor caregiving from chronic illnesses and infections among the parents. Consequently, dynamic co-constructivist culture–brain, culture–gene, and gene–brain interactions are apparent throughout this systematic review of the neuropsychology of severe malaria in African children.

1.13 Computerized Cognitive Rehabilitation Training (CCRT) for African Children with Brain Injury from Disease (Bangirana, Boivin, and Giordani)

Sub-Saharan Africa has the highest prevalence of people living with HIV/AIDS along with other comorbid and opportunistic infectious diseases that compromise brain–behavior development. The developmental impact in children is expressed either directly or indirectly within affected households and communities. Such risk factors often result in cognitive diminishment and outright impairment and disability within African children most at risk. These risk factors typically reduce the likelihood of academic success for these children, future economic opportunities, and diminish overall quality of life throughout the life span. Consequently, more attention is now being given to intervention strategies for enhancing cognitive development in at-risk children during sensitive and strategic periods of their brain/behavior development.

Possible interventions include caregiver training, physical therapy, speech therapy, and cognitive rehabilitation and training. This chapter focuses on computerized cognitive rehabilitation interventions that have recently been piloted by the authors in resource-poor settings in Uganda. The authors' review of this "proof-of-concept" preliminary research work highlights current designs, outcomes, challenges encountered, and recommendations for programmatic assessment of intervention scale-up at the school and community levels.

This chapter addresses the methodology of computerized cognitive rehabilitation training (CCRT) with African children at risk due to brain injury from severe malarial disease, although this intervention has a ready application to a host of CNS infectious diseases for which African children are at risk. This chapter also addresses the theory of how cognitive rehabilitation training exploits the positive features of brain plasticity to facilitate neuropsychological recovery from brain injury in at-risk African children. As such, it is framed within a dynamic co-constructivist paradigm at several levels. Finally, the authors provide original scientific evidence for the effectiveness of such interventions among Ugandan children affected by severe malaria and by HIV disease.

Mobile network technology with access to the internet has profoundly affected the social fabric of African over the past 10 years, more so than any other part of the world. This technology is shaping the culture–gene, culture–social, and culture–immediate individual interactions of brain/behavior development in children. This chapter illustrates one attempt to realize a culture–immediate individual benefit in the form of cognitive rehabilitation from infectious disease brain injury that can readily lend itself to scale-up through mobile network technologies providing access to the worldwide web. These technological developments have the potential of revolutionizing the neuropsychological assessment and treatment of African children in low-resource settings.

1.14 Measurement of Cognitive Outcomes of At-Risk Children Using Novelty Processing in Rural Kenyan Children (Kihara)

Each year, millions of children who live in the developing world will not reach their developmental potential. A major challenge in measuring cognitive development in African children is the scarcity of culturally sensitive neuropsychological measures. In this chapter, event-related potentials (ERPs) are introduced as an approach to measure the impact of cerebral infarct on cognitive development in rural Kenyan children with severe malaria. ERPs are brain voltage fluctuations that are associated in time with a physical or mental occurrence. They can potentially provide insight into both the early stages of information processing in brain disease, as well as an accessible technology for mapping brain regions affected by the disease. Because the ability to process novel events is fundamental in cognitive development in children, the ERP response to novelty is a potentially important and sensitive tool to brain/behavior integrity and function from a co-constructivist gene–brain level.

The author of this chapter primarily emphasizes the methodology of this domain of brain/behavior research as a practical technology with great sensitivity and power in for brain–behavior research in sub-Saharan Africa. The application of this technology relies less on cultural- and language-based approaches in ND/NP assessment. Consequently, ERP technology has ready application across divergent cultures and contexts, providing a stable and consistent neuropsychological reference point in the advancement of brain/behavior developmental science in African children.

For ERP methodology, a neural waveform representing attention to the novel event is studied in auditory and visual modes and can be further demonstrated in passive tasks where the child does not need to respond actively. Because passive ERPs are not dependent on language and may be more culturally independent than standard neuropsychological tests, they are especially useful in understanding risk and resilience factors in brain development in African children for a wide range of public health risk factors.

The utility, sensitivity, and efficacy of ERPs in profiling ND/NP in rural Kenyan children are supported by research evidence by the author as ERP is used in children surviving severe malaria. The focus of this methodological tool is largely gene–brain, and ERPs can be a sensitive brain–behavior outcome for a host of CNS diseases and treatments. However, this tool can also provide a stable and sensitive measure for evaluating culture–brain interactions as well in widely divergent public health risk/resilience settings for child development.

1.15 The Neuropsychology of Sickle-Cell Disease in West African Children (Ruffieux and Hauert)

SCD imposes a major strain on West Africa, particularly Cameroon. Patients suffering from SCD are at risk of exhibiting cognitive deficits as a result of cerebrovascular complications associated with the disease, such as silent infarcts. The high recurrence rates of cerebrovascular accidents make early detection and intervention especially important, yet neuroradiological markings are not available for most patients in Africa. A neuropsychological examination, however, may represent a quick, cost-effective way to screen for cognitive deficits in children at risk who may need urgent medical attention or neurocognitive rehabilitation.

The chapter reviews evidence from studies that pioneer the evaluation of the neurocognitive disabilities of patients with SCD in sub-Saharan Africa. This research program uses cognitive tests that are tailored to fit within the sociocultural context of Cameroon and demonstrates that patients with SCD present with a high occurrence of cognitive defects, with executive functioning and attention being specifically susceptible. As such, this chapter makes important scientific contributions to the understanding of the neuropsychological effects of this disease. This is of such great importance as a public health risk factor for children of African descent worldwide (gene–brain interactions).

Patients with SCD in Cameroon show cognitive deficit profiles that are very similar to those of patients in Western countries. Because of this, the principal findings in this chapter have significant theoretical importance in the study of common neuropathological mechanisms across divergent cultural settings at a co-constructivist culture–brain level of interaction.

Because the results show that the disease produces parallel cognitive deficits across cultures, it is suggested that cognitive rehabilitation already developed in Western and industrial countries can be reasonably adapted to be used in resource-limited countries. These findings show that this approach to the assessment of cognitive functioning could make a major difference in the health management of a major public health problem, such as SCD, in a developing country such as the Cameroon.

1.16 Evidence for a Universal Brain/Behavior Omnibus Within a Co-constructivist Paradigm

Li's dynamic biocultural co-constructivist paradigm provides an introduction to the successive chapters in this book. In a review of the neuropsychology of pediatric HIV, severe malaria, and SCD, Boivin and Giordani (2009) supported the use of this paradigm. They do so by presenting data for consistent deficit patterns in attention, working memory, and learning disabilities in children with these disorders. Despite the fact that studies Boivin and Giordani (2009) reviewed took place in different cultural settings, children at risk from diseases with a common underlying neuropathogenic mechanism had similar neuropsychological deficit profiles (e.g., malaria in African children and SCD in African and American children, HIV encephalopathies in African and American children).

Furthermore, these brain–behavior disease processes are affected in consistent and measureable ways as they relate to quality of developmental *milieu* and caregiving on ND/NP outcomes (Boivin and Giordani 2009). They conclude that risk and resilience in the brain/behavior development of children can be understood as embedded within a universal brain/behavior omnibus. The construct of a brain/behavior omnibus could provide the vital lynchpin between biology and culture in Li's co-constructive paradigm. This construct can lead to important insights into the understanding of the interface between genes and cognitive neuroscience within a cross-cultural neuropsychology of African children.

Boivin and Giordani (2009) described an "omnibus" as a computer-based processing framework that relates to or provides for many different processes all at once in achieving the functional power of the machine. However, the authors are not using the term "omnibus" to simply liken the human brain to a computer. Rather, it is a metaphor to denote the manner in which bidirectional biocultural interactions can shape brain/behavior development and plasticity across the life span, specific to the ecological needs of a given cultural context.

This understanding is at the core of Li's co-constructivist approach. We believe that the metaphor of the brain/behavior omnibus provides a unique and powerful analytical construct from which to advance scientific understanding of gene/brain interactions that are foundational to cognitive neuroscientific theory and research. It can empower a co-constructivist paradigm in ultimately revolutionizing our understanding of genes, society, brain, and cognition.

The final chapter in this book (Chap. 16) returns to this theme in order to interpret the principal contributions of each chapter. These chapter contributions are seen as providing a wealth of evidence for a universal brain/behavior omnibus as framed within a co-constructivist paradigm. The placement of a universal brain/behavior omnibus within a biocultural co-constructivist paradigm is at the gene–brain level of interactions and can be visualized in Fig. 1.1. Consideration is given in the final chapter at the conclusion of this book, as to how the principal findings of each chapter help better characterize the structural form and function of such an omnibus. We believe that taken together, the principal contributions from this book evidence how a cross-cultural neuropsychology of African children can significantly and strategically advance the field of brain/behavior science in understanding human development.

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Chapter 2
Approaches to Assessment of Very Young Children in Africa in the Context of HIV

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2.1 HIV and the Children of Africa

Although there have been major advances in the treatment and prevention of HIV disease worldwide, the HIV epidemic continues to present dire challenges to the health, well-being, and quality of life for the children of Africa. The overall burden of HIV is present across the continent and remains highest in sub-Saharan Africa. Of the 33.3 million people in the world living with HIV in 2009, 22.5 million were living in sub-Saharan Africa, including 2.3 million children (UNAIDS 2010).

Efforts to prevent and manage HIV in Africa over the past decade have resulted in some reduction of the impact of the disease. Much of this positive trajectory is due to greater, though not yet universal or consistent, availability of antiretroviral medications for HIV treatment and prevention. In sub-Saharan Africa, increased access to treatment was associated with a 20 % decrease in AIDS-related deaths between 2004 and 2009 (UNAIDS 2010), though coverage remains below 40 % for those in need of medications, leaving ample room for continued reduction in mortality. Medications to prevent mother-to-child transmission of HIV have also dramatically reduced the number of children born with HIV in recent years.

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For the 2.3 million children currently living with this disease in Africa, and for the many more children secondarily *affected* by HIV in their families and communities, there is an imperative need to understand the impact of HIV on their lives in order to better develop efficacious interventions. For children with HIV who do not have consistent access to treatment, there are health issues from and related to HIV. Studies of neurocognitive outcomes have shown that children with early HIV infection are at greater risk for disease-related encephalopathy, with measures documenting delays in development and deficits in functioning across multiple domains (Abubakar et al. 2008b; Sherr et al. 2009; Van Rie et al. 2007).

Children who are HIV-exposed, that is, children who are uninfected but whose mother is HIV-positive, are also at substantial risk for poorer developmental outcomes. HIV-exposed children in Africa currently are at risk for increased morbidity and mortality, though the potential impact on neurocognitive outcomes is inconclusive (Filteau 2009). The possible risk factors for HIV-exposed children include biological factors such as low birth weight (Wei et al. 2004) or possibly exposure to prenatal maternal infections or ARV medications. Environmental factors may also play a role in outcomes for children who are HIV-exposed, such as parental illness, which can dramatically affect the child's experience (Steele et al. 2007). Multiple additional issues related to the cycle of poverty can complicate the lives of children affected by HIV, similar to those of other children in need in Africa. Children are at risk for experiencing inadequate nutrition, decreased cognitive stimulation, caregiver depression or absence, and other chronic health issues.

Given the multiple risk factors, it is essential to follow the development of these children to determine the impact of HIV disease and treatment on their lives with an eye toward maximizing the efficacy of interventions. Disentangling the effects of the disease, other biological factors associated with HIV disease, and environmental repercussions related to HIV is extraordinarily complex but also necessary to develop appropriate interventions that directly address documented problems. Understanding these children also requires a true comprehension of the many factors in child rearing and community integrity that *support* resilience in unique ways within the diverse cultures in Africa (Marfo et al. 2011).

In developing a comprehensive understanding of the impact of HIV, interventions, and other risk factors and protective factors in children at risk in Africa, it is important to measure and track their development longitudinally. Development in most respects (e.g., cognitive, motor, social, emotional) is the result of a dynamic interplay between factors related to the biological aspects of the child and the environment in which they grow in a co-constructivist manner, described as a brain–behavior "omnibus" (Boivin and Giordani 2009). The earliest period of this dynamic developmental process is immensely important to the child's long-term outcome since it is a time of primary brain development and plasticity. Negative effects of disease or environmental stressors such as poverty can have greater impact during early development, but interventions to reduce risk factors and support corrective factors may also be more beneficial in altering the developmental trajectory (Nelson 2000; Richter 2004). Indeed, both positive and negative neural and behavioral plasticity are "among the hallmarks of individual lifespan development and foundational to a co-constructivist approach" (Boivin and Giordani 2009, p. 119). Interventions during early development are sorely needed to establish critical skills and to provide essential stimulation for children, as these early years create a foundation which can determine much of a child's long-term potential (Shonkoff and Phillips 2000).

Given the importance of early intervention for children at risk for HIV, measuring the impact of early biological and environmental interventions on later development will maximize the efficacy and utility of limited intervention resources. Although assessment methodologies for measuring the impact of risks and resiliencies in the lives of children are relatively well developed in Western countries (or other industrialized countries that have developed assessment tools), these methodologies do not necessarily directly translate to assessment appropriate for other countries, cultures, or languages. Indeed, most assessments of the children in Africa, as well as from other countries, have been exceptionally complex due to a lack of assessment instruments that were developed, standardized, and validated for each purpose (e.g., cognitive, executive function, social–emotional), country, and culture. The role of culture in neuropsychological assessment has been studied only to a limited extent (Byrd et al. 2008). The lack of systematic measurement made possible by appropriately adapted or developed culturally sensitive tools for measuring the effects of HIV on children's development threatens to negate the accurate interpretation of data, particularly across studies conducted in different countries (Sherr et al. 2009). Without reliably interpretable assessment data, Sherr and colleagues (2009) noted that it is difficult to generalize across studies and there is "no guidance from the literature on which interventions would be most appropriate to ameliorate, reduce, or avoid" the effects of HIV exposure (p. 399).

This chapter reviews the current status of assessment of very young children in Africa, with a model of the impact of exposure to HIV. Critical variables in selection, development, adaptation, and use of assessment tools for this age group will be reviewed. Specific testing instruments are not recommended, as this choice depends on the purpose and population of the assessment, but commonly used measures are discussed.

2.2 Current Approaches to Assessment

Researchers interested in assessment of very young children have historically developed a number of methods for measuring development. Ideally, assessment materials, demands, and the assessment setting, itself, should be familiar to the children, reflect the intended constructs, exhibit appropriate evidence of reliability and validity, and demonstrate sensitivity to developmental changes and aberrations. Assessment tools should also be carefully developed to sample a broad array of abilities and be standardized against a typically developing population appropriate for comparison. While tasks employed for assessment of very young children do not have the same ability to discriminate between cognitive functions (e.g., language, spatial, executive) as do neuropsychological instruments for older children, they must nonetheless be well grounded in developmental neuroscience in order to measure the effects of disease processes or environmental stressors on the developing brain. This is a challenging set of demands even for measures commonly used in developed nations, though many measures widely used in Western countries do meet these stringent criteria. The same is not the case for assessment approaches of young children in the diversity of African cultures.

In most assessment situations of young children in Africa, the ideal "test" is not available, and the costs in time and money to develop culturally specific tests are often prohibitive. Approaches to assessment have thus followed two primary paths: developing culturally consonant measures derived from existing Western measures or adapting existing measures for use with children in Africa. A third path that entails pre–post-intervention or education measurement and using the size of change as an indicator of cognitive or other domains of functioning has recently emerged with some success (Boivin and Giordani 2009). In each method, assessment stems from analysis of the specific study goals, domains to be measured, and behaviors to be observed/reported. With an understanding of the goals of assessment, the most appropriate measures can be chosen, translated, adapted, tested, and eventually implemented. At the same time, it is important to accurately measure the array of biological and environmental factors that may impact the results of an assessment.

2.3 Measures Developed Within Africa

Instruments developed in the Western context are not directly applicable to assessing children in Africa. It cannot be assumed that an instrument developed for children in the United States (USA), for example, would measure the same constructs or abilities in children in other cultures. While children of different cultures may be able to perform the same set of tasks at similar levels, they may rely on different strategies or brain pathways to arrive at their solutions. Even simple motor response speed tasks, often considered universal in the Western context, may be culturally dependent (Hedden et al. 2002; Verney et al. 2005), as some cultures may favor accuracy over speed, while others favor the reverse.

One solution is to create a new measure specifically for the cultural group to be assessed. While potentially more costly in terms of time and resources, this allows for tasks to be chosen from materials and activities that are typical in the specific setting, domains of interest to be explicitly covered (e.g., language, motor, cognitive, social–emotional functioning), and norms that can be developed from a typically developing cohort from the same region in order to more accurately reflect children's functioning relative to expectations. Examples of this strategy are the Kilifi Developmental Checklist (KDC), later modified to become the Kilifi Developmental Inventory (KDI; Abubakar et al. 2007), and the associated Developmental Milestones Checklist (DMC; Abubakar et al. 2010a) both developed in Kenya and a screening instrument developed in Malawi, the Malawi

Developmental Assessment Tool (MDAT; Gladstone et al. 2010a, b). The development of each of these instruments followed rigorous test construction procedures beginning with identifying the domains to be measured; reviewing available, largely Western measurement instruments; selecting, reviewing, and piloting potential test items; assessing reliability characteristics; and initially demonstrating evidence of validity. Focus groups were used to ensure appropriateness of tasks and acceptability of the procedures. The rigorous development processes yielded measurement instruments with evidence of reliability and validity for use in the countries in which they were developed. Given the greater similarities between cultures within Africa than between Western and African cultures, many of the tasks and materials are likely more appropriate for many groups within Africa than are Western measures. It cannot be assumed, however, that norms or content developed for one cultural group within Africa would automatically be appropriate for use in other African countries. Application of these measures with other cultures within Africa remains to be examined.

Kilifi Developmental Checklist and Kilifi Developmental Inventory: Abubakar and colleagues (2007) developed the KDC by pooling culturally and developmentally appropriate items based on a broad review of established measures. The measure was subsequently modified to form the KDI (Abubakar et al. 2008a) that focused on locomotor, eye–hand coordination, and psychomotor skills in children aged 6–35 months. An initial study suggested appropriate internal consistency, inter-rater agreement, test–retest reliability, and sensitivity to maturational change. Children with known neurodevelopmental impairments achieved significantly lower scores than a typically developing community sample, suggesting sensitivity for detecting developmental delays or deficits. Children with HIV infection had lower scores than either an HIV-exposed group or a reference group (Abubakar et al. 2009). Disease stage and weight for age were also associated with KDI scores in this group of children in Kenya.

Developmental Milestones Checklist: To assess development through parent perceptions of their children's everyday functioning, Abubakar and colleagues (2010a) developed a structured interview for parents of children through 24 months of age in Kenya. Based on existing Western measures, the development process followed a standard course of collecting, reviewing, and reducing a pool of culturally appropriate items reflecting locomotor, fine motor, language, and personal–social development. The initial psychometric studies on typically developing children in Kenya showed high internal consistency and temporal stability, as well as sensitivity to maturational changes and nutritional deficiencies. Follow-up studies revealed that the DMC was sensitive to effects of risk factors in resource-limited settings in Kenya, including limited maternal education, poor health, and limited physical growth (Abubakar et al. 2010b).

Malawi Developmental Assessment Tool: In an effort to create a simple, culturally appropriate developmental screening tool for use in Malawi, Gladstone and colleagues (2008, 2010) collected and culled potential items from both Western measures and tasks suggested by local focus groups as representative of expected developmental behaviors. The tasks were reviewed for developmental and cultural appropriateness, assessed for evidence of face and content validity, and standardized on typically developing children in Malawi. The MDAT showed adequate inter-rater agreement and appropriate sensitivity and specificity for detecting children with known developmental disabilities. Boivin and colleagues (Boivin et al. 2011a) relied on the MDAT in a study of children in Malawi with cerebral malaria (CM). Children with CM showed significantly lower scores on the MDAT relative to children hospitalized for malaria without cerebral involvement, and scores in children with CM were significantly associated with biological markers of disease severity including coma duration, seizures, and platelet count.

2.4 Measures Adapted for Use in Africa

In many circumstances, creating a new test has not been feasible or desirable, often due to study timing or costs of development. Increasingly, a research goal is also to compare assessment findings across cultural groups, such as comparing the performance of individuals within disease groups between underdeveloped and developed nations (e.g., Africa and Europe or North America). Boivin and Giordani (2009) cogently argue for the use of well-developed, neuroscientifically informed measures in a cross-cultural context in order to facilitate "methodologically triangulating the omnibus" (p. 131) toward Li's (2003) co-constructive brain–behavior framework. That is, by measuring similar developmental constructs and environmental influences across cultures, the scientific community can better approximate universal "truths" about human brain–behavior relationships and their reciprocal interactions with the environment. Choosing assessment instruments, therefore, involves adapting existing, well-developed measures for use in the cross-cultural African context. Our review of studies, nonetheless, revealed that research articles have not always noted the type or degree of test adaptations used for studies in Africa, despite the importance of this information for understanding, replicating, and extending study findings.

Test adaptation is, however, complex and the rigor used in adaptation directly impacts the quality of assessment findings and generalizability. Adaptation methods range from solely translating the language of test instructions and items to replacing or modifying materials that are not appropriate in the new context to modifying language, procedures, materials, and even measured domains, with separate studies of the psychometric properties of the adapted measure and standardization in the intended cultural context. The most commonly adapted comprehensive assessment instruments for use in Africa with very young children are the Griffiths Mental Development Scale (GMDS; Griffiths 1984) and the Bayley Scales of Infant Development (BSID 1969, BSID II 1993, BSID III 2006), with more recent introduction of an adapted version of the Mullen Scales of Early Development (Mullen 1995).

Bayley Scales of Infant Development (BSID): The BSID are the most widely employed measure of early global development in the cross-cultural context.

There has been substantial variability, however, in the extent and type of adaptations. Early studies with the BSID in South Africa suggested that it was an appropriate tool for measuring development in South African children (Richter et al. 1992) and was sensitive to major risk factors as well as corrective factors (Cooper and Sandler 1997).

Several studies in Uganda adapted the second edition of the BSID, the BSID-II, for use with children with HIV, with cultural adaptations and translation of items and instructions into Luganda, the local language. Researchers relied on the raw number of items passed, as the US norms did not apply in Uganda and did not discriminate well at the lower end of the scale (Drotar et al. 1997; Peterson et al. 2001). More recent use of the adapted BSID-II to compare HIV-infected and HIV-exposed children with healthy controls in the Democratic Republic of Congo (DRC) found that HIV-infected children had the lowest developmental achievement, healthy controls the highest, and HIV-affected children were between the two groups (Van Rie et al. 2008, 2009). A translated BSID-II (no mention of adaptations) found that both HIV-infected and HIV-exposed children in Tanzania showed lower cognitive and motor development as well as a slower developmental trajectory between 6 and 18 months than did controls, suggesting a possible cumulative or interaction effect between HIV and environmental factors such as poverty (McGrath et al. 2006).

Studies in South Africa that relied on the BSID-II with translation, though few noted specifics of the adaptations, found that motor and cognitive development in HIV-infected children were below expectation in over 97 % of the sample (Baillieu and Potterton 2008). With minimal modification of the BSID II, Potterton and colleagues (2009) found that the majority of HIV-infected children had severe motor and cognitive delays. Weight for age and treatment (highly active antiretroviral therapy—HAART) were the most important predictive factors of performance on the BSID II, though the authors hypothesized that poverty was an additional risk factor. Assessment with the BSID II administered via translator (no mention of adaptations) revealed significant motor delays in 66 % of Xhosa-speaking HIV-infected children (Ferguson and Jelsma 2009).

Griffiths Mental Development Scale (GMDS; 1984): The GMDS has been widely used, particularly in South Africa, where multiple modifications have been implemented including translation of test materials and instructions and use of interpreter as needed. Despite frequent use in Africa, there are no consistent normative data for African populations, and scores have typically been compared to the British standardization sample. Children infected with HIV who were treated with HAART in Cape Town showed no measurable change on the GMDS following treatment with HAART (Smith et al. 2008). Children who were HIV-infected children aged 10–15 months who had early antiretroviral therapy achieved better locomotor and global scores on the GMDS than did children for whom therapy was deferred (Laughton et al. 2009). The research group also found that children from low socioeconomic environments who were born to HIV-uninfected mothers showed a decrease in overall scores on the GMDS over a 10–12-month time frame, attesting to environmental influences on overall development (Laughton et al. 2010).

Mullen Scales of Early Learning (Mullen 1995): Recent studies have explored using the Mullen Scales of Early Learning as a multicomponent performance measure of early child development for children in Africa. The Mullen is a comprehensive performance test battery composed of several components reflecting gross motor, fine motor, visual reception, receptive language, and expressive language functioning. Boivin and colleagues (2011b) employed the Mullen at three points in time to measure the impact of a parenting intervention on the developmental trajectory of HIV-infected children in Uganda. Following baseline assessment, the Mediational Intervention for Sensitizing Caregivers (MISC) biweekly intervention was conducted with 60 of 120 children and their caregivers, while the remaining 60 remained in a treatment as usual (TAU) group. By the 12-month follow-up, children in the MISC group showed greater developmental growth on the Mullen composite reflecting global cognitive functioning, mostly due to improvement on the Visual Reception scale. While available data are limited for this study to date, the Mullen may prove to be an adaptable measure of multiple domains of functioning and has the advantage of a wider age range than the Bayley and less intense administration training requirements.

2.5 Guidelines for Adapting Existing Measures

Adaptations that follow a rigorous process are likely to result in better quality assessment tools. Standards have been developed to guide appropriate adaptation of measures for use in developing countries (Hambleton and Kanjee 1995; Hambleton and Patsula 1999; Hambleton 2005). Ideally, a local psychologist should be involved in the adaptation process, and local informants from different disciplines involved in assessment should participate in the process. While it is helpful to have professionals who understand development such as pediatricians and developmental psychologists, the addition of local parents and people working with young children such as nurses or teachers adds important perspective and some assurance gained through consensus. Language translations should be reviewed by a similar multidisciplinary group to insure that the intent of each task or item is correct. All items should be piloted and modified as needed. Video recording of periodic test administrations is often helpful toward monitoring problems in the way test tasks are understood and managed by children. Initial studies of adapted measures are needed to evaluate properties of reliability, including internal consistency and temporal stability. Multiple lines of evidence for validity should be completed based on internal structure (e.g., factor analysis), construct validity (e.g., convergence with measures of the same construct and divergence with measures of unrelated constructs), and ability to detect the presence of problems (e.g., concurrently diagnosed conditions) or development of problems (e.g., predict future conditions). Measures also should ideally be adequately standardized with a local cohort.

2.6 Types of Instrument Adaptations

There are many aspects of an instrument that may require adaptation. Malda and colleagues (2008) describe five different types of adaptations that can each have relevance depending on the nature or desired outcome of the proposed assessment: construct-driven, language-driven, culture-driven, theory-driven, and familiarity/recognizability-driven. Considering each of these adaptation types can systematize choices made during the adaptation process leading to more accurate measurement. Construct-driven adaptation requires considering how the intended constructs, such as "intelligence," are defined. Although the aim of assessment in Africa is often to measure "intelligence," the construct may not be defined in the same manner as in the Western context, where most tests have historically been developed. The Western concept of intelligence focuses on level of skill, knowledge, and reasoning development, while, in many parts of Africa, intelligence is defined in terms of social contributions or helping others. The concept of intelligence can also differ according to expectations for each gender. Serpell and Jere-Folotiya (2008) found that even "eco-culturally" grounded early childhood tests in their study differed in their ability to predict later outcomes such as school success and better predicted success for boys than for girls. These construct measurement differences are not limited to intellectual function. For example, simple motor speed is often considered a robust measure of neurological integrity, but some cultures emphasize accuracy as more important than speed (Hedden et al. 2002; Verney et al. 2005).

Language-driven adaptations are required when simple translation is inadequate to adapt a task. Language-driven adaptations necessitate an understanding of the construction of language and the use of words within the language. In the Western assessment context with very young children, the age at which certain vocabulary items or linguistic constructions emerge is commonly used as an index of "language" development and as an early predictor of later cognitive development. Yet, the timing with which words emerge is culturally dependent. For example, in Setswana, the native language of Botswana, color words develop much later than Western test norms suggest, as colors are not emphasized as a primary attribute with most young children (Kammerer 2010).

Theory-driven adaptations include changes in test materials or processes because the theory behind the original items would not apply in a different culture. Malda et al. (2008) have noted that digit repetition will be altered if the translation of the digit names involves a different number of syllables. In Setswana, the possessive form is more complex than the simple English addition of "'s" or "s'," so items related to possessives would not be comparable (Kammerer 2010).

Finally, adaptations for familiarity/recognizability are often required for young children who may not have been exposed to the materials used in Western early developmental assessment. Lack of familiarity with test materials could change a child's comfort, and therefore, the amount of time spent with the materials, creativity in use of them, or persistence in tasks, all of which can be part of "success" at items used with very young children. In adaptations, pictures of animals and fruit not seen in the child's environment are typically changed to those found locally. Piloting these adapted materials can be particularly important as it is difficult to choose intuitively what items will be difficult or unfamiliar for a child in a non-Western culture. For example, children in one part of Kenya would not touch certain foam materials on a measure, yet the same material was accepted by children in other parts of Kenya (Holding et al. 2004).

2.7 Considerations in Adaptation of Measures

There are particular areas that should be carefully considered in adapting measures normed outside of a country or culture including language, cultural norms for development, appropriate materials, and demonstrating validity of the adapted measure.

Language: One of the first steps in adapting a measure for use in a different country or culture is translation of instructions and items. The most common method is to translate the test into the native language of the participants then complete a "back-translation" to the original language of the test to evaluate whether meaning has been altered in translation. Translations must reflect the participants' style of language. For example, academic translations of Western words for tests may not be as comprehensible for participants who use a less formal language register. Translations may also need to vary between regions within a country or cultural groups. Particularly in developmental testing, translated items may not reflect the comprehension level of the child given cultural variations in language development, and detailed linguistic ethnographies are required to translate language tasks appropriately. For these reasons, although language is a critical marker of development, comprehensive language measures are not always included in measures either created within or adapted for a new participant group to avoid bias in results. Abubakar et al. (2008b) notes that studies of the impact of HIV on the neurodevelopmental functioning of children with HIV have often cited motor development as being a primary risk, but this finding must be viewed with caution as language development is typically not fully assessed.

Developmental levels: In assessing the suitability of items in tests, researchers and clinicians have typically piloted the tasks for acceptability by the children. Rarely, however, have the resulting adaptations been re-normed. Caution must therefore be used as the tasks may well be attained at a different developmental level when used in a new country. Even items which seem less culture-bound, such as attainment of motor milestones, have been found to differ significantly across countries (WHO 2006).

Materials: In adapting tests, most researchers try to find materials that are culturally appropriate for the children to be evaluated, as Western measures may use materials that are not part of the lives of young children in Africa. Puzzles, for example, a common task in measures designed for young children, are not a typical toy in Africa. Materials are best when familiar and recognizable. Child *comfort* in playing with materials is highly relevant to their ability to demonstrate skills with a material, even if they have typically not used a material before. For example, a child may not have used blocks, but if the blocks feel comfortable to touch and play with, the child may then try to stack them as requested by an examiner. But child reactions to materials go beyond familiar and often relate to cultural or personal associations to the object. For example, Gladstone et al. (2008) noted that the pink doll on the Denver Developmental Screening Test frightened many children in Malawi. Additionally, a plastic doll on the BSID III was well accepted by the children in Botswana, but a purple teddy bear was seen as a "monster" and was viewed as scary by many of the children (Kammerer 2010).

Validity: Adapting instruments for use with other cultural or linguistic groups typically involves changing tasks or instructions to make them more accessible and appropriate for the particular group. These adaptations typically are designed to maintain face validity of the measure or so that the adapted materials appear on the surface to be measuring the intended skill or construct. Other properties of the adapted instrument, however, may be altered by these adaptations, including reliability and validity. Further, it cannot be assumed that an instrument designed to measure a cognitive construct such as "intelligence" or "memory" in one culture will accurately measure the same construct in a different culture even if face validity appears appropriate. Children in different countries or cultures may employ different neurocognitive processes in completing a task, whether or not the task has been adapted (Sternberg 2004). The goal of adaptation should be to provide a comparable measure of the cognitive construct that is the focus of the assessment. Holding (Holding, P.A., 2013, written communication) noted that measures adapted for use in Kenya have shown that correctly managed adaptation can actually move test demands closer to the construct of the original test. This "better fit," however, requires examining the basic psychometric properties of the "new" test including reliability, some measures of validity, and often new standardization or normative studies.

2.8 Practical Constraints in Instrument Selection

Apart from the multiple theoretical and cultural issues that need to be addressed in assessing young children's development in Africa, there are also an important series of practical constraints that also require attention in choosing an assessment instrument. The World Bank toolkit (Fernald et al. 2009) notes the following issues, to which we have added considerations particularly related to assessment of very young children in Africa.

Budget: Western-based tests are often costly, both in initial purchase as well as in purchasing protocols or forms per administration. Assessment instruments vary considerably in cost, however, and some options may be less expensive or, in some cases, free. In addition, the amount of time to adapt the instruments, to train testers, and to administer each test adds to the expense of a using a particular instrument.

Copyright: Using formal published instruments requires attention to copyright issues, as these tests are licensed and have rules for use, for modifications, and often for training of the examiners. Most test publishers deal with requests to adapt measures routinely and should be contacted early in the study planning phase.

Time: The time required for administration of instruments is a particularly critical factor with young children. Young children tire easily, may not perform when tired or hungry, and often do not tolerate lengthy or demanding assessments. Many assessments in Africa have been focused on determining the impact of diseases such as HIV or malaria, which can also mean that the children to be evaluated may be sick and even more vulnerable to fatigue. Parent report measures bypass the issue of sickness or fatigue in the child, but the parent in a clinic or test setting often needs to attend to the child or other children or return to work and cannot spend long periods with lengthy questionnaires or interviews. Allowances for food, naps, child care, and/or multiple appointments should be considered.

Training: Personnel doing the assessments will most often not be trained psychologists with experience in research methods and assessment techniques. Tests vary considerably in the amount of training and testing expertise required to administer the test adequately. Some tests have been specifically developed to be able to be used with personnel such as teachers, nurses, or health care workers (e.g., KDI, MDAT), while other tests were specifically developed to be used by trained psychologists (e.g., BSID) and therefore require particularly careful monitoring to assure that the instrument is administered following the test standards. Videotaping of periodic sessions, double scoring, and use of one monitoring assessor can increase reliability of assessments. With very young children, evaluators must have the ability to relate to this age group and to make caregivers feel at ease, given much of child comfort is associated with the comfort of the caregiver at this stage.

Test setting: Choosing assessment instruments may be driven in part by the type of test setting that is available, though typically some appropriate setting can be found or created in practice. Young children can be easily disrupted by noise, extra people observing, or rooms that are associated with medical procedures. Settings that are unfamiliar to young children may be so disruptive that the assessment would not be accurate, and therefore home assessments may be advisable; at the same time, noise, seating, or other distractions at home may bias test performance (Fernald et al. 2009). Test rooms that are comfortable for young children, allow room to move and/or sit on a caregiver's lap, and are decorated in a familiar fashion are likely to be more conducive to eliciting a child's best performance. Since assessments of young children in Africa may be for health-related issues such as HIV, the rooms for testing may be connected with medical appointments but should not be in the area where uncomfortable or aversive procedures like blood draws occur.

Capacity of the respondent or rater: Respondent interviews or questionnaires may need to chosen, or adapted, to fit the skills of the respondent. For example, in some areas, literacy may be an issue and responding to written questionnaires would not facilitate accurate assessment. Similarly, observational measures by a person unfamiliar with the culture may result in inaccurate behavior ratings.

Language and cultural differences: Adapting tests to the language and culture of the children to be assessed is a mandatory part of appropriate testing. Some Western-based tests will require such extensive adaptations that the essence of what items measure can no longer be clear. Extensive adaptations also require lengthy work before the testing begins, which may not be possible, particularly for time-sensitive research or interventions. In these cases, tests created within a country or culture, or tests more easily adapted, should be chosen.

2.9 Additional Assessment Considerations

Aside from the test-focused considerations, evaluators must also consider some fundamental prerequisites that may be overlooked even in Western settings. Few studies note whether vision or hearing is screened as part of the developmental assessment. Countries in Africa differ in the amount of screening available as part of child care (McPherson and Brouillette 2008), but normal vision and hearing should not be assumed. Even if screening of any kind has occurred, good assessment practice includes brief vision (Morgan 2011) and hearing screening at the time of testing to insure that the child has adequate sensory skills to participate in the assessment. Young children in many parts of Africa are at risk for impairment in vision or hearing (Kammerer et al. 2010) due to the frequency of problems known to cause these issues. Children with HIV are at risk for prematurity, persistent ear infections, or infections such as CMV, each of which are associated with hearing loss. Although hearing was not officially screened in a study of CM in Malawi (Boivin et al. 2011a), the authors were well aware of the issue and note this factor, as hearing loss is also associated with malaria (Idro et al. 2007) and caregivers reported that some children had hearing loss. For very young children, screening is particularly important given that hearing loss or visual impairment may not yet have been discovered by caregivers.

Finally, for research and clinical assessments in any setting, participants who are found to have medical, psychological, or cognitive/developmental issues should be referred for follow-up care. This follow-up care is not possible in many parts of Africa when the appropriate services are not available. There are obviously ethical dilemmas for researchers and clinicians when faced with these situations. An important consideration in formulating an assessment project is being able to inform participants in advance as to what care will be available if problems are found. Supporting parents or caregivers in accessing local resources is essential for developmental concerns. Developing a plan for management is essential for studies when other areas are screened, such as depression, when a participant's responses may require immediate access to local resources.

2.10 Types of Assessment Approaches

Assessment may take many forms. Direct assessment with performance measures (i.e., tests) that require the child to respond to demands offers the advantage of quantifying actual skill development. At the same time, direct assessment can be time consuming in terms of administration and can be complex in African settings given the many requirements for adaptation and the lack of familiarity of "testing" for many African children.

Indirect assessment methods, such as structured observations, interviews, and rating scales completed by caregivers, offer advantages of efficiency, convenience, and lower cost, as well as relying on the observers' or raters' cultural knowledge and expectations.

Caregiver questionnaires: Assessment of very young children can be accomplished through questions asked of the caregiver about a child's typical behavior in the home setting. This method is particularly useful since very young children are less reliably cooperative or awake, and performance in an unfamiliar test setting may not be maximal. Interviewing or asking caregivers to complete rating scales in Africa is not without challenges, however, as caregivers may find the setting and demands uncomfortable, and sharing problems with children may be culturally unfamiliar. In Botswana, when caregivers were directly asked if their child had more difficulty with specific developmental tasks than other children they knew, many respondents reported no problems, even when a problem was evident (Kammerer 2009). Using the "conversational" format of the DMC produced more accurate responses.

Observational data: Structured observations of a child's behavior may provide accurate data, as the child typically would be in a familiar setting doing familiar activities. Behaviors that can be assessed in this manner are limited, however, and similar caveats apply when assessing validity and reliability of measures adapted for African setting. Structured observation methods are useful in assessing the home environment in HIV-affected children in order to better understand the impact of the disease on maternal–child interaction and the influence of the stimulation in the home setting on developmental outcomes, information critical to deciphering the role of HIV disease in neurocognitive outcomes. The Home Observation for Measurement of the Environment (HOME; Caldwell and Bradley 1984) is the most commonly used observation method for this purpose.

In addition to direct versus indirect assessment methods, it is helpful to appreciate the varied goals of available measures, such as whether an instrument seeks to measure comprehensive or global development, serves as a general screen for developmental problems, or focuses on a specific cognitive, behavioral, or social–emotional domain. Direct comprehensive measures such as the BSID and GMDS have been the primary staples in studies of HIV-affected children in Africa, as they seek to measure global development. Direct domain-specific or single-focus measures of language, executive function, or other domains have been only recently employed in Africa though this trend may increase as more measures are successfully adapted.

Screening instruments are most often indirect assessments and are frequently used with very young children given their inherent advantages of reduced time and cost and simplicity of administration. They are useful for large-scale epidemiological studies to provide a quick index of the proportion of children in a given population who have a deficit or to screen a population of children to identify those potentially in need of intervention. The most commonly used screening tool used internationally has been the Denver Developmental Screening Test and its revision, the Denver II (Frankenburg et al. 1992), which taps fine motor-adaptive, gross motor, personal–social, and language development. In HIV-infected and HIV-exposed children in the DRC, the Denver II was sensitive to global cognitive delays (Boivin et al. 1995).

Caregiver rating scales are often used to evaluate children's behavioral and social–emotional development. Social, emotional, and behavioral development is important to measure not only to assess critical aspects of child well-being but also as a reflection of physiological adaptation to disease or environmental influences on brain development. The impact of neurological insult can be reflected in emotional regulation. Perhaps the most frequently used instrument adapted for assessment of social, emotional, and behavioral development in children affected by HIV infection in Africa is the Achenbach Child Behavior Checklist (CBCL; Achenbach and Rescorla 2000), a caregiver rating scale that covers a broad range of problem behaviors. The validity of the measure in Uganda has recently been studied (Bangirana et al. 2009). Holding and colleagues (2013) developed a caregiver interview measure, the Profile of Social and Emotional Development (PSED), to assess problem behaviors in infants and toddlers in Africa based on a similar measure for school-aged children (Holding et al. 2004). The PSED has proven to be a measure that is both reliable and valid for identifying children at risk of social, emotional, and behavioral problems.

Recently, attempts to measure self-regulation, or executive function, have been incorporated in studies of children at risk in Africa. While few direct measures of executive function are available for very young children even in Western nations, there are some initial adaptations for use in African countries of the preschool version of the Behavior Rating Inventory of Executive Functions, a caregiver rating scale of young children's everyday emotional and cognitive regulation (Gioia et al. 2011).

The comprehensiveness and validity of assessment as a whole can be enhanced by using carefully selected combinations of direct and indirect approaches. Given the cautions related to each approach, using a combination of measurement types may provide a more accurate overall picture of the child's functioning. For example, the benefits and caveats of a direct comprehensive measure such as the Mullen may be balanced and extended by accompanying it with indirect structured observations such as the HOME, a developmental screener such as the Denver II, and caregiver ratings such as the CBCL. In a study of effects of antiretroviral therapy for HIV-exposed children in Botswana, an adapted BSID was chosen to allow comparison with US studies of HIV-exposed children. To add information as well as to gauge validity, a parent rating developmental scale (DMC) and social–emotional interview assessment (PSED) developed in Kenya were added (Kammerer 2010). This method demonstrated convergent validity via strong positive correlations between similar skills assessed through different measures (language with language, motor with motor) and the strong correlation of the tests with maternal factors typically predictive of developmental outcome. The complexities inherent in cross-cultural assessment of very young children often require a multi-trait/multi-method approach to develop a more comprehensive understanding of brain–behavior relationships in children at risk.

2.11 Conclusion

There have been huge strides in HIV prevention and treatment in Africa. For the millions of children who remain infected or affected by HIV, accurate neurodevelopmental assessment is critical to better understand and manage the disease and related problems. Appropriate assessment is equally required for other children in Africa impacted by disease, environmental stressors, and effects of poverty in order to develop and monitor essential interventions and avoid further loss of developmental potential (Engle et al. 2007; Grantham-McGregor et al. 2007; Walker et al. 2007). These assessments must address as well important corrective resiliencies in African cultures that may modify or ameliorate developmental problems.

There are many challenges to accurate and efficient measurement approaches for research and clinical applications in African cultures. This is perhaps more dramatic for assessment in young children, as there are many fewer well-developed measures than for school-aged children even in Western countries where the majority of assessment instruments are published. Thus, the first question is whether to develop a new instrument that is culturally specific to the target population or to adapt an existing measure to be more culturally consonant. While the former option has advantages, the later is more time and cost efficient and allows for comparison with data from studies with other cultures and diseases. Follow-up questions include whether to rely on direct or indirect assessment methods, comprehensive measures, screeners, or domain-specific measures. These may be guided by the purpose, resources, and scope of the research or clinical program. More recent studies rely on a combination of assessment approaches, including both direct and indirect methods covering overlapping domains for convergent validity while also covering unique domains for comprehensiveness.

Standards or common practices are being developed for assessment in the international context to facilitate comparison of findings across cultures, environments, and disease processes. These include a common or shared set of tools, an approach that requires multiple methods and measures and more advanced adaptation practices, expectations for demonstrating evidence of reliability and validity, as well as standardizing measures on the target population or using appropriate controls for comparison and measurement of not only neurocognitive domains of function but also environmental factors. Importantly, enabling comparisons across studies facilitates a co-constructive approach toward understanding the “brain–behavior omnibus" (Boivin and Giordani 2009) or understanding the complex relationships between genetically determined neural substrate and environmental influences across the lifespan.

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Chapter 3
Acknowledging Methodological Complexity in Assessing Children in HIV-Affected Communities in KwaZulu-Natal Province, South Africa

J.D. Kvalsvig, M. Taylor, S. Kauchali, and M. Chhagan

3.1 Introduction

Complex changes take place in the brains, thoughts, and behaviour of children from day to day and year to year as a result of disease and environmental influences. It is difficult to know which factors are primary and which are secondary in causing developmental delays at each age, how developmental trajectories are affected, and what can be remedied. More effective intervention strategies are needed to reduce what Shonkoff (2010) terms "toxic stress on developing brain circuits". The origins of developmental lags are dynamic and multicausal so the investigation and eventual interventions are unlikely to be simple. Research needs to take cognisance of this reality. A practical need exists to bring together theory and evidence from different disciplines and different regions into more comprehensive theories of child development to guide intervention.

The need for co-operation across disciplines is especially true for children living in conditions of poverty in developing countries such as in the KwaZulu-Natal region of South Africa where disease compounds the other many and various effects

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of the disadvantages under which they suffer. The term "neglected tropical diseases" is used in the health literature to describe the geohelminth infections, schistosomiasis, malaria, tuberculosis, and other infections that have not had their fair share of attention from researchers, research funders, and intervention agencies because they are prevalent in places far removed from the main sources of funding and expertise. Disease is not the only influence on development in these underdeveloped areas: the social and economic circumstances in which children are reared play their part. Most of the research data available to guide intervention emanates from the developed world where there are fewer and less intense risk factors and support services for children are more readily accessed.

Development economists (Heckman 1999; Duflo in Buchanan 2010) express dissatisfaction with the slow pace of intervention for children living in poverty as they make a strong case for investment in children as probably the most cost-effective investment a developing country can make. Duflo in Buchanan (2010) argues for more informative research to guide intervention, saying that "the solution to a particular problem in a specific situation may be unique and counter-intuitive". Many children in sub-Saharan Africa are at high risk from a number of endemic infections, poor nutrition, and a lack of good basic health and education services, and they live in a context of social and political disruption.

This chapter uses the co-construction model and the specific circumstances of children living in poverty in the province of KwaZulu-Natal, South Africa, where HIV infections are extremely prevalent, to suggest ways in which research should be undertaken for the best use of scarce resources to optimise the development of children living in poverty. The question of how best to improve the lot of the children in this province is particularly vexatious. The province appears to have many advantages which include a good rainfall, a subtropical climate, fertile soil, a well-developed industrial sector, and busy ports, and the province operates legally and programmatically in terms of a national constitution that guards the rights of children. All of this should provide a good living for its inhabitants and good care for its children. But the province is home to more poor people and has more severe health problems than any other province in South Africa. In the search for solutions to the problems of the children living in poverty, one is constantly made aware of the interconnectedness of the factors ranged against a healthy, stimulating, and happy childhood and the difficulty of designing research programmes which will point the way to feasible and effective interventions. Thus, prior to examining the ways in which HIV and AIDS impact on the children in the region, it is helpful to look briefly at the demography and health indicators of the area.

3.2 Demographic and Health Factors in KwaZulu-Natal

The province of KwaZulu-Natal is situated on the east coast of South Africa, bordering the Indian Ocean, and has an estimated 10.5 million people (HRC/UNICEF 2011). With 21 % of the country's population, it is the most populous of the nine provinces in the country and also has the largest number of children (2,902,000) living in households where the per capita income (within the household) is below the poverty line of approximately US$90 per month (SouthAfrica. Info 2011). As Horowitz (2000, p. 6) points out, poverty is a "swamping" condition for child development: "a dense concentration of disadvantaged circumstances". Thus in KwaZulu-Natal, the sheer numbers involved add significantly to the difficulties of successful interventions.

Health and nutrition are probably the most noticeable factors that differ in their importance and impact in resource-poor settings as compared to developed countries in which studies of child development have generally been conducted. In some areas of KwaZulu-Natal, the lack of services to address health and nutritional needs places major constraints on children's development. Macro- and micronutrient deficiencies, chronic parasitic infections, and frequent episodes of respiratory and diarrhoeal infections, apart from causing pain and discomfort, affect the socio-emotional and cognitive development of children in ways that are not fully understood, acting as constraints on children's mood and energy and consequently on their freedom to diversify their activities. As compared with adults, children are especially vulnerable to these conditions: they have energy needs for growth and are immunologically immature.

South African health services are working towards the Millennium Development Goals for 2019, many of which are directly relevant to the development of children living in poverty. These goals are as follows: eradicate poverty and hunger (Goal 1), achieve universal primary education (Goal 2), reduce child mortality (Goal 4), improve maternal health (Goal 5), and combat HIV/AIDS, malaria, and other diseases (Goal 6) (UN MDGs 2000). National health policies, which are designed, at least in theory, to make primary health care accessible to all, are beginning to demonstrate some positive effects. At a provincial level, programmes integrating health care for children are being implemented: primary health-care clinic nurses are responsible for health-care and mid-level workers provide home-based care. Improving the rate of immunisation for children aged <1 year has been a focus, and the immunisation rate had increased to an estimated 86 % of eligible children in the 2009/2010 reporting year (Department of Health 2010a). The Integrated Management of Childhood Illnesses, a health management tool developed by the World Health Organization, is being implemented in programmes at clinics and in the community to address morbidity and to reduce mortality of children, in line with the United Nation's fourth and sixth Millennium Development Goals (RSA/UNDP 2010).

Even given these attempts and others to improve children's health status, South Africa continues in the grips of the HIV and AIDS epidemic, hindering any advancement in the above broad developmental goals for children. For example, despite some recent improvement, an overall increase in the infant mortality rate over the past 20 years remains. Sanders (2009/2010) reports that the estimated 56 deaths per 1,000 live births in 1990 increased to 73 in 2000. Then in 2008, as a result of the Prevention of Mother to Child Transmission Programme, a decrease to 67 deaths per 1,000 live births occurred. This remains significantly above the 1990 figure, however. It is estimated that 35 % of these deaths result from HIV and AIDS, 30 % from neonatal causes, 19 % from pneumonia and childhood illnesses, 11 % from diarrhoea, and 5 % from injuries (Sanders et al. 2010). In older children, the high prevalence of infectious diseases such as tuberculosis and lower respiratory infections is associated mostly with HIV and AIDS (Sanders et al. 2010). In circumstances where the HIV epidemic has taken such a hold, many people have compromised immune systems so other infections, particularly tuberculosis, can spread more easily (Churchyard and Corbet 2008).

3.3 HIV and AIDS

KwaZulu-Natal is the province with the highest overall prevalence of HIV and AIDS in South Africa. The state provides for the treatment of all HIV-infected children, and 32,528 children in KwaZulu-Natal were reportedly receiving comprehensive HIV and AIDS treatment in 2008. This was part of an enormous campaign which provided antiretroviral treatment to the 100,000 infected children nationwide. Nevertheless, this figure is thought to represent only 54 % of the children who need antiretroviral treatment (HRC/UNICEF 2011). The increasing amount of HIV-related disease amongst public sector paediatric patients clearly places an increasing burden on health-care services and facilities (Colvin 2008).

In 2000, KwaZulu-Natal had an HIV prevalence of 39.5 % amongst women attending antenatal clinics (Department of Health 2010b). HIV in adults in South Africa is transmitted mainly heterosexually and, in children, through mother-to-child transmission with a rate of between 25 and 45 % (Coovadia 2008). A further 15 % become infected through breastfeeding (HRC/UNICEF 2011). A sustained effort to prevent mother-to-child transmission by early testing and treatment is being implemented. This is critical to improving child health outcomes (WHO 2009).

Several strategies are in place for the protection of children: treating parents and children with antiretroviral drugs, prevention of new mother-to-child infections, and better health, education, and social welfare services. None of these strategies is fully effective at present.

A key factor is early diagnosis to prevent the adverse physical and cognitive effects of HIV on children's development. Early provision of antiretroviral treatment can reduce adverse effects, but daily treatment is required, and adherence is a critical issue: the medication is required for life and failure to take every dose can result in the development of drug resistance (Moatti et al. 2004). Severe side effects from the medication can occur, and the long-term effect of the drugs on the body's metabolism is unknown.

AIDS takes a severe human toll. While 40 % of child deaths in South Africa in 2000 are directly attributable to HIV and AIDS, they are also the underlying cause for many of the deaths reported from other diseases (Bradshaw and Nannan 2006).

The epidemic in KwaZulu-Natal can now be described as a mature epidemic with many people infected.

The impact of AIDS on family structure is serious. The epidemic contributes to a situation where only 25 % of children in KwaZulu-Natal are living with both biological parents, 43 % are living with mother alone, 4 % with father alone, and 28 % are not living with parents. It is indicative of how much worse the situation is in this province than in others when it is seen that 25 % of children lose one or both parents (all causes) in contrast to another province, the Western Cape, where 8 % lose one or both parents (HRC/UNICEF 2011).

Nutritional status in affected households is also compromised: many affected households lack a secure supply of food (Altman et al. 2009) and have a diet lacking diversity, which is more common in households where caregivers are infected with HIV (Mpontshane et al. 2008).

In summary, the HIV epidemic is the overwhelming threat to the health and mental health of the children in the province. It is concentrated in certain communities and affects children's health either directly through the infection itself or indirectly through other infections which are able to gain a hold. Measures to prevent new infections and to treat those affected are only partially successful. The epidemic has its most significant impact in poor communities, where malnutrition is also a factor.

3.4 Other Infections

There are success stories in the province. One is that of controlling malaria, which used to be prevalent in the north-east and is now been all but eliminated through a regional control strategy that extends into the neighbouring countries of Swaziland and Mozambique (Sharp et al. 2007). But the strategy of spraying the walls of dwellings with DDT raises the further question of what dangers the widespread use of this and other pesticides hold for children and adults in these regions.

The province remains, however, endemic for other parasitic infections including schistosomiasis at altitudes below 300 m and soil-transmitted worm infections (Appleton and Kvalsvig 2006). Provision of sanitation and clean water helps to prevent the spread of these infections and the South African government has been active in provision of basic infrastructure since 1994. But the high rural to urban migration experienced in South Africa (as in many developing countries) results in slum conditions in some areas and these are conducive to the spread of parasitic and other infections (Houmsou et al. 2010). Soil- and water-transmitted parasites infect children in rural areas and in urban informal settlements that lack adequate water and sanitation facilities. Unfortunately the 1994 policy, which included mass treatment in schools as part of the Integrated Nutrition Programme, has not been implemented (Public Service Commission 2008).

3.5 Nutrition

Globally, 21 % of child deaths (2.1 million children) are the result of stunting, severe wasting, and low birth weight (de Onis et al. 2004). The purpose of the first Millennium Development Goal (RSA/UNDP 2010) is to reduce the number of underweight children in the under-5-year age group by 50 % between 1990 and 2015. Goal 1 (to eradicate extreme poverty and hunger) and Goal 4 (to reduce child mortality) require improvements in child nutrition (StatsSA 2010). This is critical to child survival, and lack of attention to malnutrition is contributing to the failure to achieve the Millennium Development Goals (World Bank 2006). In South Africa, as in many sub-Saharan African countries, the HIV/AIDS/TB epidemic is exacerbated by the lack of adequate nutrition (World Bank 2006). Investments in nutrition are known to have high returns, and provision of micronutrients is highly cost-effective, with community nutrition programmes being successful in preventing undernutrition in children <2 years of age (World Bank 2006). This is yet another intervention that is not being adequately addressed in the province.

In South Africa as a whole, wasting (weight for height <−2 SD), indicative of gross malnutrition as would be found in a situation of war or famine, is not a serious public health problem, but stunting (height for age <−2 SD), which is indicative of chronic undernutrition, remains persistent. Three national surveys between 1994 and 2005 report the severity of malnutrition (Altman et al. 2009). In KwaZulu-Natal, the KwaZulu-Natal Income Dynamics Study reports that of 1,146 children under 7 years of age, 1.6 % are wasted, 7.5 % are underweight (weight for age <−2SD), and 19.8 % are stunted, indicating little improvement in nutrition since 1994 (Jinabhai et al. 2006). Close to 24 % of children in KwaZulu-Natal are living in households where child hunger was reported (StatsSA 2008).

The 2005 National Food Consumption Survey (Labadarios 2000) found 64 % of children aged 1–9 years have suboptimal vitamin A status, with KwaZulu-Natal having the largest proportion affected (89 %). The national prevalence of iron deficiency in this survey was 8 %, but this varied widely from one province to another and between urban and rural locations. Programmes are in place to address these deficiencies. Children are given vitamin A at clinics when they come for their immunisations, but after the completion of the primary immunisation schedule, it is difficult to maintain the 6-monthly vitamin A supplementation. The South African government's Integrated Nutrition Programme introduced the fortification of staple foods such as maize meal with a range of micronutrients and the iodisation of salt (implemented in 2003). Children in primary schools in disadvantaged areas receive a meal every school day due to a school feeding programme initiated in 1994 (The Public Service Commission 2008).

The WHO Guidelines support exclusive breastfeeding for all mothers while ensuring that HIV-infected mothers receive antiretroviral therapy, thereby attempting to reduce HIV transmission from mother to child through this two-pronged strategy (WHO 2010). The South African health service has adopted this policy and HIV-infected mothers are particularly encouraged to follow it. However, the number of mothers practising exclusive breastfeeding in the first 6 months is on the decline in South Africa for a number of reasons. For instance, exclusive breastfeeding may be difficult for working mothers to sustain. In addition, the Prevention of Mother to Child Transmission Programme has publicly promoted exclusive breastfeeding which has had an unfortunate effect: mothers who have not revealed their HIV status fear that their families will suspect their status if they insist on breastfeeding exclusively for the first 6 months. This decline in breastfeeding has increased diarrhoeal morbidity, malnutrition, and, finally, infant mortality and is probably partly responsible for the reversal of mortality trends seen in South Africa.

3.6 Three Differentially Affected Groups of Children in Communities with High Prevalence Rates of HIV

In each of the HIV-affected areas of KwaZulu-Natal, three groups of children share certain environmental influences but are differentially affected by the epidemic and require different interventions:

- HIV-infected
- Exposed or affected
- Living in a society disrupted by the HIV/AIDS epidemic

In the epidemiological study in KwaZulu-Natal, which forms the basis for this chapter, 27 % of biological mothers report testing positive for HIV either during pregnancy or later. The national guidelines state that all children of HIV-infected mothers should be tested, but in this sample, only 41 % of the surviving 244 children (aged 4–6 years) had been tested. HIV seroprevalence amongst these preschool-aged children was 4.9 %.

3.6.1 The HIV-Infected Children

These children have specific needs over and above the stresses of living in communities or families where HIV is prevalent. Firstly, not all children are being reached for treatment either because the system fails to identify them as potentially infected when they are born or because there is slowness on the part of their caregivers to seek treatment, which could be for a variety of reasons. Secondly, children with HIV infections are at risk for neurological problems, developmental delays, and cognitive difficulties. Some of these effects may be alleviated by antiretrovirals, but some could remain. As mentioned above, malnutrition exacerbates the AIDS and TB epidemic; the biological effects of HIV include malnutrition, anaemia, and recurrent and chronic illness, indeed a vicious circle. The earlier treatment commences the better, but this happens all too infrequently.

HIV-affected children are likely to have harsh early experiences: they may lose parents to the infection, be living in a home where family members are chronically ill, have stigmatising remarks directed at them, or suffer frequent and severe illnesses. If orphaned, they may have to move to another home or an institution. They may need specialised help to build their confidence and capabilities.

In a study of orphans and vulnerable children in six AIDS-affected communities in southern KwaZulu-Natal, focus group discussions were held with parents, health workers, community leaders, and preschool workers at six sites to elicit their perceptions of orphans (Kvalsvig and Taylor 2006). Some perceived AIDS orphans as lonely, distressed, emotional, and needing the warmth of social interaction, and went out of their way to be helpful, but others said that, as a rule, orphans were treated the same as other children. A few mentioned that some people held more extreme views: they said that orphans were badly behaved or that they came from bad families because their parents had died of AIDS.

Descriptions came from all sites of the deep poverty in which many orphans were being raised, with nutritional deficits being the most frequently described physical condition. Some of the respondents realised that the emaciated state of the children could be an indication that they were HIV positive. Associated with malnutrition was lack of hygiene, obvious from the dirty and dishevelled state of some orphans. Health-care workers reported that the combination of poor nutrition, overcrowding, a lack of clean water, poor hygiene, and HIV infections gave rise to infections such as scabies, ringworm, sores, diarrhoea, and respiratory infections. In very poor households, children were seen as not being taken to a clinic or doctor soon enough when they were ill and children were seen as dying because of this delay. Children with HIV infections were viewed as not receiving the special care they needed, were often undiagnosed, or their condition was not acknowledged.

As they get older, children on antiretroviral treatment face additional unique issues. They need to understand and accept their condition and to keep taking their medication. Their families and teachers will not only have to educate them in the classroom but also to protect them from discriminatory remarks, respond to their distress, and guide them towards adulthood.

3.6.2 Children Exposed to Infection or Affected by It

Children whose parents are HIV infected or were infected and have since died, but who are not infected themselves, can be described as “affected”. They share many of the early experiences of infected children, including bereavement or living with chronically ill family members. They are likely to be living in families experiencing increased poverty because former breadwinners are not well enough to work. If they are orphans, they may have to be taken in by another caregiver, usually an aunt or grandmother, thus straining the financial resources of that person or they may have to move into institutional care.

In the study quoted above (Kvalsvig and Taylor 2006), the emotional impact on a child of living with a seriously ill parent and the subsequent bereavement was vividly described by adult participants: one respondent said "they lose hope for life". It was said that young children whose parents were seriously ill clung to their parents even though the parents had little comfort for them. For older children, caring for sick and dying parents was an emotionally distressing experience that may have left them mentally unbalanced. Respondents from all areas described two different ways in which the orphans reacted to their bereavement and change of circumstances: depression and withdrawal on the one hand or "acting out" on the other. In the former, children were described as being silent, brooding about their bereavement and losses, full of fears (particularly about being HIV infected), crying easily, showing signs of deep sorrow (*umunyu* in isiZulu), and suspecting others of taking advantage of them. They were tired all the time and didn't laugh at jokes like other children. Several respondents referred to their sensitivity: they overreacted to scolding, were easily hurt, and were short tempered and fragile. Other children were described as angry, rough, and aggressive. They behaved badly to get attention, as though that would help them to feel they belonged in their new home.

It was said that a stigma is attached to people known to be infected because the disease was known to be sexually transmitted and associated with multiple sexual partners. This stigma affected HIV-affected children as well. Children from unaffected families heard their parents gossiping and then repeated what they had heard, taunting affected children and subjecting them to ridicule.

In response to the question "How are children cared for in the community when their parents die?" it was said that some infected parents nominate a guardian, but more often the decision was made by family members after the parents have died. Most orphans reside with grandparents or aunts and some with older siblings, such as an older married sibling. There are, however, exceptions. Some older children decide for themselves where to live, and in cases where no relatives are forthcoming, the neighbours, an *induna* (traditional leader), or a social worker may make arrangements for the children. In some places there are drop-in centres where meals are provided, and in others there are community orphanages. In areas where there are community health workers, they visit homes and assist caregivers.

The respondents observed that, in some cases, children could not be placed with relatives. Sometimes people who were dying of AIDS became emotional and quarrelled with their families, which caused a rift and alienated the children from their potential caregivers. Other children had severe behaviour problems (lying, stealing, substance abuse, or making accusations against their caregivers) that made it difficult to integrate them into a new household. Others were so sick that people found it difficult to care for them at home. In extreme cases, children were abandoned or abused and left their homes to wander the streets scavenging and begging, with all the attendant risks.

Child-headed households are a special case, and these children, without the guidance and support of responsible adults, are vulnerable to life's vicissitudes in innumerable ways.

3.6.3 Children Who Are Neither Infected Nor Exposed But Are Living in an Area of High Prevalence

Between the ages of 3 and 6 years, children become increasingly socially discriminating (Cole and Cole 1993, Chap. 10). This is the age when it is common for boys to identify with other boys and prefer to play with them rather than in mixed-gender groups and girls identify games and pastimes as “for girls” and start to play these games in single-gender groups. Children categorise other children as “like me” or “not like me” in a natural perceptual process of exploring their own identity. At the time that they learn to categorise in this way, they may also learn to reject and stigmatise, and this can apply to gender, race, disability, as well as to HIV infection.

Our research in two townships in KwaZulu-Natal with children aged 3–6 years examined their attitudes towards HIV-positive children (Kvalsvig and Richter 2002). The research showed that about 70 % of the children had heard something about HIV and AIDS and a few, about 12 %, had a detailed understanding of the infection. Sixty-two percent of 3-year olds did not seem to worry about playing with an HIV-positive child, but only 46 % of the 4-year-olds were accepting of an infected child and even fewer 5-year olds (29 %). When children were shown a picture of a dejected child being excluded from playing with other children, an additional 10 % responded to the obvious sadness of the situation by saying that the child should be included in the group. While most children were unable to give coherent reasons for their answers, about a quarter was able to verbalise their fear that they or others would be infected through play, and others associated AIDS with something bad or dirty.

Our research reinforced what has been demonstrated many times in other contexts: preschool children understand the concepts of death and bereavement imperfectly and sometimes do not give the appearance of grief, but they are especially vulnerable emotionally and in every other way to the deaths of family members. Some of the children in the study (12 %) gave evidence of distress when the words HIV and AIDS were mentioned, and a few had knowledge beyond their years of threat of the disease. About half of the children understood the need to be helpful when people are ill, many were sympathetic, and a few understood the need people have for emotional support.

3.7 Living in a Society Disrupted by the AIDS Epidemic

The AIDS epidemic hampers progress in setting up systems to support children’s development in South Africa with the result that South Africa is one of the few countries expected to fail to meet the Millennium Development Goals aimed at improving child survival. The high mortality due to HIV and AIDS amongst parents results in large numbers of orphans and vulnerable children: tragically the policies and programmes developed for these children often fail to meet their needs (Phiri and Webb 2002). Phiri and Webb (2002) emphasise the urgency of dealing with the psychosocial effects of orphanhood, which are experienced by children whose mother, father, or both parents have died and who are living in poverty in communities hard hit by the AIDS epidemic. UNICEF estimated that 2.3 million children in South Africa would be orphaned by 2010 and data from the Africa Centre (Hill et al. 2008) from 2000 to 2005 shows a doubling of maternal deaths (from 3 to 6 %), a 50 % increase in paternal deaths (from 6 to 9 %), and a quadrupling of both parents deceased (from 1 to 4 %). Communities affected by the high death rate amongst parents in the most productive age group often lack the emotional, physical, and financial resources to cope with the burden. Clearly the rights of the children stated in the Convention on Rights of the Child, the South African Constitution, and the laws, policies, and programmes often do not reach down to children in homes, preschools, and schools.

These facts lead to consideration of how the workforce is affected by the epidemic in the service sectors (health, education, and social development) that work with children. As well as an increased work load, the workforce itself is affected directly through increased deaths and increased absenteeism for those infected, for those caring for family members, and for those attending funerals. There is evidence too that health workers' attitudes are affected: Marchal et al. (2005) discuss the fact that the perception of risk from working with HIV-infected patients is high amongst health workers, whether this is a realistic fear or not, and this affects the quality of care. This leads to problems of "attrition, demotivation, and absenteeism compounded by the loss of institutional memory" (p. 301). Social workers, too, are in short supply in rural areas, especially now that their duties include serving the needs of increasing numbers of orphaned.

Phurutse (2005) reported research that showed many schools in poor areas had teachers absent and dying from AIDS: 11 % of staff were infected with HIV. This confirmed that the picture of attrition and mortality was consistent with high levels of HIV prevalence and that there was "a growing loss of very many highly trained men and women … particularly in the worst affected provinces". This increased the difficulty in addressing the developmental lags amongst children that occurred in this region.

On a positive note, the South African government is one of few in Africa that provides social grants, such as the Child Support Grant and the Foster Care Grant. The Child Support Grant is an innovative support mechanism, initiated in 1998, which is available to needy children up to the age of 18 years. More children living in households where members access the Child Support Grant attend school, and children living in households where members received the old age pension receive better nutrition (Twine et al. 2007). However, a substantial number of official documents are required to access the Child Support Grant; this includes birth certificates of the index child and mother, and, in the case of orphans, the death certificate of the mother. Grandmothers or other caregivers in very poor households may have great difficulty in accessing the requisite documents. Twine et al. (2007) note that the lack of official documentation, the education level of household head, and the distance from government service offices all reduce the ability of poor households to access the grants.

Areas in South Africa differ dramatically not only in the numbers of affected children but also in the management of services, with rural areas being particularly poorly served in comparison with urban areas. In a rural situation, where early education and child-care workers feel isolated and unsure, the impact of mentoring, monitoring, and providing constructive criticism cannot be overstated. This is shown by Kvalsvig and Taylor's (2006) study in which members of the teaching staff in preschools were given a training course in dealing with children's health and behavioural problems, followed by visits from a clinical psychologist to the preschools once a month for 3 months for mentoring in dealing with particular problems. The confidence and effectiveness of the staff increased noticeably following this intervention.

Excellent programmes exist for children in distress, but they are by no means accessible in all rural areas (e.g. Isibindi run by the National Association of Child and Youth Care Workers, *ChildLine* with counsellors available for children in need, *Bobbi Bear* for sexually abused children and many others).

3.8 Social Disruption as It Affects Child-Rearing Environments in KwaZulu-Natal

The scale of the AIDS epidemic in South Africa and the tardy policy response by government to provide antiretroviral drugs in the public health sector have resulted in a high and often rapid morbidity and mortality of parents, caregivers, and children from AIDS (Bradshaw and Nannan 2006). As the scale and intensity of the epidemic escalates, more children are orphaned and the realisation of the goal of adequate care becomes increasingly difficult (Foster and Williamson 2000). In many affected communities, extreme poverty makes it unlikely that families will be able to offer healthy, nurturing environments to foster children or even that the wider community will be able to give effective support (Adato et al. 2006). The provision of care for large numbers of orphans thus fell on the state and cannot be regarded as a transient responsibility but rather one that necessitates large-scale, sustainable interventions. Public policy in South Africa is founded on a rights-based approach to the care of children, and the Child Act legislated in 2010 is in line with this approach, but in reality the sheer number of children orphaned by the epidemic has overrun the resources that the state had in place. The most striking finding from our 2006 study, quoted above, was that children's feelings were seldom addressed. This psychological damage was the most serious aspect of the report and pointed to the need for support and counselling for caregivers. Study participants described in detail the detrimental consequences of orphanhood for many children, but there was no evidence that help was at hand. In each community visited, there was awareness that some children could not be adequately cared for in family homes. Furthermore, these were often children who had disabling health or psychological problems requiring professional help, because children who were HIV infected were often affected psychologically as well as in terms of physical stamina (Potterton et al. 2009). Some respondents in the current study had noticed this and mentioned slow learning along with frequent infections and general weakness:

> There is one whose parents died and he is not doing well at school . . . he is weak and sometimes returns home before the end of the day, carried by other children.

Even some uninfected orphans in our study were tired and dispirited and consequently were not doing well at school. Respondents mentioned several other ways in which children affected by AIDS were held back in their education. Some stayed at home to look after sick parents; others were teased and bullied at school. The costs associated with preschools and schools placed a strain on families. Inability to pay preschool fees or to provide books, stationery, and uniforms for school was a common cause of children ceasing to attend.

Strategies for the care of orphans and vulnerable children remain open to controversy with community care being preferred to institutional care in KwaZulu-Natal (Phiri and Webb 2002). The consensus in these communities is that building large orphanages is not a desirable option to deal with the children who cannot adequately be raised by the extended family or neighbours, but serious thought can be given to smaller homes on a cottage system model, shelters, day care, or support groups for these most needy children. In a small study conducted during the winter months in a mountainous area of KwaZulu-Natal, Desmond and Kvalsvig (2005) found that orphans and abandoned children being raised in clustered units in the village were performing better on all tasks than orphaned children living with extended family members.

Where there are non-profit organisations and individuals committed to child care, the results for orphans are encouraging: caregivers are assisted with their applications for grants, neighbours and friends give support, and the chances of orphans making a successful transition to a new family are better. But many children are beyond the reach of these resources: community informants cite many cases where caregivers are unable to provide adequate care through poor health, ignorance, or lack of support (Kvalsvig and Taylor 2006). The lack of *good educational services* in many communities, particularly in remote rural communities, curtails the spread of literacy with the result, in this context, that child caregivers cannot take advantage of modern insights into child-rearing because their access to information is restricted: not only are they functionally illiterate, but little has been published in their home language, and there is therefore little incentive to learn to read.

Most shocking to all concerned were the reports in many areas, from community health workers and early childhood development practitioners, of child rape and incest. In some instances this was to be due to the belief that sexual intercourse with a child or young virgin could cure HIV. In other cases the rape of children was said to occur amongst people who were drug addicts or drunkards. Children whose parents were ill and who were consequently not properly supervised were most said to be vulnerable. Community workers spoke of the difficulties of accessing social workers, which made it hard to investigate or take effective action (Kvalsvig and Taylor 2006). It is clear from these accounts that the disruption of child care at family level in the affected communities is unprecedented and that existing services are struggling to provide adequate care. In the case of orphans, there do not seem to be easy answers as to how best to provide for them.

There was general agreement that community health workers, clinic staff, and traditional healers gave valuable support to families affected by AIDS, but they were not present in all areas, and local government officials played very little part in the crisis. The lack of social workers was particularly trying because access to food parcels and grants is crucial to the health and well-being of the orphans (Kvalsvig and Taylor 2006).

The observations mirror those in the general literature on orphans in Africa. Nyambedha et al. (2003) described how the social and cultural environment pertaining to child care changed rapidly as the constraints imposed by the epidemic tightened. Cultural traditions and practices for the care of non-biological children within families arose out of fosterage patterns throughout Africa, but Madhavan (2004) pointed out that there were crucial differences between voluntary fostering and the crisis-driven fostering made necessary by the untimely death of so many parents of young children. The death of a parent severed an attachment bond with consequences for the emotional well-being of the child, and this was but one of many hardships and adjustments that the child had to face.

The broader international literature suggests that in different situations different interventions might provide better solutions. It is clear, however, that, in all instances, adequate regulation and government funding are essential, but that following fashion in child care and opting for either institutionalisation or community care without a sound knowledge of circumstances and ongoing research is dangerous. The recent experience of child-rearing in large state-run orphanages in Romania gives evidence of the unfortunate consequences of institutionalisation (Chisholm 1998; Rutter 2004). The alternative of community care for children in poverty-stricken homes is also associated with high risk, however. Recent research into the relative merits of institution care for orphans as opposed to community care (Whetten et al. 2009) does not support the idea that community care is always better than institutional care. This study was carried out in five countries and involved nearly 3,000 six- to twelve-year-old orphans. Health, emotional and cognitive functioning, and physical growth were assessed. The children in institutions fared better on tests of cognition and memory and had fewer social and emotional difficulties than children cared for in the community. Children in institutions were no worse off with respect to health than orphans in community care. In their discussion, the authors noted that the institutions that have evolved in response to the waves of more recent orphans were fundamentally different in quality from the type of institutions on which the earlier studies were based. As one might expect, these results indicated that there should be provision for children in need, ranging from support services in the home to support for alternative carers who can provide foster care in small cluster homes which imitate family care, and to support to large well-run institutions.

3.9 Resilience in Children

Not all children respond to similar situations in the same way. Some are relatively unaffected by the environment (Belsky and Pluess 2009) and others are so sensitive to environmental influences that they are badly affected by adverse circumstances.

The framework for assessing a child's resilience in the face of adverse living conditions must take the child's developmental level, multiple influences on development, the risk and protective factors, and the child's adjustment into account (Armstrong et al. 2005). The concept of resilience has a long history, and the question of what risk and protective factors operate in families affected by HIV is central to the research needed to guide policy and practice for the neediest children living in HIV-affected communities in KwaZulu-Natal.

Werner and Smith (1982) defined resilient children as those growing up in adverse circumstances who, nevertheless, grew into "competent young adults who 'worked well, played well, loved well, and expected well'". These authors identified a number of factors that promoted resilience in the children of Kauai Island, Hawaii, including family size and birth spacing, the number and type of alternate caregivers, the amount of attention given to the child, structure and rules in the household, the cohesiveness of the family, and the number of stressful life events experienced by the child. Age and gender differences in the impact of adversity were observed, with boys being most vulnerable prior to 10 years of age and girls being more vulnerable at a later stage. Emotional support for the child could come from other siblings or adult family members, especially grandmothers, and they noted that "a mother's emotional stability and warmth toward her children is greater when there are more adults around to help and when she has fewer of her own children to handle".

For orphans moved from household to household or taken into institutions, stable attachment figures (such as family members or neighbours who are consistently present and supportive) are lacking. Rutter (2004) speculates that there may be a "sensitive period" early on in child development when the brain is programmed to recognise certain nurturing caregivers. In a study of institutionalised orphans from Romania adopted into middle class families at ages up to 42 months and compared with British infants adopted before 6 months of age, the level of cognitive functioning did not seem to be much affected by the institutional rearing except in extreme cases. However, the children's social and emotional behaviour was more sensitive to this early experience (Rutter 2004). "Attachment disinhibition" as described by Rutter occurred in children who did not differentiate between adults, would readily go off with a stranger, and would not check-back with the adoptive parent. This pattern was more common in the Romanian children and was associated with the duration of institution care. In a significant group, relative failure to develop selective attachments, even though there was considerable recovery of normal functioning in the sphere of social behaviour after adoption, was observed.

3.10 Child-Rearing Practices in the Context of a Particular Political and Cultural History

The starting point in this section is the need for cultural sensitivity in assessing the causes and outcomes of developmental delay. Li's conceptualisation of the interplay between culture and context on the one hand (which he describes as a "feed downward") and neurology-driven plasticity on the other (described as "feed upward") is particularly relevant to the process of applying Western child development theory to another cultural context (Li 2003). The uneasy relationship that anthropology, ethnography, and child developmental psychology have in dealing with these issues is noted, and examples from historical accounts of child-rearing practices of the Zulu people, which may have endured through the turbulent changes that mark the modern history of the Zulu, are given.

The province of KwaZulu-Natal is a meeting point of cultures from Africa, Asia, and Europe—and for many language and ethnic groups. IsiZulu is the dominant language and ethnic group in terms of numbers and political clout, but they are also the group most affected by poverty and the HIV and AIDS epidemic. For this reason the child-rearing practices in AIDS-affected Zulu communities are a central concern. National policies and government programmes for children are directed at all of the country's children, regardless of ethnic group, and this is a typical area where intercultural misunderstanding is rife and requires sensitivity. What may be viewed as neglect or abuse in one culture may be viewed as an important socialisation or disciplinary experience for a child in another culture. A rigid adherence to one cultural value system in drafting laws for the protection of children can criminalise parents for practices that are acceptable in their culture.

A lack of understanding of child-rearing across cultures is endemic amongst academic disciplines. LeVine (2007) showed in a historical overview of ethnographic studies of childhood that ethnographers and anthropologists crossed disciplinary borders and borrowed ideas from developmental psychology to direct their enquiries. The prevailing child development theorists of the day assumed that what was "normal" for children in Europe and North America had universal validity. However, anthropologists like Mead and Malinowski adopted what LeVine calls a "gadfly" role and argued that theories purporting to have universal validity are in fact culture-bound. First the theories of Freud, then Piaget's theories, Bowlby's attachment theory, and others, were examined in non-Western cultural groups, and it could be shown that at least some aspects of the theory did not apply. But the dominance of Western child development theories nevertheless had an insidious effect: Western ethnographers assessed child-rearing in non-Western groups exclusively through the prevailing theories of the day from Western child developmental psychology. This could lead to misinterpretation or missing of important features in specific cultures. This was an uncomfortable interdisciplinary relationship, and LeVine expressed the opinion that it lingers on.

Clear accounts of culture-specific beliefs about how children ought to be raised are difficult to elicit: they are often implicit in behaviour, but not easily put into words.

In a fascinating account of early childhood education in three cultures, Tobin et al. (1989) showed how cultural beliefs about how and what children ought to be taught could vary enormously. The three countries concerned were Japan, China, and America, and preschool professionals and parents from each country were asked to comment on videotaped documentaries of how the preschools were structured, what was being taught, and how children were disciplined. The participants commented first on the information from their own country and whether the teacher had handled the teaching situation adequately. The participants were then asked to comment on and critique the videotaped preschool arrangements in other countries. Their discussions brought out the cultural differences in what was regarded as being best for children, and in a number of instances, participants expressed strong dislike of the practices from another country and culture, highlighting the deep-seated emotions that can accompany cultural concepts.

An important part of assessing the causes and outcomes of developmental delays in the HIV-affected communities of KwaZulu-Natal is to try to understand how the historical patterns of rearing children in Zulu culture interact with rapidly changing political and economic circumstances. Even before the impact of the epidemic, economic and political changes had affected family life and weakened family ties.

In the past two centuries, the Zulu were swept from small pastoral groups to a highly militarised society under King Shaka and then suffered a series of defeats at the hands of the Boers and the British, which robbed them of their local dominance and status. At a time when industrialisation was taking place in Britain and spilling over into its colonies, the Zulu were increasingly marginalised in their own lands and the migratory labour system struck at the heart of families, splitting them apart. The apartheid system further weakened community life and oppression of all the Nguni tribes in South Africa reached full strength in the early seventies. Significantly, it was the *children* of Soweto who rioted against the oppressive education system in 1976 and who initiated the groundswell of opposition to apartheid that climaxed with the first democratic elections in 1994. By then, the HIV epidemic had started, and, sadly, gained momentum at a time when the government structures, which should have responded decisively, were transforming and restructuring. Families had to absorb a tidal wave of deaths of young parents, leaving children stranded in a society that was underprepared to care for them.

In any culture, childhood is not just a biological state but is defined by the general population (Kessen 1983; Liddell et al. 1990). Childhood has long been regarded as "a cultural invention" (Kessen 1983), so it is not surprising in the literature on child development in Africa to find children valued differently from Western norms and for socialisation patterns to be widely different (Nsamenang 1995). Child-rearing practices are likely to have elements which are stable and enduring, as well as elements that change with changing circumstances and cultures.

One of the strongest themes in descriptions of childhood in Zulu oral histories from the last century and before is the presence of a gender-based, age-cohort system in socialising children into the meanings and practices inherent in their society (Webb and Wright 1976). Krige (1936) recorded that children's relationships with their fathers were characterised by respect, fear, and obedience. Children spent much of their time with other children. She wrote "Zulu children are seldom lonely, for there are in the village always companions of their own age, with whom they go about and with whom their behaviour is free and unrestrained" (Krige 1936, p. 20). Young girls are taught to carry water in small containers balanced on their heads from a very early age (5 years) and later (aged 11) start helping with the crops, after being given a small hoe. Young boys follow a different socialisation pathway. They are trained by older boys successively to herd calves, then cattle, then to be mat-bearers to warriors, warriors themselves, and finally elders with family and political responsibilities (Webb and Wright 1976). Responsibility for rearing children is spread through the extended family, and children are frequently moved to other branches of the family for lengthy periods of time to be companions to the elderly or to help in other ways.

These historical accounts describe very different practices from those viewed as the norm in a modern isiZulu society, but there may be underlying ideals which persist and are embedded in the culture, and there is some evidence for this. These ideals may direct family decisions about distributed care arrangements in the home or the care of orphans and other vulnerable children when the biological parents are gone. Clearly this possibility should not be ignored in research dealing with children in this culture.

Older siblings are still seen as a major source of support for learning in Zulu society. In a study for UNICEF on the promotion of child well-being, adults from a rural community said that younger children learn fast by observing their older siblings (Dawes et al. 2004). A study of 5-year olds in rural settings showed that adult communication with 5-year olds was characterised by more power and social distance than communication from older children in an apparent continuation of the hierarchical structure (Kvalsvig et al. 1991). The 5-year olds themselves issued more controlling statements to younger children. In addition, the low levels of parental literacy might suggest that schooled siblings were preferred sources of support in this area. This suggested a disruption in the natural order of family responsibilities: parents carried greater responsibility for the well-being of family members, but their children had more opportunities for schooling and were often better informed about the modern world.

Cultural practice is constantly reshaped by circumstances, and the process may occur more quickly in urban areas than in rural areas. Cultural practice responds to microeconomic and social pressures in a way that makes it difficult to generalise.

3.11 Measuring Child Development

The preceding sections of this chapter have discussed some of the broader issues to be considered in studies of children in HIV-affected areas of KwaZulu-Natal. The seriousness of the situation for the health and well-being of children in this province is unprecedented: the apartheid years of oppression followed by a devastating epidemic have combined in a way that has serious consequences for children. Indicators and monitoring systems of the kind proposed by Dawes et al. (2007) are needed to feed into national policy development so that it is conceptually grounded, as well as based on children's rights as expressed in the South African Constitution. State intervention aimed at protecting and supporting children must be monitored using robust and reliable indicators. However, basic research has a different and more subtle role to play: it is needed for a better understanding of the primary risks leading to developmental delays and to determine what protective factors there are in these environments. Sensitive and culturally appropriate instruments and procedures are required.

The co-constructivist approach would support collecting not only biological information on health and nutrition but also indicators of social, emotional, and cognitive function in the child, as well as to assess the safety, good health, social and emotional support, and cognitive stimulation of the child's caregiving environment. The measures and procedures used should be culturally appropriate. At the present time, underlying neurological processes are usually inferred from behavioural measures and from performance on cognitive tasks, but cognitive neuroscientists recognise the need for integrating the data from recently developed neuroimaging technology with behavioural measures (Yarkoni et al. 2010) in order to shed more light on the functional development of the central nervous system in the presence of acute and chronic infections.

The difficulty of identifying principles for the selection and adaptation of measures for use in South Africa is best illustrated by the difficulties involved in selecting measures of language development (Dawes et al. 2004). In selecting a vocabulary test for isiZulu-speaking children, one could take note of the special characteristics of isiZulu as a language, such as the flexible and imaginative use of alliteration and metaphor, and take account of what is considered in Zulu culture to be a mark of a child who is competent at verbal communication in the language. This way of approaching the development of measures is intuitively preferable to importing a test but will involve a lengthy research period. As an alternative, it is quicker to use the pictures from the original Peabody Picture Vocabulary Test, to translate the items into isiZulu, and to omit those which do not translate well. This would enable direct comparison of scores with other language groups. However, Zulu children would probably respond more readily to illustrations drawn by a local artist and depicting the local version of the object.

Other language-based measures such as verbal fluency are relatively easy to construct in a particular language, but more difficult to compare across languages. The Hopkins Verbal Learning Test (HVLT) is designed to circumvent this problem (Brandt 1991). Certain words are more commonly used or easily remembered than others, but the words themselves differ from language to language. In the HVLT, the first step is to generate sets of words which are subsequently used in the memory test. This technique of using a standardised procedure for constructing measures rather than a standard measure is helpful in addressing the problem of different word meanings in different languages and cultures.

Intelligence tests are a case in point. Intelligence tests developed in the West are linked in to scholastic ability, but they are not generally suitable as a means of assessing cognitive performance in children from rural communities in developing countries (Connolly 1998). Differences in practical intelligence, on the other hand, as demonstrated by children in these communities, may be reliably recognised in the community but have little to do with the construct measured by intelligence tests. Sternberg experimented with an alternative technique of measuring children's capacity to learn rather than using a measure of what they have learned (Sternberg et al. 2002).

In the course of developing measures, it is important to look at what children actually do and say. Naturalistic observations of children in their everyday environments are particularly rich sources of information in the present context. Children may be able to rise to an occasion with a test, but the main effect of a nutritional deficit may be to lower energy levels: children may explore the environment less or be more passive socially, and this may not show up on tests. For children affected or infected by HIV and AIDS, an understanding of the extent of their social isolation, or of the support and encouragement that they receive from their families and friends, provides a more comprehensive picture of how developmental delays arise and how they may be remedied. Observations conducted in real time with a checklist or handheld computer can provide quantitative data on the amount of time spent in defined activities and social interactions, the energy levels of the children, and their emotional state. Qualitative description of the environment and the content of interactions may be noted after each structured observation period.

The dynamic systems approach (Thelen 2000; Adolph 2002) is designed to identify developmental pathways formed by the interaction of multiple subsystems such as maturation in the central nervous system, the task at hand, and the opportunities or limitations of the environment. Adolph's work involves studies of how children learn to circumvent obstacles of the type found in American houses as they achieve mastery in gross motor skills. Children in poor rural communities in Africa as a rule do not encounter the staircases or the smooth, slippery slopes, but they do meet other obstacles (uneven ground, sharp stones, and deep holes). In terms of measures of motor development, is the ability to negotiate a staircase (in the Bayley Scales, for instance, Bayley 2005) an adequate measure or do adjustments need to be made?

Conduct disorders, too, play out differently in different social environments. A study of the family and personal characteristics of aggressive Nigerian boys (Ani and Grantham-McGregor 1998) indicated that crowding, little paternal affection, and frequent physical discipline were risk factors, echoing similar findings in developed countries, but family instability and low socio-economic status were not as important indicators in Nigeria as in developed countries. The family structures are different in the two environments, as are attitudes towards corporal punishment. While the Western literature may be helpful in suggesting etiological factors and possible intervention, careful examination is needed to determine the extent to which indicators from developed countries are important in all cultures.

We need to determine which measures are transferable without adaptation from their industrialised countries of origin to technologically underdeveloped regions and to different cultures, which need some modification and which have to be redeveloped from first principles.

A number of tests with known psychometric properties have been developed in Africa. For young children, the Kilifi Developmental Inventory (Abubakar et al. 2008) has been used in several studies in Kenya and South Africa and is an attractive alternative to imported tests. The test kit is made from simple locally obtainable objects, which has the dual advantage of keeping costs low and being familiar to the children. The test procedure, too, is well adapted to African settings and a manual has been developed to allow accredited trainers to train lay-assessors. The Grover Counter Test, which is based on Piagetian principles, was developed in South Africa to assess 3- to 10-year olds' cognitive functioning levels mainly for purposes of educational placement. The child is required to sort plastic counters and arrange them in shapes, patterns, and sequences to test such cognitive processes as perceptual-motor abilities, memory, and reasoning. The administration of the test does not require many verbal instructions or responses, which makes it particularly useful for testing children with expressive language difficulties.

In the area of research on personality, temperament, or emotional regulation, the Profile of Social and Emotional Development (Abubakar et al. 2011), developed in Kenya, allows caregivers to discuss, in their own words, key areas of social and emotional functioning, with the interviewer scoring the behaviour as seriously disruptive, moderately disruptive, or not disruptive in a family context. The process lends itself to a more natural expression of the caregiver's doubts and worries about the child.

Measures for comparing different caregiving environments such as family home, foster home, and various institutional settings such as preschools are badly needed for the purposes of establishing planning guidelines for the care of children affected by HIV and AIDS and for setting minimum standards for registration of organisations. Several versions of the HOME inventory (Bradley and Caldwell 1981; Caldwell and Bradley 2003) are in use in South Africa as well as a number of checklists for assessing preschool quality.

Although imported tests are still needed, and can be adapted in some instances, psychologists working in Africa are gaining experience and confidence in developing measures; training manuals and norms are being developed and reviewed. These tests are potentially more sensitive because they are better understood by children, and they are likely to have face validity for the adults concerned (parents, caregivers, community leaders) and thus better community support and compliance in the research process.

3.12 The Co-constructivist Model

Horowitz, in an overview of the state of the art in child developmental psychology at the beginning of the twenty-first century, points out that what people call for are simple answers to complex questions. Horowitz wonders if child developmental psychology is truly developing overarching theories or whether it is simply developing a new set of buzz words: "dynamic, non-linear, systems, plasticity, life course trajectories, bio-ecological, person-in-context, reciprocal influences, mediators, connectionism, and attractors" (Horowitz 2000, p. 3). However, the ensuing decade produced a number of papers calling for integration of information on child development across disciplines and levels of analysis that use all the above words in more meaningful debate.

Li (2003) refers to the tension between "nature" and "nurture" as explanations of development that direct enquiries. He uses the term bio-cultural co-constructivism to describe the interplay of biology and culture across levels of interaction, with the concept of developmental plasticity "tuning" development. Using the metaphor of a pendulum, he maintains that research on sequencing the human genome swung public interest temporarily in favour of genetic and neuronal determinants of development, but that culture and experience are integral to the developmental process and should not be ignored. He defines culture as ongoing social processes, which produce social, linguistic, symbolic resources or materials and technology that influence development through feedback mechanisms.

A key concept in the synthesis of biological, cognitive, behavioural, and sociocultural factors in shaping the brain is the concept of brain plasticity (Li 2003). This is defined by Mahneke et al. (2006) as "the capacity for physical and functional brain change that can either be strengthened or degraded in a bidirectional manner, depending on circumstances". From a neurological perspective, the brain itself is thought of as a self-organising system, constantly adapting to its biological environment and to the social, emotional, and cognitive demands made on it (Johnson 2008).

Developments in our understanding of how in utero events can predict health problems 70 years later (Barker and Clark 1997) have given rise to a more fine-grained analysis of how early stressors influence biological functions such as stress management and immunological, metabolic, and neuroendocrine responses (Shonkoff 2010). Shonkoff calls for a new generation of public policies and practices to augment current models that emphasise enriched learning opportunities for children, parenting education, and support services for families. He points out that in the United States, the programmes based on current policies are broadly supported and have produced a wide range of desirable results. Nevertheless, difficulties include marked variability in implementation, typically modest impact, and large numbers of the children at greatest risk who do not appear to benefit significantly from them (Shonkoff 2010). He advises that the within-group variability in analyses of the implementation and the outcomes of programmes should claim our attention as much as the between-group variability.

At the end of a paper on a "unified theory of development", Sameroff (2010) quotes Albert Einstein as saying "Everything should be as simple as possible, but not simpler", an important aphorism to guide developmental systems theory at this time and a retort to Horowitz's "Person In The Street" who requires simple answers to complex questions.

Sameroff bemoans the fact that scientists try to be theoretically simple until the complexity of empirical data overwhelms them. He proposes at least four models for understanding human growth: a personal change one, a contextual one, a regulation one, and a representational one.

For the *personal change* model, he favours a stage process (after Freud and Piaget) whereby children do not only do things better as they develop, they do things differently.

In illustrating the *contextual model*, he gives us the example of the Philadelphia Project in which he was involved. Following Bronfenbrenner's (1986) socioecological model, subsystems were used in the analysis of the data: family processes, parent characteristics, family structure, and family management. This analysis model revealed that, for the Philadelphia youth sample, more risk factors predicted worse outcomes and more promotive factors predicted better outcomes—in other words it is the number of reinforcing factors and not a single causality that is important.

The *regulation model*, based on systems theory, not only views the child as active in the interpretation of experience, a self-regulation concept, but also refers to the contextual regulation. He gives an example from Thelen's dynamic systems theory of the way in which infants became able to walk. The self-regulated neurologically based co-ordination is constrained by the other-regulated muscle development. Multilevel transactional regulation can occur when the parent and child are in a transactional relationship with one another, but both are also transacting with cultural practices.

Finally he refers to the *representational model* which deals with meanings, with social representations of relationships becoming working models. He notes that the order or disorder in a family or a society's representation of itself affects the adaptive functioning of its members. Sameroff uses the first three of these models in his depiction of the unified theory of child development, saying that representation suffuses every aspect of this overarching model.

Harkness and Super (1994, p. 218) describe *context* in a model that they term the *developmental niche* which conceptualises child development in different cultural environments in terms of three subsystems: "(1) the physical and social setting in which the child lives, (2) culturally regulated customs of child care and child rearing, and (3) the psychology of the caretakers". This contextual model is particularly useful in developing countries with diverse ethnic groups. It emphasises the mediating role of culture and context in reinforcing certain developmental pathways. In this way living conditions (e.g. overcrowding) and family arrangements (extended family and community care of children) influence the way in which children are raised and the values that a society places on such qualities in a child as obedience and respect (Ogunnaike and Houser 2002) and even the qualities people in that society regard as an indication of intelligence in a child.

Bronfenbrenner's *contextual* model of circles of influence on child development is used as a way of understanding the relative strength of the *proximate and distal* influences on the course of child development (Bronfenbrenner 1986). It is possible that distal influences may be more homogeneous with respect to child-rearing patterns amongst developed countries than amongst underdeveloped countries. Developed countries have similar economies and health and education systems, and population mobility between countries is considerable. This contrasts with the relative isolation imposed on less developed countries and communities by poverty (Dawes et al. 2004).

Theories about brain development on the one hand, and the development of mind on the other, have predominantly been investigated and published separately, though some have encouraged that they be investigated together. For example, Boivin and Giordani (2009) describe co-constructivism as an "omnibus" in the sense that these theories should now be brought together in order to deepen understanding of the development of intelligence. The models described above give shape to the constructs and procedures which guide attempts to understand the development of the children who are the focus of this chapter. They give us the vocabulary to address complexity and to steer us away from answers that are too simple to be helpful.

3.13 Co-constructivism in Practice

In preceding sections of this chapter, we give an account of some of the "simple solutions" currently being applied to the children of KwaZulu-Natal. They are clearly inadequate: free access to health services or a preschool class is only successful if the quality of the service offered is good, child-care grants are only accessible if the documentation is available, and community care may only be better than institutional care if the family is financially stable and the child is not disabled or disturbed. Advocacy to encourage full implementation of the scientific recommendations regarding the programmes needed for children is required. But, as in the poverty programmes for children in the USA described by Shonkoff (2010), service delivery in KwaZulu-Natal also suffers from inadequate implementation, modest impact, and failure to reach the children at greatest risk.

In summarising the type of analyses which could be used to inform policymakers and planners in this complex situation, we take as concrete examples epidemiological studies and field trials conducted across sites in South Africa and Kenya. Our South African study, called "Asenze" and led by Davidson and Kauchali, is being implemented in five adjacent tribal areas, extending from peri-urban to deep rural, and the purpose is to examine the nature and causes of developmental delay. All 4- to 6-year olds and their caregivers in these areas are invited to participate in the study. In Phase 1, data was collected on households, caregivers, and children, and now, 2 years later, Phase 2 is under way. The same children are being reassessed during a clinic visit, follow-up information on their household and family circumstances is being obtained, and the process of their entry into formal schooling is being evaluated. Our Kenyan nutrition intervention trial (INSTAPA Work Package 6, led by Kvalsvig and Holding) assesses child development relative to micronutrient supplementation at six time points for each child, from 6 months to 3 years of age. The objective is to test the World Health Organization guidelines for iron supplementation in a malarial area, both during the year of daily supplementation and for 2 years thereafter. The two studies are in different countries, have different objectives, and work with participants of different ages, but both are longitudinal. Both studies include nutritional and physiological measures along with psychological, emotional, and behavioural measures in the developmental assessments.

Many of the principles described in the models discussed in the previous sections of this chapter have been incorporated into the study procedures, and these are summarised below:

The components of the analysis of contextual factors in our South African project fit quite neatly into the subsystems approach of the Philadelphia project: family processes, parent characteristics, family structure, and family management. We examine demographic factors in the household, maternal mental health, parenting stress, social support for the family, family violence, and order in the household.

Cultural sensitivity has been in the foreground throughout the research process. An ethnographic study, in parallel to the quantitative measures, is part of the South African study. Families and community leaders are being asked to describe and explain certain features of community life. Similar experience was gained in our Kenyan field trial involving participants in focus groups to understand infant feeding practices. An added benefit in the latter study was the inclusion of naturalistic observations that overcame some of the difficulty with direct questioning.

The selection, adaptation, and translation of measures in the South African study are the product of pilot work done in similar communities by assessors from the same cultural group as the study participants. These assessors include a core group, which has been engaged with such measures and procedures for about two decades. This group advises on cultural appropriateness and local dialect rather than purely linguistic translation. The procedures for producing an adequate isiZulu translation of the questions, information, and instructions given to children raise interesting issues. In order to have an adequate assessment of the child's ability to perform cognitive tasks, it is essential that the child understands the precise demands of the task. Ethics committees and test development agencies required translation of all instruments by accredited translators. IsiZulu, like many other languages, differs somewhat from place to place in the vocabulary and expressive habits commonly used. In addition, certain words within the language are favoured when children address one another or when adults who are experienced in working with children speak to them. In this project, translations and back-translation are done between isiZulu and English, but this is only part of the process of achieving a good understanding between the children and the assessors. It may be counterproductive to use a translation done by an accredited linguistic expert, if that person was not familiar with the purpose of the developmental measures and the words that children from that area understand. Therefore, all translations, interviews, and assessments in this project are done by isiZulu-speaking assessors experienced in working with children of this area. In addition, an ethnographic team is asked to collect information on issues of special relevance to the welfare and development of children.

Complexity: The lessons from the co-constructive approach are very relevant here. Respect for the fact that brain, mind, and culture interact constantly across what used to be construed as nearly separate levels of analysis has resulted in a choice of measures deemed to be suitable for the cognitive processes that are undergoing change and development at approximately 4–6 years of age. Biological measures in

Phase 1 of the Asenze study include both caregiver and child health and nutrition; child measures include social, emotional, and cognitive assessments; a number of family demographic and household measures are included; and finally, social environment measures include social support, order in the home, and parenting stress. These add up to a massive body of information on each child, all of which has to be summarised and tested against the specific hypotheses on which the study is based.

The intention is to use complex analyses necessary to explore the developmental pathways inherent in the local KwaZulu-Natal communities. In a study conducted with younger children on Pemba Island, Tanzania, Olney et al. (2009) used structural equation modelling and data from naturalistic observations of children to illustrate how stunting, malaria, and anaemia all affected motor activity and motor and language development in their sample. This suggested that treatment for either anaemia or malaria alone is not sufficient to optimise child development in affected children. Changes in motor development also predicted changes in child and caregiver behaviour. These rich analyses are essential to understanding the processes that may lead to developmental delays amongst the children in the Zulu communities and the remedies which should be implemented.

Sameroff's *personal change model* is represented in the particular cognitive measures selected for this study: the Grover Counter test, based on Piagetian stages and designed to show the cognitive level at which the child is functioning, and subtests from the KABC-II designed to indicate the underlying neurological function. Both of these are repeated in Phase II of the project. The regulation model is represented in groups of measures of interpersonal relationships as well as self-regulatory ones.

In addition to contemporary information, a historical account of child-rearing patterns and the suddenness of the health, social, and political changes that have impacted on the family and community context are part of the *representational model* identified by Sameroff as essential to understanding the family and community behaviours with respect to the preschool children in their midst. In the Asenze study and the INSTAPA Work Package 6, oral histories and present-day reports from parents (e.g. Webb and Wriht 1976; Ogutu et al. 2010) influenced research practice in the informed consent procedures adopted and in selecting a principal caregiver to interview regarding the child's health and development. The nature of the caregiving relationship is anticipated to have an influence on the child's developmental trajectory over time. One needs to explore how this can be accommodated in analytic procedures.

3.14 Finding Analytic Procedures

In this chapter on the value of a co-constructivist paradigm, we have tried to show in some detail how the developmental risks and protective factors for children in the province of KwaZulu-Natal, South Africa, are interconnected at various levels, within various contexts, and change over time. We are mindful of the importance of using analytic procedures that can cope with this situation, and the need for simple solutions, which are not too simple to reach the children who are most at risk.

Factor analysis, a technique developed early in the twentieth century, has traditionally been used to explore the way in which several variables in a data set interact, particularly in relation to the construct of "intelligence". The usefulness of this technique lies in the fact that it explores the data and suggests plausible linkages. Factor analysis, by whatever method, is, however, subject to the general caution that applies to complex analyses: interactions can be interpreted in different ways and it is important to consider alternative explanation.

Newer techniques such as *multilevel regressions*, *structural equation modelling*, and *growth modelling* expand the array of analytic tools that researchers can use when working with complex data. If used appropriately with due concern for problems of interpretation of the results, they can extend the knowledge base of child development within the co-constructivist paradigm.

In order to address the problem that there may be alternative models which would explain the results of the analysis, the model should be hypothesis driven, and should first be examined through descriptive and main effect analyses of the data. Handled with care, however, there are several advantages to using structural equation modelling (Brooks-Gunn et al. 2010). Firstly a distinction can be made between direct and indirect effects of the variable of interest (which in their case was the influence of maternal employment in the first year on the child's later development). If an indirect effect is found, the pathway through which it influences the outcome measure is made explicit in the model. Secondly, estimates can be made of the total effects this variable has on the outcome measure whether by direct or indirect effects. Brooks-Gunn et al. (2010) utilise this capability to good effect to distinguish between the effects of full-time and that of part-time maternal employment on child outcomes. They do this in a series of models which vary the type of outcome measure (school-readiness, language, and behaviour problems) and the age at which it is assessed (3 and 4.5 years and Grade 1), thus establishing a consistent pattern of influence.

In a different use of structural equation modelling, Dunst et al. (2007) modelled the effects of an early childhood intervention on parent and family well-being. They integrated five previously separate conceptual and theoretical approaches into a broader multivariate framework and were pleased to note that the results not only confirmed the knowledge base regarding the relationships examined in prior research but also extended it. In this process they transformed existing knowledge about the linkages from being simply "plausible" to the point where they could provide a "recipe for action".

Studies such as the above demonstrate the practical value of utilising all the available data, both cross-sectionally and longitudinally, to track the course of child development, taking account of the functionally different factors which come into play a different stages.

3.15 Conclusions

Researchers in the developing world need to produce results which have something to offer in a global context and yet yield sufficient detail on causal pathways to guide support programmes for children in localities where there are specific barriers and problems. We have tried to show in our geographical context how a general environment of poverty and disease has been rocked by political forces and a major epidemic and how this affects children and their families in both body and mind. In discussing the instruments and techniques needed to achieve a sensitive account of both the group trends and the individual variations, we strongly believe that the research participants, whether adults or children, should also be partners in the research. In concrete terms, this means that assessment instruments should reflect their concerns, as well as their responses to the tasks we ask them to perform, and that we should adopt analytic procedures which do not obscure important deviations from the norm.

Naturally, child development is concerned with change over time: different trajectories, transactions with caregivers and teachers, and transitions from one way of functioning to another. It is one thing to acknowledge complexity in child development studies in Africa and quite another to find adequate ways of working within the co-constructivist paradigm. In preparing this chapter, we have been forced to confront difficulties in devising adequate research procedures and methods and to realise that an account of this process, even if not entirely successful in achieving its objectives, can be of benefit to future research in the region.

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Chapter 4
Cognitive, Motor, and Behavioral Development of Orphans of HIV/AIDS in Institutional Contexts

Kim T. Ferguson and Melody J. Lee

4.1 The HIV/AIDS Pandemic and Institutional Care

The HIV/AIDS pandemic continues to affect the lives of millions each year. Sub-Saharan Africa remains the region in the world most heavily affected by HIV/AIDS, accounting for 67 % of worldwide HIV infections and 72 % of AIDS-related deaths (UNAIDS 2009). In 2008, more than 14 million children had lost either one or both parents to HIV/AIDS (UNAIDS 2009). Malawi is one of the countries most heavily impacted by the crisis, with an estimated 650,000 children orphaned by HIV/AIDS (UNAIDS 2009).

As orphan populations increase substantially each year, traditional African mechanisms for orphan care, which usually involve placing orphaned children into the homes of extended family, are becoming less viable. Thus, a greater reliance on the use of infant homes, also known as "crisis nurseries," has developed to address the growing number of orphans (e.g., Beard 2005). Many extended families express a willingness to care for an orphaned family member but argue that they do not have the financial means to provide for and support the basic needs of a young child (Freeman and Nkomo 2006; Miller et al. 2006). Caring for an infant or toddler is particularly challenging, given the high cost of formula and proper nutrition, amongst other basic care items. In 2003, the average cost of caring for an infant in Malawi was equivalent to US$250–$1700 (Bhargava and Bigombe 2003). This figure is poignant considering that Malawi's gross national income per capita was only US$160 in 2003 (World Bank Group 2005) and US$278 in 2008 (United Nations 2008). In fact, a relevant study in Botswana in 2003 reported that 47 % of households experienced financial hardship as a result of taking responsibility for orphan

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relatives (Miller et al. 2006). Given these challenges, some researchers argue that infant homes may be the best method of temporary support for some orphans, particularly infants (e.g., Beard 2005; Ferguson 2002). In some cases, institutions may, in actuality, provide better support for orphans with specific needs, such as physically handicapped or HIV-positive children (Subbarao and Coury 2004; Wolff and Fesseha 1998). Although other researchers and practitioners may disagree with this evaluation (see, e.g., Dunn et al. 2003), institutionalization is nevertheless becoming more prevalent in sub-Saharan Africa.

Given the increasing number of infants being placed in infant homes in Malawi, an evaluation of infants' developmental functioning within these institutions, and of the quality of care provided, is urgently needed. Yet, the majority of research to date on the developmental outcomes of children from institutionalized settings has focused primarily on poor-quality Eastern European orphanages in countries such as Romania (see, e.g., Ames 1990; Castle et al. 1999; Chisholm 1998; Fisher et al. 1997; Groza and Ileana 1996; Reich 1990; UNICEF 1993). The limited research to date in African contexts has also primarily evaluated institutions providing care, typically of poor quality, during emergency situations (Giese and Dawes 1999; Subbarao and Coury 2004). In addition, little research, be it in Western or African contexts, has assessed children while they were still living in the institution (see, e.g., Dennis and Najarian 1957; McCall 1999). And, little research has assessed children's development within institutions such as the infant homes that are now common in Malawi and other southern African countries, whereby children are placed in infant homes until the age of three (while their extended family are unable to provide for their basic nutritional needs) and are then placed back into their extended families (Beard 2005; Ferguson 2002). This research is critically needed to inform orphan care providers and policy makers in sub-Saharan Africa as to the current developmental functioning of institutionalized children.

4.2 Development in Context: Theoretical Approaches

Little research to date has evaluated the development of children living within institutional settings that provide good quality care. Thus, in assessing these children's developmental outcomes, it is essential that we develop a holistic understanding of both their institutional contexts and of the contexts of non-institutionalized children within similar regions or communities. Such an understanding should include an analysis of both physical and social environmental factors influencing each area of development at multiple levels (e.g., within both the proximal and the distal environment). In this next section, we suggest a conceptual framework within which the complex interactions between biological, physical, and psychosocial factors impacting children's developmental outcomes can be better understood and studied. Because this conceptual framework draws on a number of related cultural, bioecological, and cultural-ecological approaches, we provide an overview of some of these approaches before outlining our own. We particularly focus on Bronfenbrenner's bioecological model (Bronfenbrenner 1979; Bronfenbrenner and

Ceci 1994; Bronfenbrenner and Crouter 1983; Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998), Nsamenang and colleagues' ecocultural approach (e.g., Nsamenang 1992; Nsamenang and Dawes 1998), and Li's (2003) cross-level dynamic biocultural coconstructivist paradigm. In discussing Li's (2003) approach, we focus on Boivin and Giordani's (2009) application of the coconstructivist approach to the neuropsychological assessment of African children.

4.2.1 Bronfenbrenner's Bioecological Model

In 1974, Urie Bronfenbrenner challenged the conventional study of human development by describing developmental research as "the study of the strange behavior of children in strange situations for the briefest possible period of time." He argued that development should be studied in its ecological context or, in other words, within the actual environments in which humans live (Bronfenbrenner 1974). Later, he proposed an ecological model, now called the bioecological model, which provides a conceptual framework for studying human development in context (e.g., Bronfenbrenner 1979; Bronfenbrenner and Ceci 1994; Bronfenbrenner and Crouter 1983; Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998; see also Ferguson et al. 2009).

At the core of Bronfenbrenner's bioecological model are four interacting dimensions that should be considered when studying development in context, namely, process, person, context, and time (PPCT, see Fig. 4.1; Ferguson et al. 2009). The first of these, process, encompasses ongoing exchanges of energy between an organism and its surrounding environment over time (Ferguson et al. 2009). Most important are "proximal processes," progressively more complex, enduring, and reciprocal interactions between active and evolving human organisms and the persons, objects, and symbols in their immediate external environments (Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998; Ferguson et al. 2009). These interactions take place on a regular basis over an extended period of time. According to Bronfenbrenner and his colleagues, these proximal processes are the "engines of development" (e.g., Bronfenbrenner and Ceci 1994; Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998). Their power, however, varies as a function of the characteristics of the developing person.

In terms of the ecological context, Bronfenbrenner and colleagues have argued that development occurs within four nested and interacting systems, namely, the microsystem, the mesosystem, the exosystem, and the macrosystem (e.g., Bronfenbrenner and Morris 1998; see also Ferguson et al. 2009). The microsystem consists of the interpersonal relationships and physical settings directly experienced by the person, for example, the family, the peer group, the school, and the neighborhood. The mesosystem consists of connections between these microsystems (e.g., the relationship between children's parents and their teachers), while the exosystem is comprised of connections between settings that do not contain but directly influence the person (e.g., parental work settings). The macrosystem is the overarching pattern of micro-, meso-, and exosystems characteristic of a given culture or

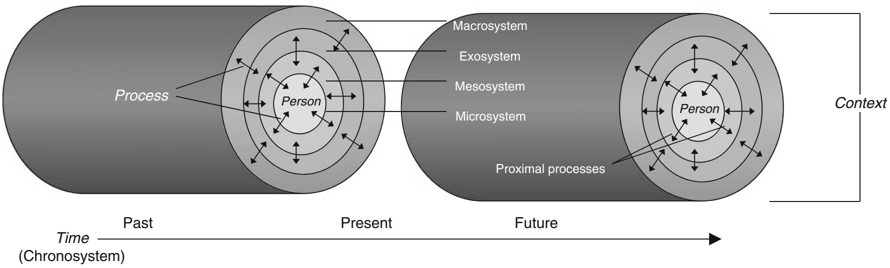

Fig. 4.1 Bronfenbrenner's bioecological model: *process*, *person*, *context*, and *time* (*PPCT*) (Reproduced from Ferguson, K. T., Kim, P., Dunn, J. R., & Evans, G. W. (2009). An ecological model of urban child health. In N. Freudenberg, S. Klitzman, & S. Saegert (Eds.), *Urban Health and Society*: *Interdisciplinary Approaches to Research and Practice*, pp. 63–91. San Francisco: Jossey-Bass)

subculture. Thus, the ecological context influences the critical proximal processes that underlie human development at multiple levels. These influences occur over time, conceptualized by Bronfenbrenner as influencing development at the micro level (i.e., continuity versus discontinuity within episodes of proximal processes), the meso level (the frequency of occurrence of these episodes over days or weeks), and the macro level (changing practices, expectations, and events in the larger society) (Ferguson et al. 2009).

4.2.2 Cultural and Ecocultural Models

Of course, Bronfenbrenner is not the only, and was not the first, researcher to argue for the importance of studying development in context. The fields of cross-cultural psychology and cultural anthropology, specifically, have studied the influences of the macrosystem (the overarching characteristics of a given culture), as well as various aspects of the microsystem, mesosystem, and exosystem that are typical of a particular macrosystem (culture). This practice began with the cultural study of the child, most notably through the research and writings of Margaret Mead (e.g., Mead 1928; Mead and Macgregor 1951) and Ruth Benedict (e.g., Benedict 1934). These writers are generally credited with founding the "culture and personality" movement (see, e.g., Harwood et al. 1995; Segall et al. 1990), which in its original form suggested that the child-rearing practices of a specific culture lead to "national personality types." This extreme formulation was later revised following work by Odum (1953) and others in anthropology, which emphasized the importance of the ecosystem in fashioning development. Inherent in this model is the idea of an ecological niche, borrowed from ecology and commonly defined as an organism's position within its ecosystem as a result of structural adaptations. Thus, in these latter models the importance of cultural adaptation was emphasized (e.g., Whiting 1977; LeVine 1973, 1977). For example, in the 1970s, Whiting and colleagues (e.g., Whiting 1977) proposed a heuristic model for psychocultural research that considered the influences of both the past history of a particular culture and the current environment on specific "maintenance systems" (such as the type of household, economic structures, social structures, and settlement patterns). These maintenance systems then influence children's learning environments (see, e.g., Whiting 1977, p. 30). At the same time, Bronfenbrenner (1979) first proposed his ecological model based on the concept of the ecosystem, although at the time cultural and developmental psychology were somewhat separate areas of study.

More recently, Super and Harkness (1986, 1997) have adapted the concept of an ecological niche to specifically study child development in context. Instead of "ecological niche," they use the term "developmental niche" to describe a child's position within his or her proximal environment. Important components of the developmental niche are the psychological characteristics of the child's parents, the physical and social settings of the child's environment, and the child-rearing and socialization practices typical of the culture in which the child lives. Similarly, in considering how the culture in which a child lives influences his or her development, Weisner and colleagues (e.g., Weisner 1996) suggest that the daily activities and practices inherent in family routines play a particularly important role. We thus return to the important influences of what Bronfenbrenner and colleagues have termed proximal processes on child development. Cole and colleagues (e.g., Cole 1996) have similarly identified cultural practices to be the proximal units of children's experience. Along similar lines, Valsiner (1987) expands on the concept of a developmental niche to distinguish different levels of developmental niches based on the interactions between the child and an adult such as a parent. The inner level structures the child's access to other aspects of the environment and his or her exposure to particular objects and events, as well as culturally acceptable ways in which he or she may act. As such, this inner level is called the Zone of Free Movement (ZFM). Within this ZFM, adults create a Zone of Promoted Action (ZPA) by promoting certain actions by the child. This ZPA is similar to Vygotsky's conception of a Zone of Proximal Development (ZPD), wherein the child can accomplish a task with sensitive instruction that he or she could not accomplish independently. Indeed, Vygotsky's sociocultural theory emphasizes the role of adults and other persons in a child's environment in shaping development, specifically cognitive development (see, e.g., Vygotsky 1934/1986).

In some ways, there has been much progress since Bronfenbrenner first argued for the study of development in ecological context (Bronfenbrenner 1974). Over the past three decades, research in human development studying child and adult behavior and development in its ecological context has proliferated (e.g., Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998; Ferguson et al. 2009). Nevertheless, there remains much additional research to be done.

In studying the ways in which various proximal processes influence child development, Ogbu (1981) has cautioned against ethnocentrism in characterizing competency. Specifically, he argues that models of competence derived from research within one cultural group (e.g., middle-class Caucasian Americans) should not be indiscriminately applied to other cultural groups, as different cultural groups may have different cultural imperatives and expectations (Ogbu 1981). For example, child-rearing practices that are considered to impact positively on child competence within one cultural group may not positively impact child development within another culture. In fact, some cross-cultural researchers have suggested that normative child-rearing practices within a culture or group are adaptive to different aspects of the environment within which they live (see, e.g., Cole et al. 1971; LeVine et al. 1994), an argument similar to the earlier cultural adaptation models already discussed (e.g., LeVine 1973, 1977; Whiting 1977; see also Segall et al. 1990). Thus, what is considered to be competent within one cultural group may not be adaptive within another (Ogbu 1981). Others have made similar arguments, particularly in the realm of cognitive development and the study of intelligence (e.g., Berry 1971, 1974, 1984, 2001, 2004; Berry et al. 1986; Cole 1996, 1999; Cole and Bruner 1971; Cole et al. 1971; Cole and Scribner 1974; Munroe and Munroe 1975; Nsamenang and Dawes 1998; Segall et al. 1990). Perhaps most similarly to Ogbu (1981), in discussing the study of child development in southern Africa, Nsamenang and Dawes (1998) contend that particular competencies may be seen differently in different cultures and contexts. Further, Berry (2004) argues that, while some basic psychological processes are universal, behavioral variations occur within different cultures as a result of cultural adaptation to the environment in which people live.

In order to effectively study child rearing and development, particularly in minority populations in the United States, Ogbu (1981) argues that a non-ethnocentric cultural-ecological model should be employed in cross-cultural research. He proposes such a model for the study of child rearing. This model is not unlike Bronfenbrenner's bioecological model, in that the specific interactions of children with adults in their immediate environment over extended periods of time are especially important in structuring child development and competencies. However, Ogbu's (1981) model differs from Bronfenbrenner's model (e.g., Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998; Ferguson et al. 2009) in its focus, as his model focuses on the nature of culturally specific child-rearing techniques and their relationship to culturally specified competencies, rather than on the interactions of an individual with various aspects of his or her environment. Thus, these two models serve different purposes in directing research on child development within its ecological context, whereby Bronfenbrenner's model is more general and therefore by nature less specific than is Ogbu's model. It is suggested here that various syntheses of these two models would be useful in considering the ecological context of infant and child development within a particular cultural group as a whole.

Similar to Ogbu (1981), Nsamenang and colleagues (e.g., Nsamenang 1992; Nsamenang and Dawes 1998) have argued for the development of non-ethnocentric theories and research programs to study infant and child development in its ecological context cross-culturally. Nsamenang (1992) remarks that the study of human behavior within the realm of scientific psychology evolved within the context of a Western worldview. Thus, Western worldviews are typically inherent in theories of development. Berry (e.g., 1971, 1974, 1984) has similarly argued that the ethnocentrism inherent in the discipline of scientific psychology has become more and more apparent as developmental researchers have attempted to generalize concepts and behaviors cross-culturally. Nsamenang consequently highlights the danger of "importing" Western models of development in the study of development in Third World contexts. This has too long and too often been the case (Nsamenang 1992, 2004; Nsamenang and Dawes 1998). In order to effectively study and thus improve the development of African children, therefore, it is essential that effective theories and methodologies based on non-ethnocentric ecocultural frameworks be developed (Dawes and Donald 2000; Louw et al. 2000; Nsamenang 1992, 2004; Nsamenang and Dawes 1998).

Nsamenang (1992) suggests that development be studied within an ecocultural conceptual framework outlined by Segall et al. (1990) and based largely on Berry's extensive cross-cultural research in Central Africa and elsewhere (see, e.g., Berry 1971, 1974, 1976, 1984; Berry et al. 1986; see also Berry 2001, 2004). This ecocultural framework includes background variables, process variables, and psychological outcome variables at both the population and individual level. Background variables include both the ecological and the sociopolitical context, which then influence biological adaptations and cultural adaptations. These adaptations then influence observable behaviors and inferred characteristics at the individual level via ecological influences, genetic transmission, cultural transmission, and acculturation. Thus, we see that this model is again a much broader generalization of human behavior as a whole than that proposed by Ogbu (1981). In fact, in considering the ecological context to be only one component of a much larger ecocultural framework, this model is also a broader generalization of human behavior than is the bioecological model proposed by Bronfenbrenner and colleagues (Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998).

Inherent in this ecocultural model is the belief that human behavior within a specific cultural context is powerfully influenced by the dominant worldview, a point emphasized by Erny (1968/1973). It is thus essential, in studying the development of African children, that we consider the conditions under which the African child lives, and specifically the nature of the child's immediate environment in terms of both physical and psychosocial settings (Erny 1968/1973; Dawes and Donald 2000; Louw et al. 2000; Nsamenang 1992, 2004; Nsamenang and Dawes 1998). In his seminal text, "Human Development in Cultural Context: A Third World Perspective," Nsamenang (1992) characterizes both broad features of Third World ecocultural contexts and more specific features of children growing up in West Africa, specifically Cameroon. In so doing, he provides a model for the intensive study of specific developmental ecologies in the Third World.

Other contemporary African researchers (e.g., Dawes and Donald 2000; Nsamenang and Dawes 1998; Kambalametore et al. 2000) have similarly highlighted the importance of understanding the ecological contexts in which children live in some detail in order to better understand development and competency. This is essential in both designing and implementing intervention programs to improve children's development that are culturally appropriate and therefore effective (Dawes and Donald 2000; Louw et al. 2000).

4.2.3 Li's Cross-Level Dynamic Biocultural Coconstructivist Paradigm

Most recently, Boivin and Giordani (2009) have argued for the application of Li's (2003) biocultural coconstructivist paradigm to the study of the neuropsychological development of African children. Within this paradigm, as in Bronfenbrenner's bio-ecological approach, Li (2003) emphasizes the interaction between the individual and his or her surrounding cultural milieu across multiple time periods (microgenesis, life span ontogeny, and human phylogeny). In doing so, Li draws from both the life span approach (e.g., Baltes et al. 1999), which emphasizes ongoing biocultural influences throughout life, and sociocultural contextual approaches (e.g., Cole 1999), which, as discussed above, emphasize the cultural embeddedness of all human activity and learning. Further, in focusing on dynamic, microgenetic interactions, Li (2003) builds on dynamic systems approaches to development, which emphasize moment-to-moment interactions between the organism and its environment (e.g., Smith and Thelen 1993). Inherent in these approaches is the active role of the organism in its own development; for example, the interaction of the infant with his or her environment, as a result of sensory-motor activity, strongly influences his or her cognitive development (see Smith 2005, for a review). This focus is similar to the emphasis on proximal processes by Bronfenbrenner and colleagues (e.g., Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998). Unlike Bronfenbrenner, however, Li (2003) focuses less on the specific influences of different levels of the ecological context, emphasizes the influences of the social over the physical environment, and further specifies the important contributions of the individual's biology in terms of genetic and neuronal plasticity. In doing so, Li draws on Gottlieb's probabilistic epigenetic approach (e.g., Gottlieb 1998, 2007), which argues that bidirectional influences within and between four levels of analysis, namely, genetic activity, neural activity, behavior, and the surrounding environment, drive development.

4.2.4 An Integrated Bioecocultural Approach to the Development of Institutionalized Children

With his coconstructivist approach, Li (2003) argues that individual development across the life span occurs through moment-to-moment microgenetic events that occur within both what he calls the proximal developmental context, which involves culturally embedded interactions, and the distal phylogenetic context, which involves culture-gene coevolution. Cole and colleagues (e.g., Cole 1996) have similarly identified cultural practices to be proximal units of children's experience. In fact, cross-cultural researchers have long emphasized the importance of understanding development within its cultural context (Cole 1996, 1999; Cole and Bruner 1971; Cole et al. 1971; Cole and Scribner 1974; Munroe and Munroe 1975;

Nsamenang 1992; Nsamenang and Dawes 1998; Ogbu 1981; Segall et al. 1990; Super and Harkness 1986, 1997). Nsamenang (1992), though, extends this approach by outlining an ecocultural framework that considers both individual and community interactions and outcomes. In addition, within this framework Nsamenang (1992) emphasizes the importance of considering cultural and environmental influences at multiple levels. Bronfenbrenner and colleagues (e.g., Bronfenbrenner and Evans 2000; Bronfenbrenner and Morris 1998; Ferguson et al. 2009) provide a detailed bioecological model that specifically breaks down the bidirectional influences of these cultural and environmental factors as they interact with the developing person. Thus, for Bronfenbrenner and colleagues, proximal processes are just one level of environmental influence, within the immediate context of the developing organism. As already mentioned, this approach fits nicely with Super and Harkness' (1986, 1997) concept of a "developmental niche," which clearly describes a child's position within his or her proximal environment.

In considering these related bioecological, ecocultural, and biocultural coconstructivist approaches, it is clear that we must understand the cultural context within which development and care take place if we are to effectively assess infant developmental functioning within institutional contexts. It is also important that we are able to evaluate interactions between the individual and physical and social environmental influences at multiple levels. Further, we need to understand prenatal, neonatal, and ongoing biological influences and interactions with the child's context before and after infant home entry. Finally, we need to understand current goals for the child within the infant home, as well as future goals for the child once he or she leaves the institutional setting. In so doing, we must recognize that institutional and individual caregivers' goals for the child may differ from each other and from those of the child's future caregivers following reintegration within the extended family network. Such differences may well lead to different expectations in terms of children's developmental functioning across multiple domains, including adaptive behavior, health, nutrition, and motor, cognitive, language, and socioemotional development.

Within each developmental domain, different aspects of development may be considered to be competent in African contexts compared to Western contexts (see, e.g., Nsamenang 1992, 2004, 2005, 2006; Ogbu 1981). For example, while Western conceptions of intelligence focus on concepts such as reasoning, communication, and physical coordination, many African communities consider such characteristics as social responsibility, generosity, cooperation, and obedience to be equally, and perhaps more, important aspects of intellectual development (Kambalametore et al. 2000; Nsamenang 1992). It is thus important to compare the developmental functioning of the institutionalized Malawian children assessed in the present study to non-institutionalized children living in similar cultural contexts, either in Malawi or in southern Africa.

Partly related to different caregiver expectations, African and Western children may also differ in their levels of competency in different domains. In fact, as early as the 1950s and 1960s, comprehensive naturalistic studies were conducted in various community settings in African and other non-Western contexts, with the goal of explaining observed variations in child developmental outcomes across different cultural-ecological contexts (e.g., Caudill and Weinstein 1969; Cole 1996; LeVine 1970; LeVine et al. 1994; Thomas et al. 1963; Whiting and Child 1953; Whiting and Whiting 1973). African researchers and other researchers in African (and Malawian) contexts have argued for the importance of considering caregivers' values and expectations of their children in assessing competence, because particular competencies may be seen differently in different cultures and contexts (Kambalametore et al. 2000; LeVine et al. 1994; Liddell 2002; Nsamenang 1992, 2004, 2006; Nsamenang and Dawes 1998; Ogbu 1981; Okumu 1999; Sawadogo 1995). However, the rapidly changing nature of contemporary African (and Malawian) culture, whereby contemporary African cultures are including some ideas from both traditional African and Western cultures and belief systems, makes it difficult to evaluate the expectations of contemporary African (and Malawian) caregivers (Nsamenang 1992, 2004; Okumu 1999). Contemporary African urban contexts are especially complex (Nsamenang 1992, 2004; Okumu 1999). Thus, there are no simple solutions in evaluating child cognitive development in African contexts (Nsamenang 2004). Nevertheless, it is important to compare the development of the institutionalized Malawian children assessed in the present study to non-institutionalized African children currently living in as similar contexts as possible.

Finally, it is important to consider current conditions in Malawi in assessing the development of Malawian children, because changing conditions may well influence children's developmental goals as well as their development in different domains (see, e.g., Nsamenang 2004). For example, with the spread of HIV/AIDS and the growing orphan problem, which has already been discussed in some detail, many more Malawian children are today suffering from their caregivers' inability to provide adequate nutrition and health care (see, e.g., Malawi National Statistical Office 2005; Maleta et al. 2003; UNICEF 2006). Respiratory diseases, such as pneumonia, as well as malaria, tuberculosis, and HIV/AIDS, are commonly experienced by Malawian children, and almost 50 % of Malawian children under five have stunted growth (Malawi NSO and UNICEF 2007; Maleta et al. 2003; UNICEF 2006; World Health Organization 2007). It may therefore be especially important, given current conditions in Malawi, to focus on children's health and nutrition and the effects of these aspects of development on other developmental domains, including motor, cognitive, language, and socioemotional development (see also Boivin and Giordani 2009, for a similar argument regarding African children's neuropsychological functioning).

4.3 Assessing Infant Development in Institutional Contexts

4.3.1 Methods

In a preliminary pilot study to begin to understand the complexity of infants' developmental functioning within institutional settings in Malawi, Ferguson (2002, 2003) assessed the motor, cognitive, and behavioral functioning of 60 (30 male, 30 female) Malawian infants and toddlers (M = 17.40 months, SD = 8.94, range = 2–35 months) living in two major urban infant homes in the Southern Region of Malawi. Thirty (15 male, 15 female) infants from each infant home participated. Twelve children were aged 0–8 months, seven aged 9–12 months, 14 aged 13–18 months, 15 aged 19–24 months, and 12 aged 25–35 months. In addition, the children's primary caregivers, the matrons in charge of daily operations, and the directors of the infant homes provided some background and demographic information.

As far as was possible, measures that had been previously successfully adapted for cross-cultural research were selected. It should be remembered, however, that many of these measures were originally developed for use in North American populations. Thus, the specific sociocultural setting to which these measures was applied was considered in both adapting measures and interpreting findings (see, e.g., Holding et al. 2004; Nsamenang 1992; Reynolds 1983; Super and Harkness 1986).

Prior to testing, all measures were translated and back-translated into Chichewa and adapted for use in Malawi by experienced Chichewa-English bilingual translators. A data collection plan was then developed in conjunction with the directors and matrons of each infant home, so as to ensure minimal disruption of normal day-to-day operations. All study procedures were described to the director and matron of each infant home, as well as to each of the child's caregivers, prior to testing and assessment, and informed consent for each infant and each caregiver was obtained. Researchers then spent several days in each infant home, so as to accustom the children and caregivers to their presence. At this time, and throughout the data collection process, observations in the form of written notes and digital photographs were collected. Each child was observed for several hours in his or her natural environment, and the various practices of and procedures at each infant home were observed and discussed with the directors and with the deputy matrons or matrons/supervisors. In addition, all available demographic and background information was obtained on each child to be assessed, including infant home admission and medical records.

Following these preliminary observations, the motor, cognitive, and behavioral development of each infant were assessed using the Bayley Scales of Infant Development, 2nd edition (BSID-II; Bayley 1993). The BSID-II was administered in both English and Chichewa. In addition, for those children within the appropriate age range, one of their primary caregivers was asked to complete the Achenbach Child Behavior Checklist for ages 2–3 years (Achenbach 1992) in English or Chichewa (whichever was their preference).

4.3.1.1 BSID-II

The Bayley Scales were used to assess motor, cognitive, and behavioral development in the present study, because these scales are easy to administer in different contexts and have been used successfully in assessing infant cognitive development in both South African (e.g., Molteno et al. 1995; Richter and Grieve 1991) and Kenyan (e.g., LeVine et al. 1994) contexts. For example, Richter and Grieve (1991) demonstrated that South African infants' cognitive development, as measured using the Bayley Scales (Bayley 1969), was positively correlated with the quality of the home environment, independent of parental socioeconomic status. Similarly, LeVine et al. (1994) found that Gusii infants' cognitive scores on the Bayley Scales (Bayley 1969) were associated with maternal holding and physical care between the ages of 12 and 24 months.

The Bayley Scales are norm-referenced, standardized scales, developed from a representative sample of the US population, and all test items have been evaluated for racial and gender bias. Specific item sets are administered to each child depending on his or her chronological age. The BSID-II consists of three scales, two of which are administered directly to the child: the Psychomotor Scale and the Mental Scale. The Psychomotor Scale assesses fine and gross motor development. The Fine Motor subtest includes items assessing fine motor skills associated with prehension, perceptual-motor integration, and motor planning and speed. Thus, children's visual tracking, reaching, grasping, and object manipulation skills, as well as their functional hand skills and responses to tactile information, are measured. The Gross Motor subtest measures children's movement of the limbs and torso. Items include assessments of static positioning (sitting, standing), dynamic movement (walking, walking up and down stairs, running, hopping, jumping), balance, and motor planning. The Mental Scale assesses each child's current cognitive development, including sensorimotor development, exploration, manipulation, understanding of object relatedness, concept formation, receptive and expressive language, and memory. A separate Behavior Rating Scale assesses examiner and caregiver perceptions of the child's responses during these interactions, thus facilitating the interpretation of the two child interaction scales.

All scales on the BSID-II were translated and back-translated into Chichewa and the BSID-II was administered in both English and Chichewa. More specifically, children were given instructions in their first language (as identified by their primary caregiver on the Child MQ) and, if they did not understand these instructions, were also given them in their second language.

4.3.1.2 CBCL/2–3

The Achenbach Child Behavior Checklist for ages 2–3 years (CBCL/2–3; Achenbach 1992) is a 100-item parent-report measure of emotional and behavioral problems, specifically Total, Internalizing, and Externalizing problems, with the Internalizing subscore indicating problems that result in the child's discomfit but are not disruptive to others and the Externalizing subscore indicating problems that are disruptive to others. It is a common measure of behavioral disturbances for children aged 2–3 years and has been demonstrated to have good reliability and validity (Thomas and Guskin 2001). Additionally, the CBCL has been found to be a valid measure of the overall mental health of children in a number of different cultures, such as Dutch, American, French Canadian, Chilean, German, and French cultures (Hannesdottir and Einarsdottir 1995). In addition, Boivin et al. (2011) have recently used a revised version of the CBCL/2–3 described here in assessments of Malawian children with cerebral malaria.

The English version of the CBCL/2–3 was translated and back-translated into Chichewa as described for the BSID-II. Items 55 ("Plays with sex parts too much") and 75 ("Smears body material") on the original English version of the CBCL/2–3 were omitted from both the English and Chichewa translations used in the present study, because these items were deemed culturally inappropriate; it was expected that these two items would have caused offence and additionally would not have been completed accurately.

4.3.2 Results

4.3.2.1 Environmental Context

Interviews with infant home directors and matrons, as well as direct observations, indicated that both infant homes aimed to create an environment that provided the child with a smooth transition into his or her extended family once circumstances and resources allowed (Beard 2005; Ferguson 2002, 2003). Unlike traditional orphanages, these infant homes emphasized reconstructing a typical Malawian family and community environment. Three "primary caregivers" were assigned to each child, with each caregiver being responsible mainly for the care of four or five children of different ages. Other caregivers within each infant home also provided some care to each child. This social structure emphasized the notion that a child's upbringing is the responsibility of an entire community and not only that of the biological mother and father. This concept of collective child rearing exists in the cultural context of many traditional African cultures and is particularly prevalent in various cultural groups that exist in Malawi.

Although a detailed assessment of infants' health and nutrition was not conducted, interviews, observations, and examination of infants' medical records indicated that most infants entered both infant homes moderately to extremely malnourished. In addition, at least 20 % of infants and toddlers at each infant home had been diagnosed with HIV/AIDS, and many had suffered from tuberculosis and other respiratory tract infections. It was thus essential in the present study to evaluate infants' cognitive, motor, and behavioral development in light of these nutritional and health risks.

4.3.2.2 Cognitive, Motor, and Behavioral Development

Table 4.1 shows mean Mental Developmental Index (MDI), Psychomotor Developmental Index (PDI), Behavior Rating Scale (BRS) total score, and Internalizing and Externalizing T scores on the Achenbach Child Behavior Checklist for ages 2–3 years (CBCL/2–3).

Table 4.1 Overall mean and standard error scores for all subjects: MDI, PDI, BRS, and CBCL/2–3 Internalizing and Externalizing *T* scores

Measure	Number of participants	Mean	Standard error
PDI	60	92.20	2.52
MDI	60	95.92	1.83
BRS	60	78.73	2.81
CBCL. Internalizing	18	65.50	1.95
CBCL. Externalizing	18	55.61	1.51

PDI psychomotor developmental index, *MDI* mental developmental index, *BRS* behavior rating scale total score, *CBCL* Achenbach child behavior checklist for ages 2–3 years (Internalizing and Externalizing *T* scores)

Table 4.2 Comparison of the experimental distribution of psychomotor developmental index (PDI) classifications to a representative US distribution using Table 7.2 in the Bayley Scales of Infant Development, 2nd edition, Manual (Bayley 1993, p. 228)

Classification	Experimental number	Representative US number
Accelerated performance	8	8.88
Within normal limits	38	43.56
Mildly delayed performance	5	6.66
Significantly delayed performance	9	0.90
Total	60	60

Both the MDI and PDI sample means (95.92 and 92.20, respectively) were significantly different from the expected mean of 100 for a representative US sample, $t(59)=2.23$, $p=0.05$ and $t(59)=3.09$, $p=0.01$, respectively. However, it was difficult to assess whether these children's motor and cognitive development was less advanced than that of non-institutionalized Malawian children. Further, these averages fall within the normal range. However, a comparison of the qualitative distribution of children's motor development scores (classified as Accelerated Performance, Within Normal Limits, Mildly Delayed Performance, or Significantly Delayed Performance) to a representative US distribution (see Table 4.2) found that the sample distribution of PDI scores was significantly different from the normative distribution, $\chi^2(3, N=60)=74.13$, $p=0.01$, primarily because a higher percentage of the Malawian institutionalized infants was classified as showing Significantly Delayed Performance than would be typical of a representative US sample. The distribution of MDI scores was not, however, significantly different from a representative US distribution (see Table 4.3).

To compare BRS scores across participants of different ages to normative BRS scores, each participant's score was classified as Non Optimal, Questionable, or Within Normal Limits, based on his or her BRS score and age in months (see

Table 4.3 Comparison of the experimental distribution of mental developmental index (MDI) classifications to a representative US distribution using Table 7.2 in the Bayley Scales of Infant Development, 2nd edition, manual (Bayley 1993, p. 228)

Classification	Experimental number	Representative US number
Accelerated performance	6	8.88
Within normal limits	44	43.56
Mildly delayed performance	7	6.66
Significantly delayed performance	3	0.90
Total	60	60

Table 4.4 Comparison of the experimental distribution of total behavior rating scale (BRS) score classifications to a representative US distribution using Table B.1 in the Bayley Scales of Infant Development, 2nd edition, manual (Bayley 1993, pp. 322–323)

Classification	Experimental number	Representative US number
Non Optimal	0	6
Questionable	1	9
Within Normal Limits	59	45
Total	60	60

Table 4.4). The BRS sample distribution was significantly different from a representative US distribution, $\chi^2(2, N=60)=17.44$, $p=0.01$. In examining the raw scores and the subsequent classifications of the present sample, the BRS scores of the present sample appeared to be, in general, higher than would be expected from a representative US sample. Overall, in the present study, a higher percentage of infants were classified as Within Normal Limits, and smaller percentages were classified as Non Optimal or Questionable, in comparison with a representative US sample. However, owing to the nature of the BSID-II, the behavioral assessment component only assessed children's behavior during the testing situation (while evaluating children's cognitive and motor development), and contained very few items. Thus, it is difficult to evaluate Malawian institutionalized children's overall socioemotional development based on these data.

Toddlers' mean CBCL/2–3 Internalizing ($M=65.50$) and Externalizing T ($M=55.60$) scores both fell within the normal range, which is set at below the 98th percentile, at a T score of 70. One-sample t-tests, however, indicated that both the Internalizing T score and the Externalizing T score sample means were significantly different from the theoretical expected means of 50, $t(17)=7.95$, $p=0.01$ and $t(17)=3.71$, $p=0.01$, respectively. Additionally, the actual mean Internalizing and Externalizing T scores for the present sample appear to be higher (less optimal) than those expected from a representative US sample. However, due to the small sample size ($n=18$) and the lack of a comparative normative distribution, it was difficult to ascertain whether the mean participant scores were comparable with normative means.

Table 4.5 Intercorrelations between age, MDI, PDI, BRS, and CBCL/2–3 Internalizing and Externalizing *T* scores

	Age	PDI	MDI	BRS	CBCL. Int	CBCL. Ext
Age	/					
PDI	0.29*	/				
MDI	0.04	0.69**	/			
BRS	0.38**	0.46**	0.40**	/		
CBCL. Int	–0.15	–0.34	–0.34	–0.46	/	
CBCL. Ext	0.10	0.19	0.12	–0.18	0.45	/

PDI psychomotor developmental index, *MDI* mental developmental index, *BRS* behavior rating scale total score, *CBCL* Achenbach child behavior checklist for ages 2–3 years (Internalizing and Externalizing *T* scores). Higher MDI, PDI, and BRS scores are more optimal; higher CBCL/2–3 scores are less optimal

*$p<0.05$; **$p<0.01$

4.3.2.3 Associations Between Cognitive, Motor, and Behavioral Development

Not surprisingly, cognitive, motor, and behavioral scores on the BSID-II were significantly associated (see Table 4.5). Interestingly, both motor and behavioral scores were also associated with age, with older children receiving higher scores on both measures. Somewhat surprisingly, especially because CBCL/2–3 scores assess behavior, CBCL/2–3 scores were not significantly associated with any of the other scores, including BSID-II behavioral scores.

4.3.3 Discussion

In the present study, the BSID-II was successfully adapted to evaluate the cognitive and motor functioning of institutionalized Malawian infants, as evidenced by the expected correlation between cognitive and motor development scores. Overall, it appears that institutionalized Malawian infants' cognitive and motor development were slightly less optimal than representative US samples. However, mean scores for both assessments were within the normal range. It should also be noted that these mean differences largely resulted from a higher number of children receiving very low scores (Significantly Delayed Performance). In fact, the distribution of cognitive scores in the present study was not found to be significantly different from that of a representative US sample. In addition, it should be noted that motor development was positively associated with age. The facts that motor development scores in particular were lower than a representative US sample, that older children received higher scores on motor development than did younger children, and that many infants entered these infant homes moderately to severely malnourished suggest the need for a more detailed evaluation of infants' health and nutrition prior to infant home entry, as well as during the institutionalization period. Because older infants are likely to have been institutionalized for longer, and thus have had a longer time to recover from prior malnutrition, in evaluating the motor and cognitive development of infants within institutional settings, it is particularly important to consider the amount of time an infant has lived within the institution. This is especially important in comparing institutionalized Malawian infants' development with that of non-institutionalized Malawian infants because, given that many caregivers place their infants within institutional settings because they cannot afford to provide adequate nutrition, it is certainly plausible that the average institutionalized infant would be more malnourished upon infant home entry than the average non-institutionalized infant.

Unfortunately, the results of this study cannot be compared to those for non-institutionalized Malawian infants, because these data do not exist. Quite obviously, this is an important avenue for future research. The most recent related data available come from an assessment of the motor and cognitive development of 305 urban South African infants aged 2–30 months and the relationship between children's environmental quality and these outcomes (Richter and Grieve 1991). Children aged 2–17 months had an average score of 107.8 on the cognitive scale of the first edition of the Bayley Scales (Bayley 1969), while children aged 18–30 months had an average score of 101.9 (Richter and Grieve 1991). These average scores were slightly higher than the standard mean of 100 and were higher than the mean scores observed in the present study.

Interestingly, the institutionalized Malawian infants assessed in the present study had more optimal behavioral development, as assessed by the BSID-II, than a representative US sample. However, the CBCL/2–3 scores of the subset of toddlers assessed ($n = 18$) were less optimal. This could suggest increasing behavioral problems with age, but the findings also could relate to differences in parent/caregiver reports. Clearly, a more extensive evaluation of socioemotional and behavioral development is needed.

4.4 Future Directions

The results of the present pilot study are a necessary first step in evaluating the cognitive, motor, and behavioral development of institutionalized Malawian infants. However, further work is needed in order to fully understand the quality of the physical and psychosocial environment provided for these children, their developmental functioning, and the relationship between specific dimensions of environmental quality and particular developmental outcomes. Because the number of institutionalized infants in southern Africa continues to grow, this research is desperately needed.

Future research should begin by evaluating interactions between the individual and physical and social environmental influences at multiple levels. To do so, effective environmental assessment tools are currently being developed for this population (see, e.g., Ferguson 2008, 2010; Ferguson and MacAllister 2008). Further, understanding prenatal, neonatal, and ongoing biological influences and interactions with the child's context before and after infant home entry is needed. One first step in doing so will involve evaluating infants' health and nutrition before infant home entry, at infant home entry, and over a period of months following infant home entry. Infants' cognitive, motor, and socioemotional development should then be evaluated in light of both past and present health and nutrition.

More detailed and culturally relevant assessments of infants' language development and socioemotional development are also sorely needed. This is particularly important because, in the present study, in looking at individual language items on the Mental Scale, children's language development appeared to be especially delayed (Ferguson 2002, 2003). However, the fact that these infants were bilingual must be taken into account. In addition, it was clear in the present study that evaluations of infants' behavioral development were somewhat inadequate.

Language development and assessment are comprehensively reviewed in another chapter in this volume, but a brief mention will be made of assessments of infants' language development that have been developed or are in the process of being developed, within the last several years. First, a revised version of the Bayley Scales, the BSID-III (Bayley 2006), now includes a separate Language Scale (comprised of the Receptive Communication and Expressive Communication subtests). This scale includes items from the BSID-II (Bayley 1993) Mental Scale that were identified as measuring primarily language skills. In addition, some additional items of the BSID-III were adapted from the Preschool Language Scale—Fourth Edition (PLS-4, Zimmerman et al. 2002). These items were added in order to provide greater content coverage of general language development. Similarly, the Language Scale of the Malawi Developmental Assessment Tool (MDAT; Gladstone et al. 2010), which includes many similar items to those included in the BSID-III, may prove useful and has the advantage that it has been specifically developed for use in Malawian (albeit rural) contexts. However, both of these assessments are somewhat limited in scope (in particular, the MDAT includes only a few items for infants, because it has been developed for use with a wider age range of children) and have been developed to assess monolingual infants and children. Therefore, the inclusion of other assessments, including the Child Multilingual Questionnaire (MQ; Virtual Linguistics Lab, Lust, 2005 Personal Communication), which assesses children's home and language environments, as well as children's productive (expressive) and receptive language, may be warranted. In addition, to better evaluate infants' receptive and expressive vocabularies, the MacArthur–Bates Communicative Development Inventories (short forms) for infants and toddlers in English (CDI/Infant Short Form and CDI/Toddler Short Form—Form A, Fenson et al. 2000) as well as adapted versions in Chichewa (see, e.g., Ferguson et al. 2005) may prove useful. The MacArthur–Bates CDIs are widely used parental report scales designed to yield information on children's overall language development. In addition, the scales have been successfully adapted for use in a number of different languages, including Chichewa (Ferguson et al. 2005; Moreno-Vega 2004). The Infant and Toddler versions in Chichewa (CDI/Infant and CDI/Toddler) have undergone extensive development, and some pilot data assessing both institutionalized and non-institutionalized urban Malawian infants and toddlers have been collected on earlier versions of both forms (Ferguson et al. 2005).

In evaluating infants' socioemotional functioning, again the BSID-III may prove useful, because this newer version includes the Social-Emotional Scale, a parental questionnaire adapted from the Greenspan Social-Emotional Growth Chart: A Screening Questionnaire for Infants and Young Children (Greenspan 2004). This scale assesses young children's acquisition of social and emotional milestones. Items include assessments of children's self-regulation and interest in objects and people around them, their ability to engage others and establish relationships, their use of emotions in an interactive and purposeful manner, and their use of emotional signals and/or gestures. However, this scale has been developed for use in Western contexts. Thus, the Social Scale of the MDAT may also prove useful, because this scale has been developed for use with rural Malawian populations. Given that, as already noted, the MDAT includes only a small number of items for infants, the development of additional assessments of infants' socioemotional functioning within Malawian institutional and urban contexts will be important (see Kambalametore et al. 2000, for some related work in this area).

Finally, in effectively evaluating institutionalized Malawian infants' environments and current developmental functioning, we need to understand current goals for the child within the infant home as well as future goals for the child once he or she leaves the institutional setting. As has been mentioned above, institutional and individual caregivers' goals for the child may differ from each other and from those of the child's future caregivers following reintegration within the extended family network. Such differences may well lead to different expectations in terms of children's developmental functioning across multiple domains, including adaptive behavior, health, nutrition, and motor, cognitive, language, and socioemotional development.

4.5 Conclusions

In the present study, the overall developmental functioning of 2- to 35-month-old infants and toddlers living in the two major urban infant homes in the Southern Region of Malawi was evaluated and compared to that of other institutionalized and non-institutionalized children. This is the first study to assess the developmental functioning of orphaned children in Malawian infant homes, which are becoming more common with the rising number of orphans in Malawi resulting from the HIV/AIDS pandemic. This research therefore provides a foundation upon which future work assessing the overall development of orphaned children in southern Africa can be built.

Consistent with findings from previous studies of African and non-African institutionalized children, the institutionalized Malawian children assessed in the present study showed delays in motor and cognitive development. They also had more optimal behavioral development than a representative US sample. However, without any comparative development data from a non-institutionalized Malawian population, which is not yet available, it was difficult to evaluate whether the institutionalized Malawian children presented with delayed motor and cognitive development in comparison with their non-institutionalized Malawian counterparts.

In conclusion, this research suggests that the introduction of specific interventions to improve the developmental functioning of young institutionalized children in Malawi may well be needed, especially in the domains of motor and cognitive development. However, a more extensive evaluation of institutionalized Malawian infants' developmental functioning and of the relationship between their developmental functioning and the quality of the physical and social environment of these institutions is sorely needed. Given the increasing number of orphaned infants being placed in institutions because their extended families are unable to provide for their basic nutritional needs, this research is essential in ensuring the best possible development for young Malawian children.

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Chapter 5
Factors Contributing to the Psychosocial Adjustment of Ugandan Preschool Children with HIV/AIDS

Rachelle A. Busman, Connie Page, Evelyn Oka, Bruno Giordani, and Michael J. Boivin

5.1 Impact of HIV/AIDS on the Children of Sub-Saharan Africa: Developmental Implications

In Uganda, about one million children are orphans with one or both parents dead due to HIV/AIDS. In fact, a new child is orphaned every 14 s in Uganda (Ronald and Sande 2005). The number of children who are themselves infected with HIV is 110,000, most likely through mother-to-child transmission (MTCT) (UNICEF 2008). HIV/AIDS infection has many different developmental implications.

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The impact of HIV/AIDS on cognitive development and psychosocial development will be addressed. Other dynamic contextual factors will also be considered in the development of preschool children with HIV/AIDS.

5.1.1 Cognitive Development

Children with HIV are at increased risk for developmental disabilities (Speigel and Bonwit 2002). This is especially true for children infected via mother-to-child transmission (MTCT), given that their central nervous systems are not fully developed when they contract the virus. Depending on the severity and progression of the central nervous system involvement, children with HIV may present with impairments that are diffuse and pervasive or impairments that are specific in nature (Armstrong et al. 1993; Knight et al. 2000). Therefore, when assessing the cognitive functioning of children with HIV, it is imperative to examine both global (e.g., intelligence quotient) and specific (e.g., processing speed, visual-spatial) domains of functioning.

In terms of language development, children with HIV tend to have difficulty with expressive language, although problems with both expressive and receptive language abilities may be present (Woodrich et al. 1999). Affected children may have decreased spontaneous and responsive vocalizations (Wachsler-Felder and Golden 2002). More generalized language impairments center on limited verbal, emotional, and motor expression. In general, pediatric HIV compromises the acquisition of language and development of language milestones. In school this may translate into the need for speech and language therapy in order to participate in and benefit from the educational setting (Papola et al. 1994). Further investigation is needed, however, to identify consistent language impairments that should be the target of early intervention.

Research on the cognitive functioning and academic achievement of young children with vertically transmitted HIV has produced inconsistent results. Some studies report that by school age, IQ scores of children with HIV are in the low-average range compared to uninfected peers who generally are within the average range (Speigel and Bonwit 2002). Papola et al. (1994) found that over half of the school-age children with HIV/AIDS that they tested were in the borderline cognitively impaired range of intelligence. Furthermore, children with HIV experiencing neurological impairment and associated cognitive delays are believed to experience continued neurological deterioration into adolescence. Ongoing cognitive deterioration has been shown in children with HIV/AIDS who have lost previously attained motor milestones (Landau and Pryor 1995).

To illustrate, Smith and colleagues (2006) collected data from 569 children between 3 and 7 years of age with HIV infections across several diverse demographic locations, including sites within Massachusetts, New York, Texas, Puerto Rico, and Illinois. These researchers reported that young children with HIV scored lower than controls on all domains of cognitive development. This was only true, however, if the children had also exhibited an AIDS-defining illness. These data suggest that children may only be at increased risk for poor cognitive outcomes if they have also had a severe illness associated with advanced stages of AIDS (Smith et al. 2006). By medically treating and preventing rapid disease progression for children with vertically transmitted HIV, the development of cognitive deficits may be significantly attenuated.

There is still much to be learned about children with HIV who survive into school age without severe cognitive complications. It is important to understand cognitive functioning because of its association with quality of life and ultimately survival. In fact, cognitive impairment can substantially affect survival, with about a threefold increased risk of death among children who are cognitively impaired (Zickler 2009).

5.1.2 Cross-Cultural Consistency

Some cross-cultural studies already have been conducted to understand the contextual impact of HIV on cognitive development. These studies provide important information on the cross-cultural consistency of neurocognitive development of individuals with HIV/AIDS. Similar impairments in abstraction/executive function, information processing speed, and learning have been reported in China and the United States (Cysique et al. 2007). In other studies including Nigerians with HIV infection, the patients exhibited a wide variety of neurological manifestations including cognitive impairment, peripheral neuropathy, and lower motor neuron facial palsy (Imam 2007).

Boivin and Giordani (2009) provide evidence for similar patterns of deficits in attention, working memory, and learning across cultures (African and American children) in children exposed to cerebral malaria and sickle-cell disease. Cross-cultural studies have also shown similar differences in brain development depending on caregiving characteristics such as age, relationship to the child, or mental health. Boivin and Giordani (2009) argue that these findings, suggesting some consistency in certain aspects of cognitive neurodevelopment in the face of chronic illness across different cultures, are consistent with Li's (2003) co-constructivist framework and that such research is evidence for a universal brain/behavior omnibus that drives plasticity across the life span.

5.1.3 Impact of Environment on Cognitive Development

The presence of the disease, alone, may not automatically lead to negative cognitive outcomes. Other environmental factors play a role in the expressed cognitive ability of children with HIV/AIDS. Hochhauser and colleagues (2008) tested the hypothesis that children in conditions of high environmental risk would be at greater risk for the cognitive complications related to immunosuppression. They found that children in highly stressful environments are at particular risk for HIV-associated cognitive decline. Highly stressful environments are thought to negatively impact adherence to medication, and conversely, environments with reduced stress may provide some degree of neuroprotection (Hochhauser et al. 2008). Thus, it is imperative to examine the cognitive abilities of young children with HIV with careful consideration of the context in which they live. Furthermore, identifying potentially modifiable environmental factors that play a role in cognitive development provides a logical avenue for intervention.

5.1.4 Psychosocial Development

Psychosocial adjustment is a multifaceted construct that refers to the mental health, or "a state of successful performance of mental function, resulting in productive activities, fulfilling relationships with other people, and the ability to adapt to change and to cope with adversity…" (U.S. Department of Health and Human Services 1999, p. 4). Children with HIV face many psychosocial consequences that are often exacerbated by frequent hospitalizations, poor social support, and lowered school performance. Some of the challenges faced by children with HIV include the loss of cognitive abilities, physical impairments, social stigma leading to rejection and isolation, and the fear of death (Landau and Pryor 1995). Psychosocial adjustment and cognitive impairment also may interact, themselves, in the adjustment of children with HIV. Carter et al. (2003) found that adults with HIV/AIDS who exhibited depression and medical symptoms also presented with increased cognitive complaints. Children with HIV/AIDS may exhibit this same relationship between depressive symptoms and cognitive deficits, although this has not yet specifically been studied.

HIV/AIDS infection carries a significant social stigma that evokes fear and discrimination towards children with the disease. In Uganda where there has been an open HIV/AIDS awareness policy for over 20 years, the stigma is still high (Bateganya et al. 2008). Children and families must also deal with issues centering on disclosure of the medical condition, which can further perpetuate discrimination secondary to the disease (Wiener et al. 2000).

The cognitive, physical, and social effects of HIV can contribute to infected children experiencing more subjective distress than uninfected children. This distress has been associated with resulting dysphoria, hopelessness, preoccupation with the illness, and poor body image (Brown et al. 2000). Affected children are prone to more anxiety and depression than uninfected children, and their parents also report increased conduct and hyperactivity problems. Children with HIV also have been found to suffer from disruption in attention and concentration, and severe social withdrawal (Armstrong et al. 1993).

In one study looking at the service needs of school-age children with HIV within the Bronx, 42 % of children were found to exhibit formal psychiatric diagnoses that included mood disorders (depression and anxiety), attention deficit hyperactivity disorder, and adjustment disorder (Papola et al. 1994). The authors of this study also found that as children grew older, they tended to exhibit more problematic emotions and behaviors (Papola et al. 1994). However, these findings are not consistent throughout the literature, with many of the discrepancies explained by differences in the population being studied. For example, one study conducted within the United States reported that among children with HIV, behavior problems decreased as the child aged (Franklin et al. 2007). Another study conducted within the United States concluded that there were no differences between the HIV and control groups with the exception of internalizing behavior problems that were actually exhibited by the control group (Bachanas et al. 2001). Within this study the variables that did make a difference when considering the psychosocial well-being of children with HIV/AIDS were stress, age, and coping strategies employed.

Similarly, Mellins and colleagues (2003) in their study of 307 children with vertically transmitted HIV did not find a link between HIV status and behavior problems, though biological and environmental factors were important in predicting behavioral problems (Mellins et al. 2003). This finding highlights the need to consider behavior of children with HIV within the geographical context.

As evidence of the emotional impact of HIV on the Ugandan child, a study of Ugandan AIDS orphans in a rural district had higher levels of anxiety, depression, and anger than their non-orphan counterparts. Symptoms exhibited by the AIDS orphans that were indicative of clinical depressive disorder included vegetative symptoms, feelings of hopelessness, and suicidal ideation (Atwine et al. 2005).

5.1.4.1 Psychosocial Adjustment and Caregiving Context

There is evidence to suggest that children infected with HIV who are living with a caregiver other than their biological mother demonstrate elevated internalizing behavior problems, presumably because of the mother's illness/death (Bachanas et al. 2001). In fact, researchers who failed to show internalizing behavior concerns or somatic complaints when using the CBCL as a measure of psychosocial well-being of children with HIV/AIDS speculated that this could be due to the fact that the children in their study were all cared for by their biological parents (Franklin et al. 2007). In other words none of the sample had lost their primary caregiver to the disease as is common in other resource-poor regions such as Uganda.

In a study conducted by Pelton and Forehand (2005) of 105 African American children from New Orleans 6–11 years of age, the behavior of children whose parents were living with HIV was contrasted to the behavior of children whose parents had died of AIDS. Relative to children who were still living with their biological parents, those who were orphaned exhibited significantly more internalizing and externalizing problems (Pelton and Forehand 2005).

Many children with HIV within the African context live with caregivers other than their parents. Within Uganda it is not uncommon for households to be headed by grandparents who have traditionally been the recipients of financial support from their adult children (Nyesigomwe 2006). Though these alternative caregivers largely value their role in child rearing, they may not understand the importance of continued stringent medical care for the HIV-infected children they are looking after (Jones et al. 2005) or may be unable to meet their emotional, educational, nutritional, or medical needs because of advanced age and frail condition (Nyesigomwe 2006).

Caregiving takes place within a social context, and thus, it cannot be appropriately studied without attention paid to the conditions of poverty that may compromise child outcomes (Dawes et al. 2007). The death of parents with HIV/AIDS and the subsequent taking-in of their children, often by grandparents, have exacerbated household poverty (Hodge 2008). In South Africa, where the HIV/AIDS epidemic has been an ongoing struggle, caregiving has been recognized as a significant determining factor in psychosocial adjustment. If children receive quality care, they are more likely to exhibit social and behavioral adjustment, as well as intellectual achievement (Richter et al. 2004).

No matter who the primary caregiver of the child is, he/she has a role in the development and proper adjustment exhibited by the child. For example, psychological distress exhibited by the caregiver has a negative impact on the adjustment of the child, with the child exhibiting more internalizing behavior problems (Bachanas et al. 2001). Continued examination of the impact of the caregiver on the psychosocial resiliency of children living with HIV/AIDS is paramount.

5.1.4.2 Socioeconomic Status

One of the contextual variables that can have a large impact on the psychosocial well-being of children is socioeconomic status (SES). The measure is used to understand how people within a community compare in terms of monetary income, the ability to meet the basic needs of the family members, and the level of education. Measures of SES have been shown to account for differences in performance, health, and overall well-being across illnesses.

Poverty has been established as a risk factor, associated with negative child outcomes especially for children under the age of 5 years and those in extreme and enduring poverty (Owens and Shaw 2003). Poverty also has been identified as one of the barriers preventing mothers from following through with care for their HIV-exposed infants in South Africa (Jones et al. 2005) and has been found to impact adherence to daily drug regimens among HIV-infected children in Uganda (Bikaako-Kajura et al. 2006). Nongovernmental organizations (NGOs) in Uganda have put substantial effort into helping families improve their economic situation in the hopes that it will lead to benefits in other aspects of life. For example, loans are given to families to start farms and other businesses that can then sustain an improved quality of life. Although the benefits seem to be apparent, it is not clear what impact family SES has on the psychosocial adjustment and subsequent quality of life of a child living with HIV/AIDS. Thus, it is important to understand the SES differences within the population and how it impacts the psychosocial adjustment of children with HIV/AIDS.

5.1.4.3 Psychosocial Adjustment and Child Variables

Bachanas et al. (2001) collected measures of psychological adjustment through caregiver report and child self-report of school-age children infected with HIV. The researchers found that age was a significant predictor of the children's self-reported psychological adjustment. Younger children were shown to exhibit poorer psychological adjustment, but even when the data were analyzed without the youngest children (6 and 7 years of age), age was still significantly correlated with scores of psychological adjustment (Bachanas et al. 2001).

Another study focusing on caregiver reports of maladjustment found that aggressive behaviors of children with vertically transmitted HIV significantly decreased as the children grew older (Franklin et al. 2007). Age may be a reflection of adjustment to the diagnosis of HIV, caregiver adjustment over time, adjustment to the earlier death of a parent, or entry into school (Franklin et al. 2007).

Another hypothesis for differences in psychosocial adjustment based on increasing age is the concomitant increase in the sophistication of cognitive skills with age that may improve a child's ability to cope with HIV-associated stressors. As the child ages and develops more sophisticated cognitive abilities, he/she is able to employ more sophisticated forms of coping (Engel and Melamed 2002). For example, older children are better able to manage their emotions using cognitive mediational control (Wertlieb et al. 1987), because they are felt to be more aware and able to label internal emotional states than can younger children. Younger children may not understand that they can regulate their emotions and are unable to see this process modeled by others because of the internal nature of emotional regulation (Compas et al. 1991). The role that increased age plays in terms of increased psychosocial adjustment, however, has yet to be clarified in resource-poor settings such as sub-Saharan Africa.

There is limited research investigating the potential impact of gender on quality of life for individuals living with HIV/AIDS in resource-poor African settings. Most of the research to date has been conducted in adults, with men reporting more positive feelings about their future than women (Chandra et al. 2009). To illustrate, men also are more likely to report feeling content and having positive experiences as compared to women (Chandra et al. 2009).

Women living with HIV also have been found to be more vulnerable to depressive symptomatology (Cook et al. 2002), show more patterns of sleep impairment, and have greater symptoms of anxiety (Junqueira et al. 2008) than men. In a large-scale study based in the United States, differences in health-related quality-of-life (QoL) scores were collected for men and women, throughout the course of HIV/AIDS treatment. Women reported lower health-related QoL scores than men in all domains, except social functioning at baseline. At 40 weeks of treatment, women still had lower scores in all QoL domains except overall health (Mrus et al. 2005). However, both men and women showed equivocal improvements in QoL over the entire course of treatment.

Although it appears that men are able to adapt to the disease more readily than women, some studies have identified strengths that women demonstrate over men when coping with HIV/AIDS. For example, women have been reported to show more strength in social functioning (Mrus et al. 2005) and score significantly higher than males on scales measuring domains of forgiveness, spirituality/religion, and personal beliefs (Chandra et al. 2009).

5.2 Theoretical Framework: Stress and Coping Model for Predicting Psychological Adjustment in HIV-Infected Children

In order to better understand the relationship between factors that may contribute to the psychological adjustment of children with HIV, Bachanas and colleagues (2001) developed a model of stress and coping. This model is used in this chapter to organize the ecological factors that are thought to contribute to the well-being of the child with HIV. The model also fits into the cross-level biocultural coconstructive framework described by Li (2003) to understand development.

In his framework Li argues that development is a dynamic process that is influenced by culture throughout the life span (life-span ontogeny) and through evolution (human phylogeny). Similarly, Bachanas et al. (2001) describe the psychosocial adjustment of children with HIV/AIDS by focusing on key health, and demographic parameters, as well as caregiver and child characteristics. This model by Bachanas and colleagues is also the organizing framework in the following chapter in this volume, which focuses on psychosocial adjustment of school-age rural Ugandan children with HIV.

Demographic parameters are important to consider throughout child development. Children are constantly interacting with the environment in which they are raised, and thus, development is impacted by the dynamic interactions experienced within that environment (Masten 2006). Some of the demographic information that may play a role in the child's development include the child's age, gender, weight for age, and family socioeconomic status. As noted earlier, research has shown that age and gender of the child can determine expectations for behaviors and day-to-day interactions. Living with HIV/AIDS may have very different effects on children of different ages and genders.

For example, studies conducted in resource-limited settings have found a significant association between weight for age and psychomotor functioning (Abubakar et al. 2008b). Weight for age also mediates the relationship between socioeconomic status and developmental outcome (Abubakar et al. 2008b). Furthermore, Abubakar and colleagues (2009) found that weight for age was an easily measurable benchmark in developmental monitoring for providing appropriate intervention. The family's socioeconomic status and ability to meet the needs of the child as well as all of the family members also may impact psychosocial adjustment.

Children in advanced stages of HIV/AIDS are thought to be at the greatest risk for negative developmental outcomes. Health parameters are specified as the degree to which the disease has progressed within the child and reflect the potential for symptoms and medical complications. Researchers have found that the most informative measures of disease progression are CD4 cell counts and viral load, as they are the best predictors of mortality (Rouet et al. 2003).

Within the stress and coping model, caregiver characteristics are also considered important in understanding the psychosocial development of children with HIV. In their model of stress and coping, Bachanas and colleagues (2001) focus on the adaptation process of the caregiver. Specifically, they consider the stress level of the caregiver, the coping strategies that are used, and the overall family functioning. These factors are thought to be important because children are continually interacting with their caregivers and families, and thus, the caregiver can impact the child's development (Masten 2006). There is a reciprocal relationship between the child and caregiver in which the child can influence the caregiver and is also influenced by the reactive behavior of the caregiver. Caregiver characteristics (e.g., anxiety, depression, and quality of interactions) all play a role in the psychosocial adjustment of the young child.

Child characteristics or personal qualities (e.g., cognitive ability, motor development) are also important within the stress and coping model. Conceptualized from the developmental psychopathology literature, the child is an active part of his or her own development. According to the core "agency" principal, there is a relationship between the brain development and the independence exhibited by the child (Masten 2006). One can use neuropsychological assessment to investigate this process, in that it gauges a child's ability to think and learn while navigating and functioning within the physical and social environment.

Motor development also has been found to be an important part of this navigational and functional process and is often delayed in children with HIV in sub-Saharan Africa (Abubakar et al. 2008a). The impact of motor development delay can subsequently impair other neuropsychological domains of child functioning in African children with HIV (Abubakar et al. 2008a).

All of the factors discussed above can be considered integral parts of the coping and stress model and consistent with Li (2003) co-constructivist framework. This is because this paradigmatic framework emphasizes the dynamic roles of the child, the caregiver, and the overall environment in contributing to the psychosocial well-being of children with HIV/AIDS.

5.3 Analyzing the Stress and Coping Model of Psychosocial Well-Being in HIV Children

The model for stress and coping developed by Bachanas and colleagues (2001) was used to guide the collection of data and develop research questions for a model study of the psychosocial functioning of preschool-age children with HIV in a Ugandan rural setting. A model of this approach and the measures used is presented in Fig. 5.1. In order to understand the factors related to the psychosocial well-being

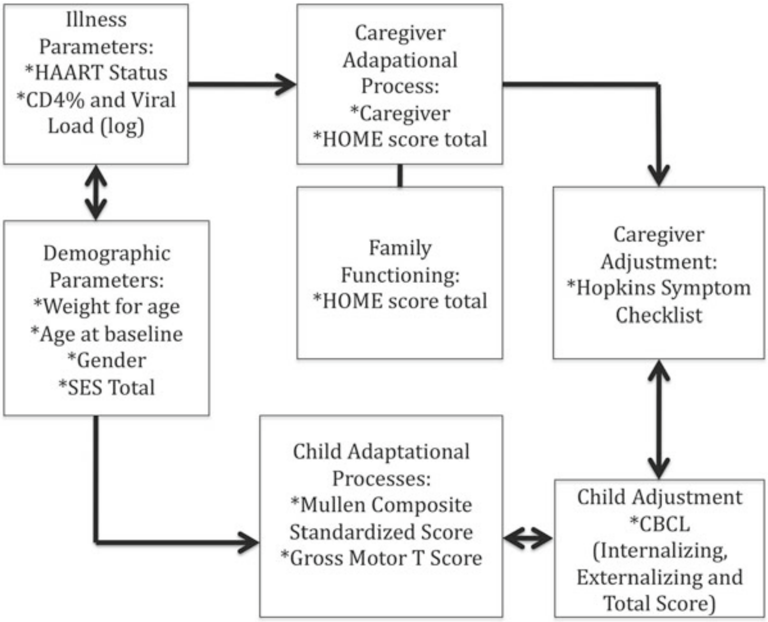

Fig. 5.1 Summary model of child adjustment. The strongest relationships exist on the left-hand side of the figure between caregiver emotional well-being (HSCL measures of depression/anxiety) and child psychosocial adjustment (CBCL global scales). HOME caregiving quality scores are related to caregiver depression/anxiety. The child's psychosocial adjustment is related to the overall cognitive ability of the child as measured by the Mullen composite score. HIV illness parameters as indicated by HAART treatment status and weight-for-age physical growth are predictive both of HOME quality provided by the caregiver and of the child's overall cognitive ability and development

of preschool children in Uganda with HIV/AIDS, following research questions were addressed:

1. What health and demographic factors are important to the caregiving environment?
2. What health and demographic factors are important to the cognitive development of young children with HIV/AIDS in Uganda?
3. What health and demographic factors are related to caregiver adjustment (depression and anxiety)?
4. Which variables (home environment, cognitive development, caregiver adjustment) are important to the psychosocial outcomes (internalizing, externalizing, and total behavior problems) of young Ugandan children with HIV/AIDS?

This study considers many mediating factors, including health variables, demographic variables, home environment variables, caregiver variables, and child factors within a single model. The relationship between these variables is organized using Bachanas and colleagues' 2001 model of stress and coping, which fits with the cross-level dynamic biocultural co-constructivist paradigm discussed by Li (2003).

5.3.1 Methods

Baseline data from a longitudinal study of the effectiveness of a caregiver training of HIV-infected mothers in a rural Ugandan setting is used to provide a snapshot of the psychosocial well-being of preschool-age Ugandan children. In Uganda it is mandatory for pregnant women receiving care through a Ministry of Health facility to be tested for HIV/AIDS. Children were included in the study if they were between 1 and 5 years of age and not yet attending school. Their parent gave written consent to being in the study through all appropriated institutional and local approvals. If there was more than one child of the appropriate age in the household, they were all included. Children and families were excluded from the study if the child had a medical history of serious birth complications, severe malnutrition, bacterial meningitis, encephalitis, cerebral malaria, or other known brain injury or disorder requiring hospitalization or continued evidence of seizure or other neurological disability. Caregivers were also assessed for mental illness or disability to ensure that they could participate in the study.

All of the study measures were collected as baseline assessments as caregiver/child dyads were enrolled in the study. The one exception was a questionnaire evaluation of anxiety/depression of the caregiver, collected 6 months after the other baseline assessments occurred.

5.3.2 Participating Child/Caregiver Dyads

Participants included 119 children ages 1–5 years and their primary caregiver. The average age was 3½ years with a standard deviation of 1.3. Sixty-five of the participants were male (54.6 %) and 54 were female (45.4 %). Children in the study were mostly cared for by their biological mother (59.7 %). Grandmothers cared for 32 of the children (26.9 %), and 16 children (13.4 %) were being cared for by a stepmother, father, aunt, or uncle. Eighty of the children (68 %) are not on antiretroviral medication at the time of assessment, and 38 (32 %) were on Trimune highly active antiretroviral therapy (HAART).

5.3.3 Measures Used in the Present Model Analyses

The Caldwell Home Observation for the Measurement of the Environment (HOME) scale was developed to provide specific information about the home and caregiving environment as a stimulus to the learning and development of young children (Caldwell and Bradley 1979). It has been validated for use within the Ugandan context (Bangirana et al. 2009a). Through both caregiver report and direct observations, this measure characterizes the developmental milieu and caregiving style within the child's home.

The Mullen scales of Early Learning were used to assess different developmental domains of children from birth to 68 months of age (Mullen 1995). The scales include Gross Motor (up to 36 months only), Visual Reception, Fine Motor, Receptive Language, and Expressive Language. The four Mullen scales with a cognitive performance component (Fine Motor, Visual Reception, Receptive Language, and Expressive Language) were used to derive the Early Learning Composite (g), which is a general measure of fluid intelligence in early childhood. The Early Learning Composite has been found be highly correlated with the Bayley Mental Development Index ($r = 0.70$), in validation studies (Mullen 1995).

The Achenbach Child Behavior Checklist (CBCL) for preschool-age children is used to obtain caregiver's reports of their 1½–5 year-old child's competencies and behavior problems. Ratings by a parent are completed on 99 problem items, which combine to make the following scales: Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Attention Problems, Aggressive Behavior, and Sleep Problems. These scales are then used to derive composite scores for internalizing (emotional), externalizing (behavior towards others), and total behavior problems.

The CBCL has been widely used throughout child and adolescent psychiatry and pediatrics (Achenbach et al. 2008; Achenbach and Rescorla 2001) and has been adapted to the Ugandan context (Bangirana et al. 2009b). The scale is administered to the primary caregiver in an interview format. During the interview the items are read in the local language of Luganda by a study team member, and the caregiver indicates the extent to which the child displays the behavior.

Standardized-for-age *Z* scores (WAZ) was used as a measure of nutritional well-being and overall physical health as it relates to pediatric HIV African children (Abubakar et al. 2009). The Hopkins Symptom Checklist (HSCL) is a 25-item scale to assess the emotional well-being of adults (15 depression items and 10 anxiety items). This scale has previously been utilized to assess the emotional well-being of Ugandan adults in HIV-affected communities (Bass et al. 2006; Derogatis et al. 1974a, b) and in other studies of adult depression in sub-Saharan Africa (Bolton et al. 2003, 2004), yielding scores for the severity of caregiver depression and anxiety. The child's relationship to the primary caregiver was classified into three categories that naturally arise in the population: mother, grandmother, and others (made up of stepmothers, aunts, fathers, or uncles).

For all children in the study, the stage of HIV infection was monitored through multiple means. The highly active antiretroviral treatment (HAART) status of the child was measured, and a 5 ml blood draw was used to obtain CD4+ T-cell counts and viral load.

5.4 Statistical Evaluation of the Ugandan HIV Early Childhood Assessments Within the Bachanas et al. Model

Using a Mann–Whitney statistical comparison of independent samples, there were no statistically significant differences between boys and girls for the CBCL domain scores (internalizing, externalizing, or total behavior problems). When looking at the number of children within the sample that were considered in the borderline and clinical range according to the CBCL cross-cultural norms (Achenbach 2010), about half of the sample was experiencing some internalizing behavior concerns. Specifically, 66 (55.5 %) of children were in the normal range for internalizing behaviors, while 22 (18.5 %) were in the borderline rage, and 31 (26.1 %) were in the clinical range.

For externalizing behaviors only 13 children were in the borderline (11) or clinical (2) range. For total behavior concerns, 80 (67.2 %) were in the normal range, with 19 (16 %) in the borderline range, and 20 (16.8 %) in the clinical range. There were no significant differences between boys and girls in the clinical or borderline range for internalizing, externalizing, or total behavior concerns.

Neither caregiver anxiety nor depression scores significantly differed among the principal caregiver groups (biological mother, grandmother, others). Likewise, there were no significant differences in HOME scores among the three caregiver groups.

5.4.1 Predicting Caregiving Environment

When only health predictors are considered, the child's HIV viral load level is a significant predictor of HOME quality using a linear regression model. SES as measured by material possessions in the household was significantly predictive of HOME quality for our study children, with a linear regression model ($P < 0.01$).

5.4.2 Predicting Cognitive Development

HAART treatment status was significantly related to poorer performance on the composite Mullen score (overall cognitive ability) after adjusting for WAZ, gender, and HOME (analysis of covariance model—ANCOVA). This meant that clinically less stable children with HIV necessitating HAART were also at risk in terms of cognitive ability. Higher viral load level in children not on HAART was also significantly predictive of lower cognitive performance on the Mullen scales. Consistent with Abubakar et al. (2009), lower standardized weight for age was highly predictive of poorer performance on the Mullen composite cognitive performance and on gross motor development. Viral load and HAART treatment status were also significantly predictive of gross motor development and an ANCOVA model. Detailed statistical results from these analyses can be found in Table 5.1.

5.4.3 Predictors of Caregiver Adjustment Within the Present Model

The impact of health and demographic variables were considered separately for both caregiver anxiety and caregiver depression. In separate stand-alone linear regression analyses, less clinical stability for the child as indicated by HAART therapy and higher viral loads were predictive of higher depression and anxiety in the caregivers.

Table 5.1 Predictors of cognitive and gross motor skills

Dependent variables	Mullen composite cognitive ability			Mullen gross motor scale		
Predictors	Unadjusted	Adjusted	Adjusted (SES omitted)	Adjusted for age only	Adjusted	Adjusted (SES omitted)
Age				0.000	0.000	0.000
Viral load	0.929	0.327	0.412	0.168	0.031	0.029
Weight-for-age *Z* score	0.002	0.003	0.004	0.000	0.004	0.004
SES	0.408	0.329		0.802	0.921	
Gender	0.258	0.587	0.513	0.131	0.039	0.036
HOME caregiving quality		0.332			0.712	
HAART status	0.040	0.045	0.046	0.151	0.034	0.013
Gender by HAART		0.391	0.356		0.024	0.023
R-squared		13.5 %	14.4 %		67.5 %	67.5 %
Sample size		108	108		109	109

An analysis of covariance (ANCOVA) is presented below for the predictors (left-hand column) of the two predicted dependent variables (DVs). The two DVs are the Mullen Early Learning Composite score (Visual Reception, Fine Motor, Expressive Language, Receptive Language) standardized by age and the raw score for Mullen Gross Motor scale using age as a covariate, since norms were only available up to 33 months of age for standardizing the scale score. *P* values are present for both unadjusted and adjusted ANCOVA analyses, with and without SES. *P* values less than 0.05 are statistically significant

5.4.4 Predicting Psychosocial Outcomes Within the Present Model

To understand which of the ecological variables are important to psychosocial outcomes, internalizing, externalizing, and total behavior problems were considered separately. Caregiver depression, anxiety, and HOME quality of caregiving scores were significantly predictive of CBCL internalizing and total symptoms for the children (Table 5.2).

5.5 Summary of Bachanas Model Fit Within Present Study Sample

Figure 5.1 presents a schematic overview of the principal significant statistical relationships relevant to the Bachanas et al. model, as summarized in the previous sections and as detailed in Tables 5.1 and 5.2. The strongest relationships exist on the left-hand side of the figure between caregiver emotional well-being (HSCL measures of depression/anxiety) and child psychosocial adjustment (CBCL global scales). HOME caregiving quality scores are related to caregiver depression/anxiety.

Table 5.2 Predictors of cognitive and gross motor skills

Dependent variables	CBCL internalizing symptoms			CBCL total symptoms		
Predictor	Unadjusted	Adjusted with anxiety	Adjusted with depression	Unadjusted	Adjusted with anxiety	Adjusted with depression
Viral load	0.109	0.674	0.591	0.651	0.451	0.408
Weight-for-age *Z* score	0.818	0.756	0.974	0.321	0.572	0.442
SES	0.902	0.211	0.185	0.229	0.023	0.016
Gender	0.797	0.822	0.625	0.472	0.840	0.722
HAART status	0.068	0.685	0.702	0.496	0.756	0.700
Caregiver	0.381	0.544	0.500	0.357	0.319	0.272
Gender by HAART status		0.722	0.639		0.246	0.451
Gender by caregiver		0.225	0.293		0.129	0.228
HOME caregiving quality	0.006	0.030	0.024	0.045	0.074	0.061
Caregiver anxiety	0.015	0.028		0.078	0.098	
Caregiver depression	0.027		0.040	0.042		0.045
R-squared		17.2 %	16.5 %		16.7 %	18.0 %
Sample size		99	99		97	97

An analysis of covariance (ANCOVA) is presented below for the predictors (left-hand column) of the two predicted dependent variables (DVs). The two DVs are the Achenbach internalizing symptoms and the total symptoms. *P* values are present for both unadjusted and adjusted ANCOVA analyses with anxiety or depression (not both together because of colinearity problems). *P* values less than 0.05 are statistically significant

The child's psychosocial adjustment is related to the overall cognitive ability of the child as measured by the Mullen composite score. HIV illness parameters as indicated by HAART treatment status and weight-for-age physical growth are predictive both of HOME quality provided by the caregiver and of the child's overall cognitive ability and development.

5.6 Health and Demographic Predictors of Cognitive Development

Children with HIV are at increased risk for developmental disabilities (Speigel and Bonwit 2002), consistent with the data presented in this chapter that demonstrated that specific health and demographic variables (i.e., poorer clinical stability as indicated by lower weight for age and need for HAART) impacted children's overall cognitive development and ability. A linkage between medication status, as a surrogate for progression of HIV/AIDS, and lowered developmental cognitive scores also would be expected, as children are not put on medication until their illness reaches a significant level (i.e., elevated viral load and CD4 count, as well as an AIDS-defining illness). Thus, it makes sense that with increased symptoms from more aggressive disease course, represented by the need for HAART, would come decreased cognitive scores, as was found in this sample of Ugandan children with HIV/AIDS. This is consistent with the findings of Smith and colleagues (2006) who reported significantly lower cognitive development scores for children ages 3–7 years with HIV/AIDS and exhibiting an AIDS-defining illness.

Similarly, weight for age as a measure of physical health and development was significantly predictive of Mullen gross motor and cognitive developmental outcomes for our study children. WAZ has also been linked to psychomotor outcomes for HIV-infected children in Kenya, with healthier children exhibiting higher psychomotor skills (Abubakar et al. 2009).

5.6.1 Psychosocial Outcomes for Young Ugandan Children with HIV/AIDS

The psychosocial child outcome variables chosen for the study presented in this chapter were internalizing, externalizing, and total behavior concerns from the CBCL. Not surprisingly, the caregiving environment played a role in both internalizing behaviors and externalizing behaviors exhibited by the young Ugandan children with HIV/AIDS. Specifically, children's internalizing behavior concerns were influenced by the caregiver's anxiety, depression, and the quality of the interactions within the home environment. The total behavior concerns exhibited by the study population were related to the caregiver's depressive symptoms and the caregiving environment, but were also influenced by the socioeconomic status of the family. These findings are consistent with other research carried out in South Africa, a country strongly affected by the HIV/AIDS epidemic. In this setting, caregiving quality, perhaps as mediated by strength of caregiver/child attachment, has been identified as a key factor in the psychosocial adjustment of children. If children have quality care, they are more likely to exhibit social and behavioral adjustment, as well as intellectual achievement (Richter et al. 2004).

There were no significant predictors for externalizing behavior concerns in this study. On the other hand, there were few children reported by their caregivers to exhibit externalizing behavior concerns, restricting the range of responses and reducing the power to obtain significant findings. Children are reported to exhibit significantly more internalizing behaviors than externalizing ones. However, it also may be the case that caregivers are more concerned about the internalizing behaviors and do not feel that externalizing behaviors present as significant a problem to the family. This suggests that researchers may be better served to focus interventions for children with HIV/AIDS and their caregivers on anxious and depressive symptoms and not be as concerned with aggressive or externalizing behaviors.

5.7 Conclusion: Bachanas et al. Model Within a Co-constructivist Paradigm

Given the psychosocial, motor, and cognitive development delays faced by a significant proportion of our present sample of rural Ugandan HIV study children, it is imperative to understand the ecological factors contributing to the psychosocial adjustment of these children. The Bachanas et al. model provides a useful framework for doing so, and our study findings were consistent with this overall model. Such a framework also provides a vantage point for identifying strategic points of intervention for these at-risk children.

The results from this study show a dynamic relationship between demographic variables, health variables, caregiving variables, and child psychosocial development (see Fig. 5.2). This can be used for identifying interventions. For example, both internalizing behavior concerns and total behavior concerns are influenced by the caregiving environment or the quality of the home environment as measured by the quality of interactions between the caregiver and the child. Children's internalizing behaviors also were influenced by the caregiver's anxiety and depression. Boivin and colleagues are presently in the first year of an NIH-sponsored randomized controlled clinical trial (RCT) of the effects of a year-long caregiver training

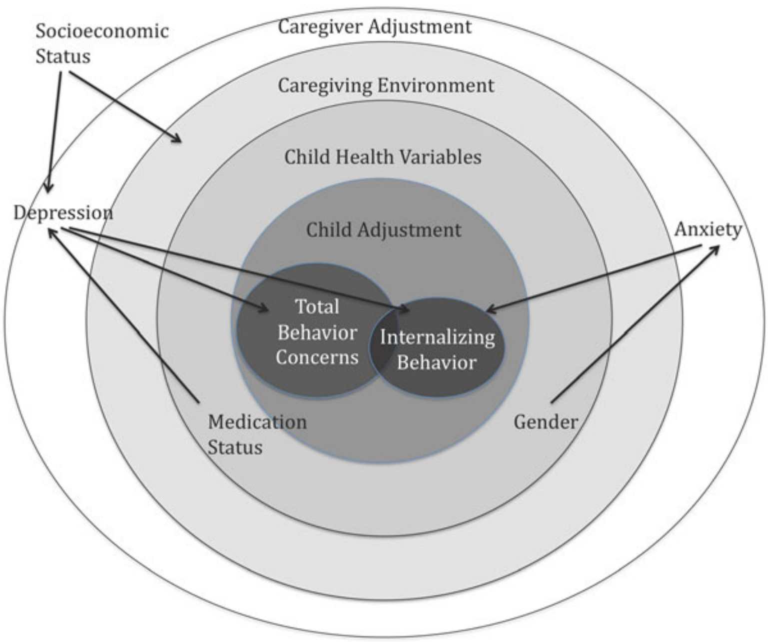

Fig. 5.2 Outcomes: ecological model of factors contributing to psychosocial development of young children with HIV/AIDS

intervention for caregivers of rural Ugandan children with HIV and caregivers of children uninfected but born to infected mothers. This study will evaluate the impact training to improve caregiving in the home, on quality of caregiving, emotional well-being of the caregiver and child dyad, and subsequent developmental outcomes for the child. The present model indicates that caregiver training may be the single most strategic point of intervention for these outcomes (Fig. 5.1).

This model approach is also consistent with the biocultural co-constructivist framework described by Li (2003). Like this framework these results emphasize the dynamic interplay between the child and his/her environment in psychosocial development.

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Chapter 6
Examining the Psychosocial Adjustment and School Performance of Ugandan Children with HIV/AIDS

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6.1 Impact of HIV/AIDS and Resilience of Those Afflicted

Every day, 1,100 children around the world are infected with human immunodeficiency virus (HIV), most as a result of mother-to-child transmission (MTCT) of the virus [United Nations Program on HIV/AIDS (UNAIDS) 2007]. In 2007 alone, an estimated 420,000 children worldwide were newly infected almost exclusively through MTCT (UNICEF 2008). Despite the improving availability of medical interventions to decrease the incidence of MTCT, UNAIDS found the

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total number of children living with HIV had reached 2.5 million in 2007; 1 million more than was estimated in 2005. Children now make up approximately 7.5 % of the 33.2 million people worldwide living with HIV/AIDS (UNAIDS 2007). Many of these cases are in sub-Saharan Africa where the problem is compounded by a lack of resources and the presence of many other life-threatening diseases.

HIV/AIDS has a widespread impact on the children of Uganda in particular, where about 1 million children are already orphaned and a new child is orphaned every 14 s due to the AIDS epidemic (Ronald and Sande 2005). Furthermore, over 100,000 children in Uganda are infected with HIV/AIDS (UNAIDS 2007). No cure for the virus is known, and being infected means increased medical needs and decreased life-span. Fortunately, children are beginning to receive care in many ways.

The devastating AIDS epidemic is receiving global attention, which has led to better pharmacological treatments that are implemented early on and in conjunction with other vital care addressing nutrition. The Ugandan government has been responsive to the epidemic by making the problem a priority, allowing for the implementation of new medical interventions and through public campaigns to curb the devastation (Kirumira 2008; Ruzindaza 2001). Within Uganda, nongovernmental organizations (NGOs) such as Child Health Advocacy International (CAI) and Global Health Uganda (GHU) have pioneered social programs targeted at helping to improve the lives of children and families living with HIV/AIDS. NGOs have been instrumental in providing care around the world and delivering more aid to developing regions than all United Nations organizations combined (Chaplowe and Engo-Tjega 2008). These new interventions have been successful at identifying children with the virus and prolonging life, but much more is needed to understand and ultimately improve the quality of life of children living with HIV/AIDS.

A Luganda proverb from a tribe within Uganda, “Akakyama anamera tekagololekeka,” is translated as “That which is bent at the outset of its growth is almost impossible to straighten at the later age” (Kilbride and Kilbride 1990). This proverb aptly describes the harmful effects of HIV/AIDS on the lives of children infected at birth. The developmental effects can be seen in children’s cognitive ability and psychosocial adjustment. Children may exhibit global cognitive impairments, specific deficits in attention, and specific deficits in visual-spatial functioning (Smith et al. 2006). Numerous studies have reported the psychosocial consequences suffered by children diagnosed with HIV including externalizing (e.g., hyperactivity, aggression) and internalizing (e.g., depression, anxiety) behavior problems (Bachanas et al. 2001; Franklin et al. 2007; Misdrahi et al. 2004). However, the emphasis in the literature on cognitive and emotional dysfunction exhibited by children infected with HIV has recently shifted to a focus on the positive outcomes demonstrated by many of these children. For example, children with HIV/AIDS have been found to exhibit normal cognitive functioning if they do not have an AIDS-defining illness such as an opportunistic infection, a disease affecting the central or peripheral nervous system, malignancies, or wasting syndrome (Smith et al. 2006) or if they do not experience high environmental stress (Hochhauser et al. 2008). Although children with HIV may exhibit elevated levels of maladjustment relative to a non-infected population, the majority of these children do not. In a study by Bachanas and colleagues (2001), despite being born with HIV/AIDS, 75 % of the infected children did not show signs of externalizing (behavior towards others) or internalizing (emotional adjustment) problems, suggesting behavioral and emotional resiliency.

Resilience refers to an individual's ability to recover from, adapt, and remain strong in the face of adversity (Boyden and Mann 2005, p. 6). Focusing on the resiliency of children amidst diverse risks and life circumstances can be important in leading to and informing intervention (Ungar 2008). However, specific information guiding the conceptualization of risk and resiliency within resource-poor regions of the world dealing with a chronic illness such as HIV is limited. Liebenberg and Ungar (2008) point out that the challenge to resilience researchers is that positive outcomes vary according to context and culture. Data presented in this chapter is provided as an example of how cultural context can be used to better understand factors associated with psychosocial adjustment and school success in a rural setting.

Bachanas and colleagues (2001) have proposed a model of stress and coping that can be used to better understand factors underlying resilience (e.g., psychological adjustment) in the face of HIV in a given cultural context. Their model considers key ecological factors that contribute to children's adjustment, including illness parameters, caregiver characteristics, demographic parameters, and child characteristics. Although this model has not been used in sub-Saharan Africa, this chapter uses this approach as a guide to better understand factors that may buffer the negative impact of HIV in Uganda.

Psychosocial adjustment defines the adaptive functioning of individuals. A person is considered to be well adjusted if he or she demonstrates positive social skills, normal psychological functioning, and is able to meet the demands of the environment adaptively (Achenbach et al. 2008). Within this view, the extent of psychosocial adjustment in children in the face of some environmental stressor can then be characterized by the presence or absence of internalizing and externalizing behavioral problems. Internalizing disorders reflect "problems within the self, such as anxiety, depression, or somatic complaints without known medical cause and withdrawal from social contacts" (Achenbach and Rescorla 2001, p. 93). Externalizing behaviors on the other hand involve conflicts with others and violations of expected behavior (Achenbach and Rescorla 2001). A reliance on the presence or absence of internalizing and externalizing behavior problems, alone, is a narrow approach to mental health when examined in isolation. The stress and coping model provides a way of understanding internalizing and externalizing behaviors in context: in relation to children's unique environmental circumstances and characteristics. As applied in this chapter, the stress and coping model illustrates how the caregiver and the socioeconomic context play an important role in children's adjustment to HIV within a resource-poor region, such as Uganda.

6.2 Theoretical Framework for Understanding Psychosocial Adjustment of Children with HIV/AIDS

Children learn to think, speak, and behave within a sociocultural context through interpersonal interaction (Boyden and Mann 2005). This environment can then have both positive and negative influence on a child's development. "Resiliency" describes a child's ability to thrive and develop successfully despite negative life circumstances. Research conducted on psychosocial adjustment of children in the face of an adverse condition such as HIV/AIDS should only be done when considering the "dynamic interplay of individual and social forces" (Liebenberg and Ungar 2008, p. 7). Bachanas and colleagues (2001) use their model of stress and coping for predicting psychological adjustment in children with HIV. Their model is derived from the work of Thomas (1987) who recommended a theory-driven model to guide research on children with chronic illnesses. Increased technological ability to save lives through medical interventions has led to an increase in children living with chronic conditions (Thomas 1987). Living with a chronic condition can have a negative impact on psychosocial functioning, because prolonging life does not automatically mean that individuals are able to live quality lives. As a consequence, chronic illness becomes a critical risk factor for psychological adjustment and quality of life (Thompson and Gustafson 1996).

The stress and coping model developed by Bachanas and colleagues (2001) provides a model that can be followed in research predicting psychological adjustment of school-age children with HIV. The model emphasizes the importance of all of the ecological factors that contribute to the child's adjustment, including demographic parameters, caregiver characteristics, illness parameters, and child characteristics.

The demographic parameters within Bachanas and colleagues' (2001) model of stress and coping include the child's age, gender, and family socioeconomic status. All of these measures have a direct impact on the child's adaptation process, which, in turn, influences the adjustment of the child. The importance of these parameters is set forth in the work of Bronfenbrenner (1979) and demonstrates continued importance within Masten's (2006) developmental psychopathology framework. According to this framework, demographic parameters are important to consider because throughout development, children, as living systems, are continually interacting with the contexts in which they are a part. In this way, typical development, and transversely, psychopathology, is due to the complex interactions between the systems that the child is a part of as well as between the child and the contexts in which the child is embedded (Masten 2006). The child's age may determine the responsibilities and day-to-day tasks of that child, thus impacting expectations for typical development. The gender of the child is also a contextual variable that carries different expectations for behavior and typical adjustment depending on whether the child is male or female. Living with a disease such as HIV/AIDS can thus have differing effects on children depending on gender. The family's resources and ability to meet the needs of the child with HIV/AIDS, as well as all of the family members, also can significantly affect psychosocial adjustment. Any one of these demographic variables can serve as a risk or protective factors, and all must be considered within the larger model of stress and coping as it applies to children living with HIV.

Caregiver characteristics are also of key importance to the adjustment of the child. In their model of stress and coping, Bachanas and colleagues (2001) focus on the caregiver adaptational process which consists of stress, coping strategies, and family functioning in influencing child adjustment. According to the "systems principal," children are thought of as social beings who are continually interacting with their families, peer groups, schools, and larger systems (Masten 2006). Children are thought to be part of a codependent relationship in which they influence the regulation of others' behavior while at the same time being regulated by their relationships with others. Thus, children can influence a caregiver and then subsequently be influenced by his or her reactive behavior (Masten 2006). When considering the protective qualities of caregiving in a child's adjustment to HIV/AIDS, the relationship of the child to the caregiver can be important. Within Uganda, the AIDS epidemic has significantly affected the traditional caregiving system. Although positive outcomes are associated with the care of the biological mother, many children are orphaned and in the care of a grandparent or alternative caregiver. In such cases, caregiving may vary in quality (O'Hare et al. 2005; Ssengonzi 2009).

The illness parameter is specified as the HIV status of the child. This can be defined as the presence or absence of the virus and the mean the progression of the disease within the body. As the disease progresses more symptoms and difficulties are experienced by the child. In fact, by definition, the category of disease is associated with the symptoms experienced by the child, with children in later stages presenting with more medical complications. Research on the best ways to measure disease progression supports the use of two different factors: CD4 cell count and viral load. These measures have been found to be the best predictors of mortality in developed countries as well as sub-Saharan Africa (Rouet et al. 2003).

The final piece of Bachanas' (Bachanas et al. 2001) stress and coping model of child adjustment represents the characteristics or personal qualities of the child. These include expectations and coping strategies. Expectations can be measured as the health locus of control, the child's generalized expectations concerning where control over his or her health resides. Coping strategies are considered palliative (passive) or adaptive (active). The resulting coping strategy is dependent on a child's age and relative cognitive capacity. Masten (2006) defines the "agency" principle as the child being an active agent in his or her development, showing increasing independence with brain development and learning. Strong cognitive skills are protective and aid in the coping process, whereas deficits in cognitive ability are a risk for psychosocial maladjustment. Thus, understanding the child's ability to think and learn as they navigate their environment is important in understanding the factors contributing to the overall psychosocial adjustment of the child when faced with chronic illness.

Ultimately all of these variables contribute to the primary outcome variable for the stress and coping model (Bachanas et al. 2001), child adjustment. Together they make clear the need to understand the psychosocial adjustment of children according to the context of which they are a part. This view is also endorsed by Li (2003) as he argues for a co-constructivist approach to understanding development. In his holistic and multidimensional approach, Li (2003) states that culturally imbedded interactions (proximal developmental context) as well as culture-gene coevolution (distal phylogenetic context) are a part of individual development. Boivin and Giordani (2009) apply this approach to cross-cultural neuropsychology with African and American children and also argue for a universal brain/behavior omnibus that drives developmental plasticity.

In light of the work of Li (2003) as well as that of Boivin and Giordani (2009), Bachanas and colleagues' model can be organized into two systems of influence: the *caregiving context* composed of the caregiver and socioeconomic status and *child illness parameters* composed of characteristics such as the disease progression and cognitive ability. These systems of influence can be used to identify factors that ultimately promote resiliency in the face of risks such and HIV/AIDS.

6.3 Examining Psychosocial Adjustment and School Performance

The purpose of this study is to present a model for examining developmental outcomes (i.e., psychosocial adjustment and educational success) of Ugandan school children living with HIV/AIDS in relation to the social and cultural contextual factors that promote resiliency, based on the stress and coping model (Bachanas et al. 2001). Having HIV/AIDS is associated with a plethora of negative outcomes; thus, it is important to identify the protective factors that promote resiliency. The stress and coping model, though appropriate and relevant, has not been applied to a resource-poor region, such as Uganda, where the epidemic of HIV has had far-reaching effects. Furthermore, the model's focus on positive outcomes and resiliency promotion represents a positive change from past emphasis in the literature from resource-poor regions that tended to focus on pathology and dysfunction in the face of chronic illness. The first step to the model presented in the chapter is the identification of the internalizing and externalizing behavior problems that children with HIV/AIDS experience, as representing the level of psychosocial adjustment. The second step then examines the factors that best predict successful psychosocial adjustment, resilience, in the face of HIV. Understanding the predictors of successful adjustment to chronic illness, such as HIV, can inform the development of interventions to promote resiliency in the face of illness. The research presented as an example in this chapter (a) explores the caregiving context and role of illness parameters in children with vertically transmitted HIV/AIDS within Uganda and (b) identifies the factors that may be linked to successful psychosocial functioning and school performance, all within the unique context of a resource-poor setting.

6.3.1 Methods

Children were recruited through Child Health Advocacy International (CAI), an NGO serving children with HIV and families in Kayunga District, a poor rural district about 80 km northeast of Kampala, Uganda. Recruitment in the CAI home healthcare program is done through a voluntary counseling and testing (VCT) outreach program to the communities throughout Kayunga District. CAI and the Kayunga District Hospital sponsor this free HIV testing service. School-age children with a CD4 percentage of less than 15 %, or in stage 3 with an HIV-associated life-threatening illness, are eligible for highly active antiretroviral therapy (HAART) treatment through the HIV clinic at Kayunga Hospital. The care, however, is contingent on having a parent or legal guardian/caregiver who is willing to have the child commence antiretroviral therapy (ARV) treatment and who is committed to adherence to the strict regimen.

Children 6–16 years of age with HIV/AIDS and enrolled in the CAI program were eligible with appropriate consent, to participate in this study. To ensure only the inclusion of children who contracted the virus from their parents, only children who had been diagnosed in early childhood (i.e., prior to achieving sexual maturity) were eligible for enrollment. Based on a brief medical history questionnaire and CAI medical chart review, children were excluded if they exhibited a medical history of serious birth complications, severe malnutrition, bacterial meningitis, encephalitis, cerebral malaria, or other known brain injury or disorder requiring hospitalization or continued evidence of seizure or other neurological disability. Although CAI provides school fees for children who are enrolled in the program, only 45 of the 60 children participating in this study were attending school.

6.3.1.1 Child Behavior Checklist

Children's social emotional wellness was measured using the Child Behavior Checklist (CBCL) 6–18 years. The CBCL is an instrument on which parents/caregivers rate a child's competencies and problem behaviors. The CBCL yields a composite score for a child's internalizing and externalizing behaviors. An overall score for total behaviors combines scores for internalizing, externalizing, and the other three syndromes (*social behavior problems, thought problems, and attention problems*). This score provides an indication of the overall functioning of a child.

Extensive research on this tool has shown inter-interviewer and test-retest reliabilities and internal consistency to be high (Achenbach and Rescorla 2007a; Achenbach et al. 2008). The Achenbach assessments have been translated into more than 75 languages and have been used in thousands of published studies in over 65 societies (Berube and Achenbach 2007). These data have been used to develop a multicultural supplement that allows users to compare children's scale scores with normative samples from various societies (Achenbach and Rescorla 2007b). For this study the normative data from Ethiopia (sub-Saharan Africa) was used to derive standard scores and determine if the children are in the clinical range. The CBCL has also been used in the research of medical conditions, specifically being used in HIV research (Berube and Achenbach 2007). For this study the CBCL was translated and back-translated with the assistance of a child psychologist from Mulago Hospital in Kampala, Uganda, so that versions were available in Luganda and English. The scale was presented in interview format, and because English is taught within the education system in Uganda, most caregivers were more comfortable with English than Luganda.

6.3.1.2 Kaufman Assessment Battery for Children: Second Edition

The Kaufman Assessment Battery for Children—Second Edition (KABC-2) was chosen for this study because it is a comprehensive assessment of cognitive ability that has been adapted and validated in other studies in diverse populations to assess the effects of infectious diseases on cognition (i.e., Bagenda et al. 2006; Boivin 2002; Boivin et al. 1995, 2007; Boivin and Giordani 1993). The measure has demonstrated good construct and predictive validity in these applications (Giordani et al. 1996; Bangirana et al. 2009).

For this study, Luria's neuropsychological approach was used in order to look at Sequential Processing, Simultaneous Processing, Learning, and Planning. Internal consistency and reliability coefficients are high for the KABC-2 factor scores and subtests (Kaufman and Kaufman 2004). For this study nine subtests of the KABC-2 were administered to all participants and were used to look at four primary subscores of cognitive functioning: Sequential Processing, Simultaneous Processing, Planning, and Learning. All four areas of cognitive functioning were used in the analysis because socioeconomic status and gender may have differing effects on these specific cognitive ability areas. The KABC-2 data does not have normative data for the population studied; thus, it was used as a comparative within-group measure rather than a normative measure of intellectual functioning.

6.3.1.3 Socioeconomic Status

SES takes into account an individual or family's relative economic and social position within their own society. The measure used for this study was developed by researchers at Mulago Hospital in Kampala, Uganda, who are familiar with the quality of home environments in Kayunga in order to assess the resources available within the home for the child living with HIV/AIDS. The measure focuses on the access to resources and asks questions to assess the type of home the family lives in, if they have year-round access to food and, if so, what type; and, finally, what possessions the family owns that are seen as status symbols within their district. Numerical values are assigned to each question: possessions, ways of living, and food eaten such that higher scores represent higher SES status.

6.3.1.4 Disease Progression

All children who were part of the study underwent a 5 mL blood draw at the local hospital, within one week of testing, in order to evaluate HIV status as well as progression of the disease, according to previously published procedures (Kiwanuka et al. 2008). Treatment was provided by the CAI home healthcare program, and free medications were supplied by the Makerere University-Walter Reed Project (MUWRP) in Kayunga through support from the US-AID President's Emergency Plan for AIDS Relief (PEPFAR) initiative. Decisions for instituting HAART were based on evaluation of the CD4 T cell counts and viral load by treating physicians at Mulago Hospital, allowing medication status to reasonably represent disease progression.

6.3.1.5 School Performance

All of the children within the study had access to schooling because CAI paid for their school fees, uniforms, and books. In Uganda, all of the children attending school are given a class rank by their teachers, comparing their performance to that of their classmates. Using class rank allows researchers to see how the children are doing in school as compared to their classmates without HIV/AIDS. For the purposes of this study, children were put into four categories of school performance based on their class rank: (1) not attending school, (2) below average, (3) average, and (4) above average.

6.3.2 Results

6.3.2.1 Sample Characteristics

This study focused specifically on quality-of-life issues as outcomes for these children and examined the caregiving context and the child illness parameters as predictors. The number of children in the study by gender and age is represented in Fig. 6.1 by a histogram. The participants consisted of 60 children (36 girls and 24 boys) ranging in age from 6 to 16: median age = 9.8 years.

Similar numbers of boys and girls had average and higher SES; however, more girls than boys were in the lower SES group. Children with average SES were equally distributed among all types of caregivers. Among children with lower SES, the largest number was being cared for by a grandmother. Most children in the highest SES group lived with a caregiver other than their mother or grandmother. Most children performing below average or not attending school exhibited lower SES. In the study sample, 37 children (61.7 %) were not on HAART (severe disease progression group), while 23 children (38.3 %) were not on medication.

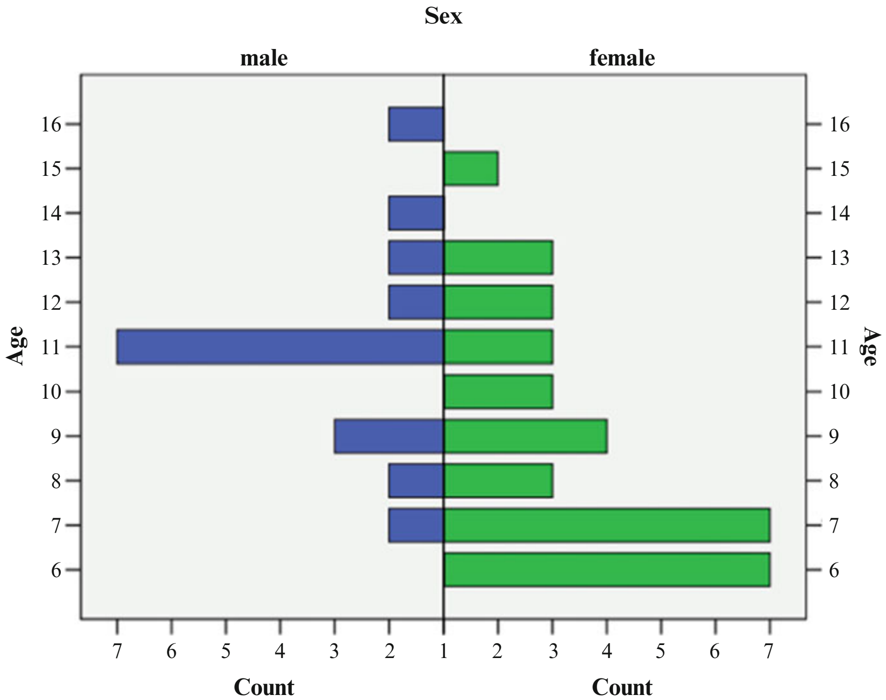

Fig. 6.1 Histogram of children by gender and age

6.3.2.2 Caregiving Context

The primary caregivers varied with 17 (28 %) of the children being raised by the biological mother, 24 (40 %) by a grandmother, and 19 children (32 %) by someone else including uncles, sisters, and other distant relatives. A similar pattern of caregivers was found for girls and boys. The caregivers for children at different ages varied however, with children more likely to be cared for by their biological mothers at younger ages and by a grandmother or other relatives at older ages (see Fig. 6.2). To examine if the child's age and SES predicted the likelihood of children living with either their mother or another caregiver, a direct logistic regression was employed. The full model containing both age and SES as independent variables was not statistically significant, $\chi 2$ (2, $N=59$) = 5.06, $p=0.079$, indicating that the age and SES did not predict whether children were cared for by their biological mother versus another caregiver.

6.3.2.3 Child Illness Parameters

As previously noted, medication status was used as a surrogate for disease progression, with children who were on medication being in the more advanced stages of

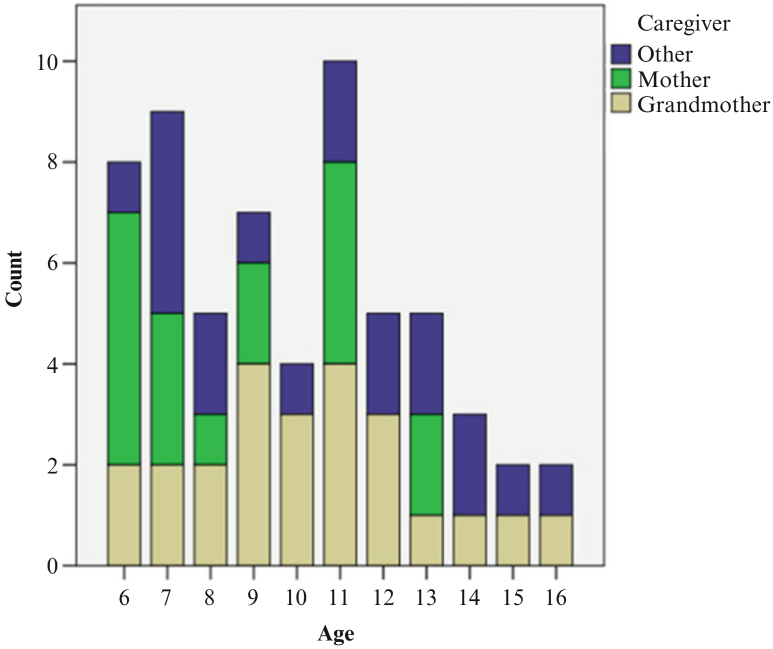

Fig. 6.2 Histogram of the number of children by caregiver and age

the disease and children not yet on medication being in a less advanced disease state. It was hypothesized that as the disease progresses more cognitive deficits develop, so that children on medication would have significantly lower cognitive scores in all four K-ABC areas measured (Sequential Processing, Simultaneous Processing, Learning, Planning) than children not yet taking medication.

As predicted, a statistically significant multivariate effect for SES was observed: $F(4,53)=4.88$, $p=0.002$; Wilks lambda = 0.73; and partial eta squared = 0.27. Follow-up univariate tests revealed a significant main effect for SES on Learning ($p<0.001$) and Planning ($p=0.002$), indicating that SES had an effect on children's Learning and Planning abilities as measured with the KABC-II. However, SES did not have the same effect on Simultaneous ($p=0.031$) and Sequential Processing ($p=0.107$). Contrary to prediction, the multivariate main effect for medication group (disease progression) was not significant, $F(4,53)=0.461$, $p=0.764$; Wilks lambda = 0.97; and partial eta squared = 0.034, suggesting that in this population, disease status did not predict neuropsychological performance.

6.3.2.4 Psychosocial Adjustment and School Performance

School performance was examined by transforming class rank into a percentile rank. Percentile rank was then split into four categories of analysis: (1) not attending school ($n = 15$); (2) below average, a percentile rank of 1–40 ($n = 18$); (3) average, a percentile rank of 41–60 ($n = 14$); and (4) above average, a percentile rank of 61–100 ($n = 13$). No statistical differences in the percentages of parents, grandparents, or other caregivers responding to the CBCL were noted across the four school performance groups. Grandmothers were equally represented across groups. Mothers made up half of the caregivers within the below-average group. Two mothers were reported each in the group of children not attending school and in the above-average group. Within the group of children not attending school, the largest group of reporters was other caregivers. Other caregivers were represented in all other school performance groups.

In order to characterized the relationship between psychosocial adjustment, as represented by internalizing and externalizing scores, and school performance, a MANCOVA was used to assess the differences in internalizing and externalizing behavior problem scores from the CBCL (checking first for multicollinearity of these variables) and school performance categories, using age as a covariate.

After accounting for age in the analyses, none of the main effects for externalizing behaviors were significant: school performance: $F(3,49) = 1.59$, $p = 0.204$ and gender: $F(1,49) = 0.105$, $p = 0.747$. As seen in Table 6.1, after adjusting for age a significant interaction effect (school performance and gender) was observed for externalizing behaviors: $F(1,49) = 4.38$, $p = 0.008$, using a Bonferroni-adjusted alpha level of 0.017 (partial eta squared = 0.21). These results suggested that boys and girls have different externalizing behavior scores based on their school performance. Externalizing behavior problems among girls decreased with higher levels of performance in school. Girls in the above-average performance group had the lowest average externalizing behavior concerns. Boys, on the other hand, presented a more complex pattern. Boys with above-average school performance actually had the highest average externalizing behavior problem scores, in the borderline range of clinical significance. The next highest scoring group were those boys who are no longer in school, with the other groups falling between. None of the main effects for internalizing behaviors were significant: school performance: $F(3,49) = 1.67$, $p = 0.185$; gender: $F(1,49) = 2.815$, $p = 0.1$; and age: $F(1,49) = 0.045$, $p = 0.833$. The interaction effect for internalizing behaviors did not reach significance using a Bonferroni-adjusted alpha level of 0.017, $F(3,49) = 2.978$, $p = 0.04$.

6.3.2.5 Factors Contributing to Psychosocial Adjustment and School Performance

The CBCL was completed for 58 of 60 children in the study, with the two children not completing the scale appearing to be random occurrences. Using the CBCL multicultural norms for sub-Saharan Africa to characterize difficulties in adjustment, eight children (14 %) scored in the borderline range for internalizing behaviors: five boys and three girls. Eleven (19 %) of the children, five boys and six girls, scored in the clinical range for internalizing behaviors. Four children (7 %), equal numbers of boys and girls, were in the borderline range for externalizing behaviors.

Table 6.1 Test of between-subjects effects to assess psychosocial adjustment and school performance by gender and age

	Dependent variable	Type III sum of squares	df	Mean square	F	Sig.	Partial eta squared
Corrected model	Internal	1,211.36	8	151.42	2.23	0.041	0.267
	External	960.35	8	120.04	2.06	0.058	0.252
Intercept	Internal	11,023.58	1	11,023.58	162.4	0.000	0.768
	External	10,778.47	1	10,778.47	184.97	0.000	0.791
Age	Internal	3.05	1	3.05	0.045	0.833	0.001
	External	4.58	1	4.58	0.079	0.780	0.002
School group	Internal	340.68	3	113.56	1.63	0.185	0.093
	External	277.89	3	92.63	1.59	0.204	0.089
Gender	Internal	191.09	1	191.09	2.82	0.100	0.054
	External	6.11	1	6.11	0.105	0.747	0.002
School performance *Gender	Internal	606.17	3	202.06	2.98	0.040	0.154
	External	765.6	3	255.2	4.38	0.008	0.211
Error	Internal	3,326.23	49	67.88			
	External	2,855.05	49	58.27			
Total	Internal	181,752	58				
	External	176,963	58				
Corrected total	Internal	4,537.57	57				
	External	3,815.4	57				

* Signifying the interaction effect between school performance and gender

Eleven children (19 %) were in the clinical range, including four boys and seven girls. As seen in Table 6.1, on the Total Behavior Problems Scale, 14 % of the children were scored in the borderline range (two boys and six girls), and 14 % were scored in the clinical range (three boys and five girls).

Considering the stress and coping model presented earlier, multiple regression was used to help understand what factors contribute to psychosocial adjustment. Separate regressions were conducted for internalizing behaviors and for externalizing behaviors. Based on the previous discussion, cognitive functioning (child illness parameter) and the relationship of the caregiver to the patient (caregiver context) were considered to represent important predictors. Because of the already mentioned association between age and relationship with caregiver, age was not added to the regressions. Similarly, SES was not included due to its relationship with cognitive outcomes as found in the analyses on child illness parameters. The multiple regression for externalizing behaviors revealed that the overall model was not statistically significant, $F(2,55)=2.85$, $p=0.067$, although the model for internalizing behaviors was significant $F(2,55)=3.12$, $p=0.048$. Caregiver and cognitive score explained a modest 10 % of the variance in internalizing behaviors. Using the semi-partial correlation coefficients, almost all (10 %) of the total variance in internalizing behaviors was uniquely explained by cognitive score. Children with higher cognitive functioning had fewer internalizing behavior problems. Caregiver accounted for only 0.4 % of the variance in the model (see Table 6.2).

Table 6.2 Nominal regression to assess variables contributing to externalizing behaviors

Model	Standardized coefficients beta	*t*	Sig.
Constant		34.078	0.000
Caregiver	−0.305	−2.372	0.021
SRTotalCog1	−0.027	−0.207	0.837

Most children not attending school were less than 8 years of age. Children ages 9–14 were more likely to be attending school than their younger or older counterparts. Only 50 % of the 15- and 16-year-olds were attending school. A logistic regression with a multinomial set of procedures was used with the dependent variable being school rank and the predictor variables being caregiver and cognitive scores. The model was significant, $\chi 2$ (9, $n=60$) = 22.63, $p=0.007$, accounting for between 31.4 % (Cox and Snell) and 33.6 % (Nagelkerke R squared) of the variance in school performance. The likelihood ratio test of individual parameters showed that caregiver was not a significant factor in the model, $\chi 2$ (6, $n=60$) = 7.68, $p=0.263$; however, cognitive score was a significant factor, $\chi 2$ (3, $n=60$) = 14.75, $p=0.002$. Using children in the "above-average" group as a reference, cognitive scores were significant for the group of children not attending school ($p=0.002$) and for those in the below-average performance group ($p=0.015$). The odds ratio for cognitive scores of children not attending school was 0.427, indicating that as the cognitive score of children decreased by 1, the odds of being in the *not attending school group* increased by a factor of 0.427. Similarly, for children in the below-average group, as the cognitive score decreased by 1 point, the odds of being in the below-average group rather than in the above-average group changed by a factor of 0.542 (see Table 6.3). Thus, as cognitive scores increased, the probability of not attending school or being in the below-average performance group decreased.

6.3.3 Discussion

The purpose of this study was to examine the nature and predictors of the quality of life of children with vertically transmitted HIV/AIDS in Uganda considering variables of interest as specified in a stress and coping model of resilience. In understanding the concept of resilience in the face of HIV, age and survival beyond the point of transmission must be considered, but in field studies relationships are often hard to quantify. For example, in this sample of children 6–16 years of age, the fewest participants were from the 14- to-16-year-age range. This finding could reflect poorer survivorship in this group; however, length of life may not reflect disease progression, but instead reflect the quality of care they have received in the community throughout their lives. Because CAI had been involved in the region for about 2 years, meaning that none of the children in the study had received care in

Table 6.3 Parameter estimates of variables contributing to school performance with the above-average performance group as the reference category

School performance group[a]		*B*	Std. error	Wald	df	Sig.	Exp(*B*)
Not attending school	Intercept	0.088	0.613	0.021	1	0.886	
	CogScore	–0.851	0.280	9.229	1	0.002	0.427
	Mother	0.611	0.973	0.394	1	0.530	1.842
	Grandmother	0.228	1.316	0.030	1	0.863	1.256
	Other	0[b]			0		
Below-average school performance	Intercept	0.147	0.600	0.060	1	0.806	
	CogScore	–0.613	0.252	5.920	1	0.015	0.542
	Mother	–0.023	1.022	0.000	1	0.982	0.978
	Grandmother	1.858	1.119	2.758	1	0.097	6.413
	Other	0[b]			0		
Average school performance	Intercept	0.146	0.593	0.061	1	0.805	
	CogScore	–0.405	0.236	2.933	1	0.087	0.667
	Mother	0.232	0.953	0.060	1	0.807	1.262
	Grandmother	1.092	1.153	0.898	1	0.343	2.982
	Other	0[b]			0		

[a]The reference group is above-average school performance
[b]This parameter is set to zero because it is redundant

the critical first few years of their lives, more children may have died in the older age group because of lack of early care availability, rather than actual severity in comparison to children in areas where care would be available. In addition, because these children may have survived without the same level of care as other comparison groups, they actually may represent a robust group of survivors.

Although no reason is clear for the disparity in gender, the majority of children in the study were girls. Other researchers in this community feel this reflects the general gender makeup in this area, but this has not been described in the literature.

The child disease progression analysis revealed that the disease had not progressed to critical levels in many of the children. The majority, 62 %, of the children in the sample had sufficient CD4 cell count and low viral load and were not yet on medication. This was a surprising finding because these children were at least 6 years old and had had the HIV virus since birth. These results suggest that this group of children could be more resilient to disease effects, successfully living with HIV/AIDS and sufficiently healthy not to require medication.

Regarding psychosocial adjustment, one third of children in the sample demonstrated internalizing behavior problems (either in the borderline or clinical range as compared with same-age peers), using the sub-Saharan norms on the CBCL (Achenbach and Rescorla 2007b). These findings were consistent with a study of Ugandan AIDS orphans in a rural district who also exhibited high levels of anxiety, depression, and anger (Atwine et al. 2005).

Schooling plays an important role in childhood quality of life. The majority of children with HIV/AIDS in this study were attending school, though 25 % of children were not, even though school fees did not have to be paid by caregivers. It has been suggested that cost was one of the largest barriers to attending school for children with HIV/AIDS in Uganda (Nyesigomwe 2006; Whyte 1998). The substantial proportion of children not attending school in our study without the burden of school fees suggests that there are other reasons why they are unable to benefit from an education. This finding is consistent with results of a study commissioned by the Ugandan Ministry of Education and Sports exploring the dropout rates (Nakiyingi et al. 2003). According to the report, 61 % of children enrolled in primary 1 had dropped out by primary 5, with the highest rates of dropout occurring in the first year. Although the perceived reasons for dropout are complex, the most commonly cited hypotheses among community members were the competing attraction of income-generating activities and marriage-related factors. The children who had dropped out most commonly cite the lack of school requirements and the loss of parents as reasons for dropout (Nakiyingi et al. 2003).

6.3.3.1 Caregiving Context

SES did not appear related to relationship of the child and caregiver nor did it decrease as children aged. These socioeconomic results are reassuring, because they demonstrate that children within the sample were not worse off financially if their mother was no longer the primary caregiver. Previous research has reported that taking-in children exacerbates household poverty (Hodge 2008) and that poverty, with this finding being linked to lowered adherence to daily drug regimens among HIV-infected children in Uganda (Bikaako-Kajura et al. 2006). Within our sample, children did not appear to face financial hardship if living with a caretaker other than their biological mother. The financial stability of families in the study may also be due to the involvement of CAI, as the extra assistance that program provides may boost the family's SES.

6.3.3.2 Child Illness Parameters

In this study, children who were on medication did not exhibit lower cognitive functioning in any of the domains examined (Sequential Processing, Simultaneous Processing, Planning, and Learning). These results are consistent with several adult studies within sub-Saharan Africa reporting that ART medication use and the medical support that accompanies it were correlated with increased neurocognitive performance and improved performance in executive functions (Sacktor et al. 2006, 2009). The results from this sample of children suggest that medications may contribute to cognitive resiliency, as well as medical well-being. However, many studies gauging the neuropsychological benefit of medications in children found that medication alone is not sufficient to reverse the inevitable neurocognitive decline that accompanies HIV/AIDS (Koekkoek et al. 2008; Shanbhag et al. 2005).

Another explanation for the cognitive resilience of children in more advanced disease states noted in the current study may be that they are a robust survivor group with a less aggressive form of the disease.

As hypothesized, SES did have an effect on cognitive functioning of children, accounting for 27 % of the variance observed in this study. Children with HIV are at increased risk for developmental disabilities (Speigel and Bonwit 2002), and those who have fewer resources (lower SES) may be in even greater jeopardy of developing cognitive deficits. These results are consistent with the research of Hochhauser and colleagues (2008), in which they found that children in highly stressful environments are at particular risk for HIV-associated cognitive decline.

Of the specific cognitive domains examined, only two, Learning and Planning, were significantly associated with SES. Learning was measured with the Atlantis and Rebus subtests on the KABC-2, which emphasize attention and concentration, the coding and storage of information, and require participants to generate strategies to learn and retain new information (Kaufman and Kaufman 2004). The Planning construct was measured using Pattern Reasoning and Story Completion, subtests evaluating nonverbal reasoning and planning skills as well as hypothesis testing. As a domain, Planning is thought to assess high-level decision making and executive functioning processes (Kaufman and Kaufman 2004). Both of these domains have been shown to be important to successful everyday functioning in children (Kaufman and Kaufman 2004), and the linkage to SES suggests that support, such as it is available through CAI or other similar interventions, may contribute importantly to psychosocial adjustment by bolstering resources available to families (Fig. 6.3).

6.3.3.3 Factors Contributing to Psychosocial Adjustment and School Performance

Externalizing and internalizing behaviors were considered separately in the analyses. Analyses for externalizing behaviors showed that children being raised by someone other than a grandmother or mother had the highest externalizing behavior scores, followed by those being cared for by their mother. Children being cared for by their grandmothers had the lowest average externalizing behavior concerns. These results were unexpected and show the complexity of the caregiving context. Children who were still with their biological mother had been predicted to show the fewest externalizing behavioral concerns; however, if their mother was sick and unable to provide adequate care, the children may have been acting out more. The group of children with their grandmothers exhibited the fewest behavior concerns. This may be due to the grandmother's involvement from the time the child was young, leading to a more secure attachment with his/her caregiver.

The model for understanding predictors of internalizing behavior revealed that both caregiver and cognitive scores were associated with these problems. Children's cognitive scores were the best predictor of internalizing behavior problems. Children who have the ability to employ more sophisticated coping strategies based on their cognitive capabilities may demonstrate fewer internalizing behavior concerns. These results are consistent with theories that psychosocial adjustment is based on

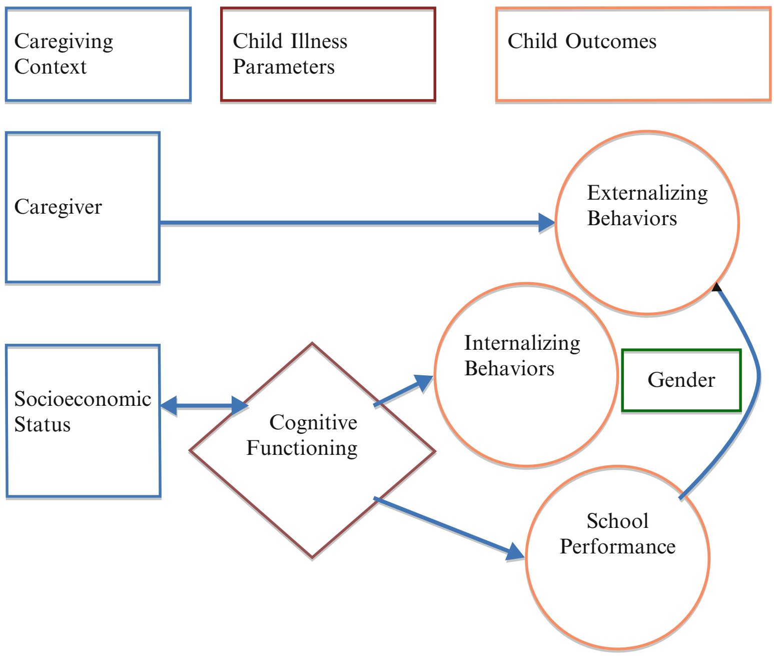

Fig. 6.3 Results: connecting the caregiving context, child illness parameters, and child outcomes. Vectors are provided only for significant covariate relationships in the path analysis. Caregiver category (mother, grandmother, other) is significantly predictive of symptoms of behavioral problems (CBCL externalizing); socioeconomic status significantly predicts overall cognitive ability (KABC-2), which in turn predicts both school performance and emotional well-being for the child (CBCL internalizing). The relationship between school performance and externalizing behavior symptoms is modified by gender, indicated by a significant interaction effect between school performance and gender in predicting externalizing symptoms

the child's cognitive ability to cope with environmental stressors (Engel and Melamed 2002; Wertlieb et al. 1987).

The school performance of children in this sample was correlated, as expected, with their cognitive scores. Children with higher cognitive skills were more likely to be doing well in school. Regardless of who was caring for the child, the child's cognitive ability score was the strongest predictor of school performance. These results are consistent with those found by Franklin et al. (2007) in which children with HIV/AIDS exhibited academic achievement in line with their cognitive ability scores.

6.4 Future Directions

Data presented in this study demonstrates the complexities of the stress and coping model, but supports a broad consideration of possible predictors of increased resilience that can then suggest important directions for intervention. More complex analyses will be needed to support or expand the findings in this chapter within a resource-poor setting such as sub-Saharan Africa, which will require increased sample size and a wider array of variables to be considered within a stress and coping model. On the other hand, results of this study support the careful study of the interactions among possible predictors and the need to carefully select variables for analyses to avoid confounding or other issues with interpretation. Path analysis statistical techniques, for example, provide a methodology for large sample sizes and multiple variables to be considered to better understand the intricate connections and causal relationships facing researchers in resource-poor settings. The well-being and health of the primary caregiver, the coping strategies used by caregivers, and the quality of the patient's relationship with the caregiver are areas suggested by the results of the analyses presented here to be important areas for exploration. Techniques that enhance caregivers coping and family interactions may be particularly effective interventions in the sub-Saharan Africa setting. Better understanding of caregiver characteristics may inform interventions most successfully, particularly because the placement of the child is usually beyond the control of the helping organization.

The successful development of cognitive skills also was suggested by the research presented here, to be an important factor in predicting successful psychosocial adjustment and school performance. Future research should focus on developing cognitive skills, including, for example, more advanced computer-based techniques that can reach a number of children through different mediums from computers to cell phones (Boivin et al. 2010). Because of the effect that cognitive skills have shown to have on important outcome measures such as internalizing behaviors and school performance, the development of interventions in these areas is increasingly feasible and clearly beneficial.

6.5 Conclusions

In Uganda the AIDS epidemic has infected over 100,000 children (UNAIDS 2007), yet there is a paucity of research studying children's quality of life and factors important in guiding the development of meaningful interventions. Data from this chapter demonstrates that Bachanas and colleagues (2001) model of stress and coping can be applied to children with HIV/AIDS within a resource-poor setting and can help to better frame the dynamic environmental and personal factors contributing to child outcomes.

Data presented in this chapter did not reveal a clear relationship between age, SES, and caregiver status. As children's SES increased, it was discovered that so did their cognitive scores regardless of whether or not their infection had progressed to a stage where they needed to take medication. Although more investigation is necessary, SES may represent a neuroprotective factor to be considered in studying and designing interventions for children and their families living with HIV/AIDS in resource-poor settings. The lack of differences between children on and off ART on cognitive test measures also suggests important lines of investigation.

Data presented in this chapter clearly emphasizes the importance of caregiving context (SES and caregiver) and child illness parameters (cognitive functioning, medication) in planning for meaningful intervention for children with HIV/AIDS within a resource-poor setting, such as Uganda. When targeting the well-being of children in Uganda living with HIV/AIDS, organizations should look beyond medical intervention, alone, and recognize the importance of social programs that focus on the caregiving environment and cognitive functioning of the child.

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Chapter 7
Screening for Neurodisability in Low-Resource Settings Using the Ten Questions Questionnaire

Erin E. Lorencz and Michael J. Boivin

7.1 Introduction to the TQQ

Information on child disability in resource-limited settings is prominently lacking. One reason for this is the lack of infrastructure and resources necessary to allow screening tools to be validated using established follow-up measures. One of the screening tools that has been developed for use in such settings is the ten questions questionnaire (TQQ). Published initially in 1986 as part of the International Pilot Study of Severe Childhood Disability (Belmont 1986; Stein et al. 1992), the TQQ has since been subject to very little change (UNICEF 2008). It has become the most widely used screening tool for childhood disability in low- and middle-income countries (Maulik and Darmstadt 2007). The questionnaire is composed of ten items that are asked to the child's caregiver. It includes five questions addressing cognitive development, two questions relating to motor development, and one question each regarding vision, hearing, and seizures. Each item is a yes/no question. The screen is considered to be positive if any of the questions are answered with a positive response. A current version of the TQQ can be found in the appendix of Durkin et al. (1995).

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7.2 Adaptation and Validation of the TQQ in the Cross-Cultural Context

The TQQ has been used in a number of cross-cultural contexts. Perhaps most prominently, the UN has included the TQQ to monitor child disability in its Multiple Indicator Cluster Survey (MICS) used to gather information on the status of women and children in developing nations. Results of the survey in 20 developing countries for 2005–2008 were compared with variables such as education, wealth, and nutrition as well as with sociodemographic information (UNICEF 2008).

The implementation of the TQQ as part of the MICS has led to the detection of a greater number of potential disabilities in children who are not breastfed, are not given vitamin A supplementation, show stunted growth or malnutrition, and have lower education in a range of 18 developing countries (Gottlieb et al. 2009). Countries participating in this survey included Albania, Bangladesh, Belize, Bosnia and Herzegovina, Cameroon, Central African Republic, Georgia, Ghana, Iraq, Jamaica, Mauritania, Mongolia, Montenegro, Sao Tome and Principe, Serbia, Sierra Leone, Suriname, TFYR Macedonia, Thailand, and Uzbekistan (UNICEF 2008).

Other studies have also used the TQQ to identify children at risk for disability and analyzed those who screened positive against potential risk factors. A Saudi Arabian study used the TQQ to identify children up to 15 years of age with childhood disability (Milaat et al. 2001). Additional information was gathered in order to gain a general epidemiological understanding of disability in the region, including variables such as birth order, familial disability, and etiology of disease as perceived by the family. Risk factors for disability were also identified under the assumption that those screened positive were actually disabled as verified by clinical neurological exam. These risk factors included families with many children, parental age, and familial disability. The point prevalence of disability as detected by the TQQ was 36.7 per 1,000 children. Both the prevalence and the risk factors associated with disease as reported in this study were similar to those that are known in Saudi Arabia.

In Southern Nepal, a study using similar methodology found that children small for gestational age and preterm at birth were more likely to have a positive TQQ screen (Wu et al. 2011). In this study, an additional question was added to the TQQ to address behavioral problems. The question asked specifically about tantrums, aggression, and relational difficulties.

In the three of these studies, the TQQ was used to identify children with disability rather than as a screen that identifies children at risk who are then followed up with diagnostic measures. This approach may be appropriate for gathering epidemiological information, including prevalence and risk factors in a population. However, using the TQQ in this way is limited by its inability to diagnose childhood disability. Therefore, if an intervention is planned to offer the children with disability, more thorough measures should be employed before that takes place, as is the case in the studies below.

7.3 Use of the TQQ as a Screening Tool

Others have used the TQQ to identify children at risk for disability and then confirm the findings with follow-up testing, as described below.

7.3.1 Screen for Intellectual Disability and Mental Retardation

In Karachi, Pakistan, the TQQ was used to screen for intellectual disability in a study looking at prevalence of and risk factors for mental retardation in children 2–9 years old (Durkin et al. 1998). Modified nonverbal scales in the Stanford–Binet intelligence scales along with a physician's assessment were used to follow up with children who screened positive on one or more of the questions on the TQQ. The results of the validation component of this study are discussed below under Sect. 7.4. The physician's assessment included developmental history and observation of the child's language, following instructions, motor development, and general behavior. Final diagnosis of mental retardation was based on the presence of both cognitive and adaptive deficits as well as IQ. Severity of disability was determined by IQ. Prevalence of serious mental retardation was 19.0 per 1,000 children (95% CI 13.5–24.4) and 67.3 per 1,000 children (95% CI 48.9–81.8) for mild retardation.

Factors associated with a diagnosis of mental retardation were lack of maternal education, a history of perinatal difficulties, neonatal infections, postnatal brain infections, or traumatic brain injury, and malnutrition at the time of the study. For cases with confirmed disability, only 3.7% of children had been given an evaluation or services previous to identification using the TQQ. Thus, this study demonstrated the TQQ's utility in identifying new cases of disability in this population.

7.3.2 TQQ Screen for Neurological and Developmental Disability in Africa

The TQQ has been used to screen for intellectual disability in children living in rural Northern Province, South Africa (Christianson et al. 2002). The TQQ was followed up by an evaluation by a neurodevelopmental pediatrician and clinical geneticist. The children who were determined to be at risk for disability upon clinical evaluation were then given the Griffiths Scale of Mental Development and a test of general intelligence quotient (GIQ), the latter of which determined the severity of developmental disability.

Further classification of the disability was then carried out as the researchers gathered information about disease etiology and associated disabilities. The prevalence of moderate intellectual disability in this population was 29.1 per 1,000 children, while that of severe intellectual disability was 6.4 per 1,000 children. While numbers with which to compare these are lacking for this population, it is similar to estimated rates of childhood intellectual disability in Zambia, a nearby nation in Southern Africa.

Another team in KwaZulu-Natal, also in rural South Africa, used the TQQ as a preliminary screen for childhood disability in children under 10 years of age (Couper 2002). For children under 2 years of age, six questions asking about development were added in order to make the screen more appropriate for younger children. The children who screened positive were followed up for diagnostic measures by occupational therapists. The disability rate in this population was 60 per 1,000 children, similar to that in similar locations throughout the country.

A rural Kenyan study looked at prevalence of neurological disability and impairment in children ages 6 through 9 years (Mung'ala-Odera et al. 2006). Follow-up was done using a battery that tested both nonverbal and verbal abilities, including intellectual and developmental maturity, information processing and impulsivity, auditory short-term memory, processing, visual-motor coordination, and visual-spatial perception, long-term memory, receptive vocabulary, verbal comprehension, and picture-word associations. A physical exam and neurological exam were also performed on each child. Comprehension, expression, and the child's phonological system were tested as the speech component. Final diagnosis of neurological disability was based on the child's *z*-score in relation to other children of comparable age. Neonatal insult was found to be a significant risk factor for neurological disability.

7.3.3 Screen for Vision/Hearing Disability

Most of the above studies also addressed hearing and vision disability that was screened by each of the individual vision- or hearing-related questions. In Kenya, all children were evaluated for visual and auditory disability regardless of whether or not they screened positive on either of the two sensory disability questions specifically (Mung'ala-Odera et al. 2006). Likewise, all children in the Pakistan study were evaluated for sensory impairment (Durkin et al. 1998). In Northern Province, South Africa, all children underwent a visual exam but only those determined by the clinician to be at risk for auditory impairment underwent diagnostic hearing tests (Christianson et al. 2002).

Presumably because of the specific questions about vision and auditory problems as well as the broad nature of the other questions, some of the children who screened positive actually had a disability that was strictly auditory or visual in nature. However, one limitation shared by these three studies was that no analyses were included as to whether specific TQQ questions showed a relationship with purely auditory or visual impairment. This sort of determination would be difficult since the number of children diagnosed with purely sensory deficits was low and there was significant overlap between groups of children with sensory impairment and those with cognitive impairment in all three studies. Nevertheless, this effect demonstrates that the TQQ may be helpful in screening for sensory deficits, effectively flagging children in need of follow-up clinical evaluations.

7.4 Validation of TQQ as Screen for Disability

When one is screening a population, both the sensitivity and specificity are important. Sensitivity is an indication of how well the screen detects cases, while the specificity measures the ability of the screen to limit detection to only actual cases. A high sensitivity in this case ensures that few screened children with actual disability will be missed, and a high specificity means that fewer resources will be used to follow up and diagnose children who do not have a disability. Ideally, a screening tool will have both a sensitivity and specificity as close as possible to 1.00, which means that the tool is able to detect all cases of disease (no false negatives) and only detects cases where disease is actually present (no false positives). Durkin has shown that the TQQ can be helpful as a screening tool in various settings (Durkin et al. 1994) because of the reasonable sensitivity and specificity of this measure when validated against subsequent clinical neurological and developmental evaluation. Studies carried out in communities in Bangladesh, Jamaica, and Pakistan showed varying utility for the TQQ in different communities.

7.4.1 Overview of Methodology of Cross-Cultural Validation Studies of TQQ

In Bangladesh and in Pakistan, those who screened positive along with a random sample of those screened negative on the TQQ were administered follow-up testing. The follow-up testing used the nonverbal scales of the Stanford–Binet intelligence scales. The Denver Developmental Screening Test (DDST) was used for those who were unable to be tested with the Stanford–Binet. In addition, caregivers for each child also completed the Child Disability Questionnaire. The children's intelligence quotient scores were used to classify them into mild, moderate, or severe ranges of mental retardation.

In Jamaica, the DDST was used to assess 2–5 year-old children, and the Woodcock-Johnson Psycho-Educational Battery, McCarthy Scales of Children's Abilities, and Peabody Picture Vocabulary Test were administered to children ages 6–9 years. Developmental history, language function, ability to follow instructions, motor skills, and behavioral factors were all assessed by a physician, and diagnoses were based on consensus of the psychologists and physicians (Thorburn et al. 1992).

In rural North India, a validation study was performed portions of the Wechsler Intelligence Scale for Children (WISC) ages 6–9, the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) for 2–5 year olds, and the Expressive

Language Milestone Scale (Singhi et al. 2007). The results of these validation studies are listed below in the following sections, according to the type of disability detected.

7.4.2 General Cross-Cultural Disability Findings with TQQ

Sensitivity for serious disability of a general nature was 1.00, while specificity was 0.74 in India (Singhi et al. 2007). Sensitivities for disability in Bangladesh, Jamaica, and Pakistan were reported according to specific type and are given below. Specificity for any serious disability was 0.92 in Bangladesh, 0.85 in Jamaica, and 0.86 in Pakistan (Durkin et al. 1994).

7.4.3 Cognitive Disability

Sensitivity for cognitive disability of any severity was 0.82 in Bangladesh and 0.84 in Pakistan, but only 0.53 in Jamaica (Durkin et al. 1994). However, sensitivity for Jamaican children with a serious cognitive disability who also had another noncognitive disability increased to 1.00, while this effect was not seen in sensitivity analyses at the other two sites. It is not surprising that children with noncognitive disabilities in addition to their cognitive disabilities may be easier to detect. However, the observation that this was only true in one community out of the three indicates that there may be a difference in the etiology or manifestation of disability most often encountered in each community. It may also suggest differences in perception of disability by the caregivers. The TQQ was perfectly sensitive to severe cognitive disability in Bangladesh, Jamaica, and Pakistan (Durkin et al. 1994).

7.4.4 Motor Disability and Seizures

In Bangladesh and Jamaica, sensitivity was 1.00 for serious motor and seizure disabilities, while it was 0.84 in Pakistan (Durkin et al. 1994). Sensitivity for seizures was 1.00 in all three populations.

7.4.5 Auditory and Visual Impairment

In Jamaica, the sensitivities of the TQQ for vision and hearing disability were both perfect, while it was much lower in Bangladesh (0.57 for vision and 0.46 for hearing) and Pakistan (0.59 for vision and 0.70 for hearing). Durkin notes that this could be due to differences in the proportion of children with sensory disabilities who had already been diagnosed through other referrals and services and received treatment. In Jamaica, where children with serious vision or hearing disabilities are more likely to have been previously identified, caregivers are much more likely to identify their child with a serious sensory impairment as disabled on the questionnaire. Notably, children in all three populations were three times more likely to screen positive if they had already been treated for their visual or auditory disability than if they had not (Durkin et al. 1994).

7.4.6 *False Positives in TQQ Screen*

Many children who turned out to be cases of false positives for sensory disability were found to have other problems, such as infections, malnutrition, and mild cognitive disability in Durkin and colleague's (1994) study, arguing for the need to follow up such cases, even if the actual sensitivity of the TQQ is low in some situations. Eliminating those two questions from the survey actually decreased the sensitivity for all disabilities (Durkin et al. 1994.). In India, half of those classified as false positives on any of the questions had minor speech problems or malnutrition-related delays (Singhi et al. 2007). Although these children did not have actual sensory disabilities, resources used to follow up on such children did find significant developmental needs.

7.5 Validation as a Screen for Neurological Impairment in an African Context

Mung'ala-Odera's prevalence study of 6–9 year-old children in rural Kenya also included a validation component (Mung'ala-Odera et al. 2004). Those screened positive by the TQQ, along with a sample of those screened negative, were followed up with the list of tests and medical evaluations described above. Sensitivity and specificity, respectively, were 70.0% and 71.4% for moderate to severe cognitive impairment, 71.4% and 98.3% for motor impairment, 100% and 92.9% for epilepsy, 87.4% and 87.5% for auditory impairment, and 77.8% and 98.0% for visual impairment. Positive predictive values for each category of disability were low, however (≤33%).

7.6 Cultural Considerations and Adaptation

Assessment of child development can be difficult in countries outside of Europe and North America when the tools frequently used are developed in these contexts. Gladstone's work in Southern Malawi showed that a number of specific milestones routinely used to measure child development are inappropriate for children in rural sub-Saharan Africa (Gladstone et al. 2010). For example, North American expectations of intelligence often emphasize literacy and counting, while the Malawian ideals focused on obedience and independence. Making toys was seen as an appropriate way of measuring fine motor skills in Malawian children, while North American tests often assess this by the child's ability to write or stack blocks (Gladstone et al. 2010).

Clearly, some western-specific measures of child development cannot be extrapolated to all populations. However, the TQQ asks questions that are sufficiently general and may be less culturally dependent. The question addressing cognition asks about comprehension when a task is given to the child. Children's activities are compared to other children their age so that in any context, a caregiver can interpret the question based on what is culturally appropriate in that situation.

Some issues remain, however, related to appropriateness of the TQQ in different populations. When adapted to a rural Ugandan context, one translator noted that questions about delays in achieving developmental milestones are likely to be construed in relation to the child's siblings (E. Ssebyala, personal communication, April 18, 2011). It is not common to keep records of when Ugandan children start to walk, for example, unless it is significantly delayed in relation to when older siblings did so. If there is more than one delayed child in the family, or if the child with the impairment is the first born, this could make the screening tool less sensitive. Conversely, those who had children who achieved milestones significantly early could falsely identify subsequent children as delayed.

In administering the TQQ in rural Kenya in the Kigiriama language, Mung'ala-Odera found that some questions were misunderstood by caregivers (Mung'ala-Odera et al. 2004). As suspected was the case in Uganda, because estimation of developmental milestones typically uses siblings for comparison, some mothers whose other children started doing things earlier said that the child being screened was delayed when in fact the child was not (Question 1). Other insights revealed that the notions of hearing and attention were easily confused when a question was asked about the children having trouble hearing (Question 3). The question was sometimes interpreted as asking about inattentiveness rather than hearing difficulty. A third question (Question 4) also turned out to be ambiguous when translated, confusing the intended meaning of "understanding instructions" with "obeying instructions."

7.7 Use and Validation in Rural Uganda

We added the TQQ to a list of neurodevelopment assessment tools while studying neurodevelopmental disability in HIV-positive rural Ugandan children 2–6 years of age. The other measures used included the Mullen Early Childhood Scales, Color Object Association Test (COAT), Achenbach Child Behavior Checklist (CBCL), and Early Childhood Vigilance Test (ECVT). We analyzed the data according to each of the TQQ questions' correspondence with items in each of the tests, which are described below.

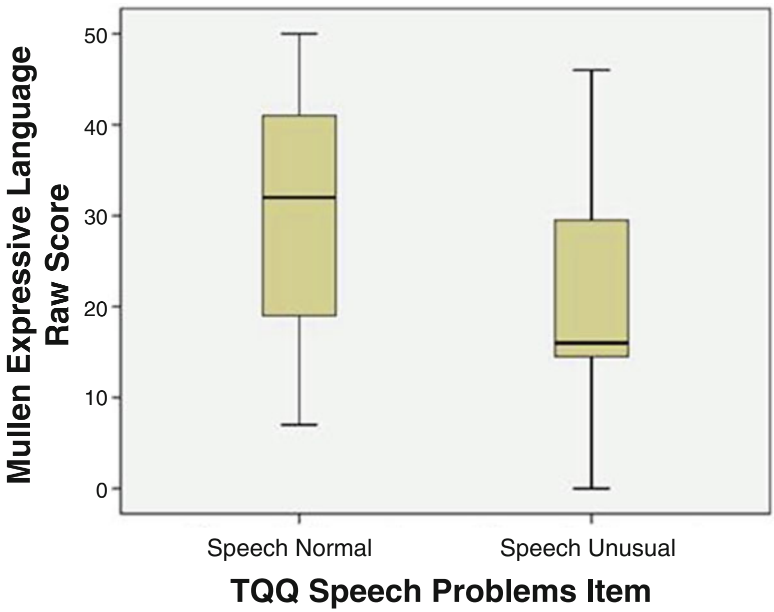

Fig. 7.1 These are *box* plots comparing preschool rural Ugandan HIV-positive children screening positive or negative on the TQQ "Speech problems" item, on the Mullen Early Learning Scales Expressive Language scale. The *upper and lower* boundaries of the *box* represent the first and third quartile of that group, and the *box* is bisected at the median (second quartile). The *upper and lower* range of scores for each group extends above and below the *box* for that group. The TQQ speech difficulties positive and negative groups differed at the $P<0.05$ level using a Mann–Whitney test of between-group nonparametric statistical difference. Speech problems on the TQQ were predictive of poorer Mullen Expressive Language performance

The Mullen is intended for use in assessing children from birth to 68 months and provides scores for the developmental domains of Gross Motor (up to 36 months), Visual Reception, Fine Motor, Receptive Language, and Expressive Language (Mullen 1995). The Early Learning Composite provides a measure of *g*, the general measure of fluid intelligence thought to underlie cognitive ability in general. It is derived from the standardized *T* scores of the four cognitive scales (Visual Reception, Fine Motor, Receptive Language, and Expressive Language). In validation studies, the Early Learning Composite has a correlation coefficient of 0.70 with the Bayley Mental Development Index measure. The TQQ question about difficulties with speech showed a significant correlation to the Mullen domains of Expressive Language, Receptive Language, Visual Reception, and Fine Motor, while the question about difficulties in walking was significantly related to the Mullen Fine Motor and Gross Motor domains. The TQQ question about learning and the question about listening to instructions showed a correspondence to Mullen Expressive Language (Figs. 7.1, 7.2, 7.3, and 7.4).

The Mullen provides an alternative dimension since it gives a scaled score rather than a dichotomous outcome. Therefore, sensitivity and specificity

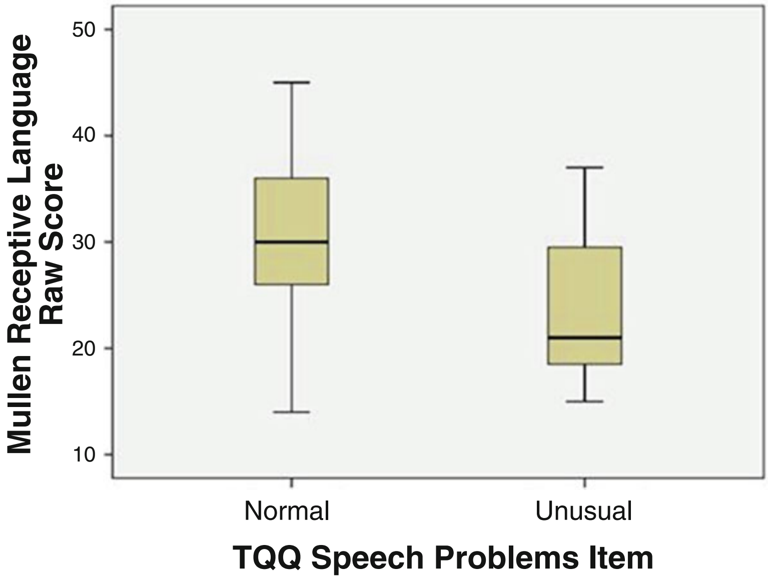

Fig. 7.2 These are *box* plots comparing preschool rural Ugandan HIV-positive children screening positive or negative on the TQQ "Speech problems" item, on the Mullen Early Learning Scales Receptive Language scale. The *upper* and *lower* boundaries of the *box* represents the first and third quartile of that group, and the *box* is bisected at the median (second quartile). The TQQ speech difficulties positive and negative groups differed at the $P<0.01$ level using a Mann–Whitney test of between-group nonparametric statistical difference. Speech problems reported on the TQQ were predictive of poorer Mullen Receptive Language performance

analyses would not be appropriate for analyzing the data. All five domains of the Mullen corresponded with a positive screen on at least one TQQ item. However, each one of the TQQ questions was not significantly correlated to a specific Mullen domain.

The COAT is an experimental test which evaluates declarative (explicit) memory in children during the toddler and preschool years (Jordan et al. 2008). The principal outcome measures from the test are the immediate memory score and an overall total recall or learning score. Poorer performance on the COAT was significantly correlated to the TQQ question about hearing difficulties.

The results of the analysis of the TQQ with the Mullen and COAT which showed a significant relationship are listed in Table 7.1.

The **CBCL** is one of the most widely used instruments in **child** and adolescent psychiatry and pediatrics (Achenbach 2010; Achenbach and Rescorla 2000). It has previously been adapted to the Ugandan context by our study team (Bangirana et al. 2009). The principal outcomes from this assessment are total number of internalizing (e.g., depression, anxiety, somatic complaints) and externalizing symptoms (e.g., aggression, rule breaking, obstinacy/defiance, withdrawn). The TQQ showed no correlation with the CBCL.

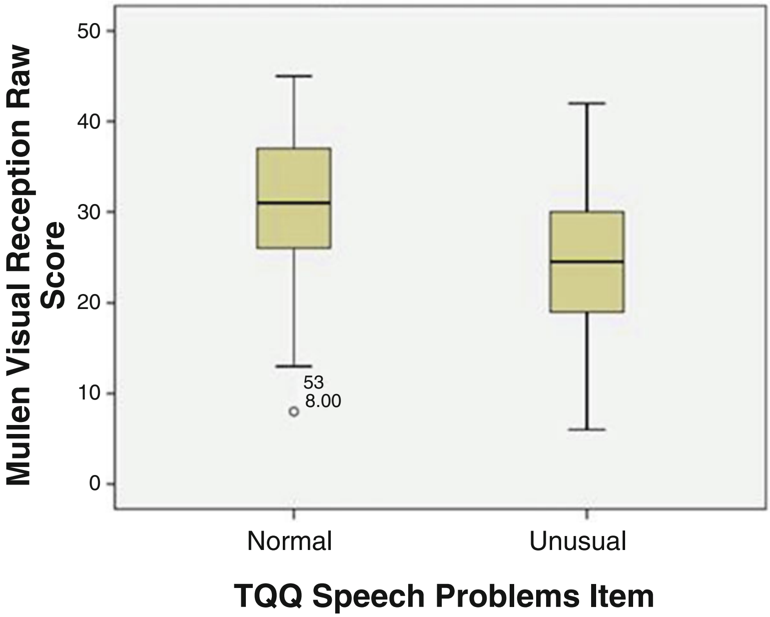

Fig. 7.3 These are *box* plots comparing preschool rural Ugandan HIV-positive children screening positive or negative on the TQQ "Speech problems" item, on the Mullen Early Learning Scales Visual Reception scale. This scale includes a number of test items pertaining to visual-spatial and object-recognition memory. The *upper* and *lower* boundaries of the *box* represent the first and third quartile of that group, and the *box* is bisected at the median (second quartile). Individual outliers are plotted below the lower bracket for the range of scores for that group. Speech problems reported on the TQQ were predictive of poorer Mullen Visual Reception performance ($P < 0.05$)

The ECVT is an experimental measure of vigilance used in preschool children to evaluate sustained attention (Goldman et al. 2004; Zelinsky et al. 1996). We found no significant relationship between the ECVT and the TQQ.

Considering the correlation with the Mullen and COAT items, the TQQ may be useful in screening for developmental disability as well as memory deficits in children with HIV. The lack of correspondence of the TQQ to either the CBCL or the ECVT suggests that the TQQ may be less helpful when screening for psychiatric manifestations of disease, as compared to neurological, neurocognitive, or neurodevelopmental dimensions of disability or delay.

7.8 Summary

In some cases, the TQQ was used without follow-up measures to identify potentially disabled children. This approach is most practical for gathering epidemiological information such as prevalence and risk factors in a large number of

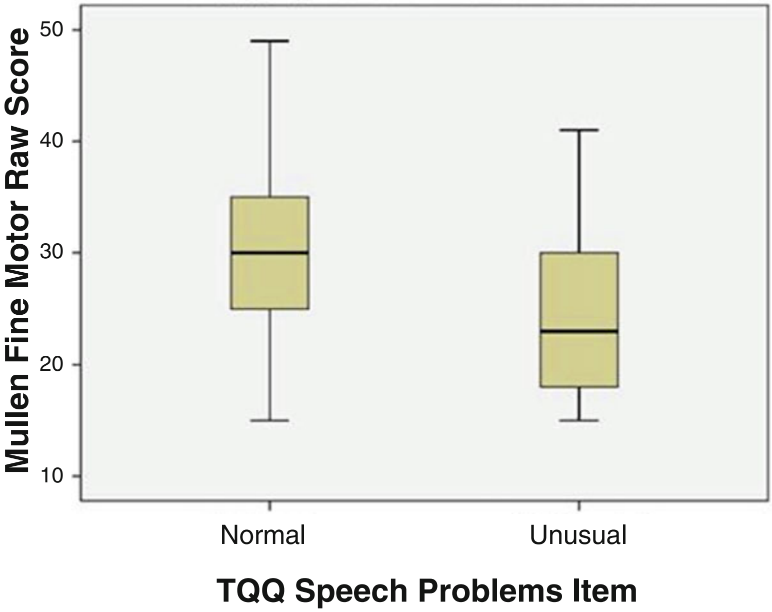

Fig. 7.4 These are *box* plots comparing preschool rural Ugandan HIV-positive children screening positive or negative on the TQQ "Speech problems" item, on the Mullen Early Learning Scales Fine Motor scale. This scale includes a number of items testing the child's ability to remember spoken actions or demonstrated motor movements. The *upper* and *lower* boundaries of the *box* represent the first and third quartile of that group, and the *box* is bisected at the median (second quartile). The TQQ speech difficulties positive and negative groups differed at the $P<0.05$ level using a Mann–Whitney test of between-group nonparametric statistical difference. Speech problems reported on the TQQ were predictive of poorer Mullen Fine Motor performance ($P<0.05$)

Table 7.1 Relationship of TQQ items to Mullen and COAT items

TQQ question	Number positive ($n=113$)	Mullen Early Childhood Scales	Color Object Association Test
#9: Unusual speech	20 (16.8%)	Expressive language ($p=0.04$)	Total memory ($p=0.028$)
#8: Understandable speech	25 (21%)	Expressive language ($p=0.004$) Composite ($p=0.01$)	Immediate memory ($p=0.023$) Total memory ($p=0.009$)
#5: Walking difficulties	25 (21%)	Gross motor ($p=0.01$)	–
#3: Hearing difficulties	15 (12.6%)	Receptive language ($p=0.01$) Composite ($p=0.01$)	–
#7: Learning difficulties	18 (15%)	Expressive language ($p=0.026$) Visual reception ($p=0.035$) Fine motor ($p=0.013$)	–

P value is based on student *t* test for two independent samples for one-tailed test on age-adjusted (*T*) scores children, such as in the UNICEF report, where follow-up on all the positive screens would be exceedingly difficult. It should be emphasized that results of these studies indicate which children are *at risk for* disability rather than which children have a disability. Others have used the TQQ to screen for disability in order to identify groups who should be assessed further. This is a practical and efficient use of resources that eliminates the costly and time-intensive process of thoroughly testing each child in a population. The TQQ has been validated in several low-resource settings for identifying children with disabilities. The sensitivity has been shown to be adequate as a screening tool, while the data also show that its usefulness is limited to that purpose. Those identified to be risk for disability should be referred for diagnostic evaluation with more thorough methods. This is particularly important as TQQ false positives often appear to relate to the prevalence of other health issues that may require immediate attention.

7.9 Discussion and Conclusion

The TQQ is an effective tool for identifying childhood cognitive, motor, sensory, and seizure disability in low-resource settings. In validation studies, the TQQ consistently detected most cases of disability. The format and general nature of the questions are such that the questions can be translated and adapted for use in a variety of cultures without relying on specific questions that may be culturally inappropriate.

The data show that using the questionnaire to gain information on specific types of disabilities may be overestimating its function. One explanation for this is that tests such as the Mullen used by professionals to assess specific disabilities are quite different from the observations that caregivers make. Observation of a delay in one developmental area may actually be an indicator of disability or delay in another area. As a result, the TQQ is useful to identify children at risk for disability, but not necessarily as a predictor of a specific kind of disability. This is consistent with Durkin's findings discussed above that the TQQ questions concerning vision and hearing impairment were important components for detecting non-sensory disability as well (Durkin et al. 1994).

As neurodisability research in resource-limited settings increases, the TQQ may prove to be an important resource, particularly for large-scale screening in the context of epidemiological surveys or studies. Continued validation work as well as information about reliability and consistency in observer ratings and individual item analyses will be required. Further research investigating the utility and validity of the TQQ in different low-resource settings and in different cultures and with different languages also will be necessary to better understand the limitations of the tool and whether reasonable adjustments to existing items or further inclusion of other items would be necessary.

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Chapter 8
Language Development in Sub-Saharan Africa

Katie Alcock and Nuala Alibhai

8.1 Introduction

The study of language development in sub-Saharan Africa has a variety of motivations. The topic may be of interest for theoretical and/or for applied reasons. Even more than the study of cross-cultural developmental psychology, crosslinguistic studies have the power to identify situation-dependent and situation-independent aspects of development, a fact which has been realized for some years (Slobin 1985). In addition, studying children's language is, of course, highly relevant for other aspects of development, and most researchers in behavioral development would acknowledge the tight link between language development and other aspects of development. Although here we will not examine literacy and will only review a small proportion of the literature on spoken language in school-age children where it elucidates other points, early spoken language abilities are highly predictive of preschool and school performance in typically developing children, including those at risk and those in poverty (Hoff 2003; Locke et al. 2002; Molfese et al. 2001; Noble et al. 2005; Pan et al. 2004; Rescorla et al. 2000), and in a setting where children have limited opportunities for education, it is important to maximize school readiness.

Language development is also arguably one of the most rapid aspects of development, and shows great variability between children (Bates et al. 1995; Fenson et al. 1994, 2000), as well as being sensitive to a number of negative factors that are more common in sub-Saharan Africa, including HIV infection, cerebral malaria,

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meningitis, and other causes of brain injury and dysfunction (Baker et al. 1996; Bates et al. 1997; Brouwers et al. 2001; Davis et al. 1997; McNeilly 2005; Wolters et al. 1997). Its study, therefore, in recent years has become an essential part of studies of child development outcomes following exposures and interventions in the prenatal period and infancy (Abubakar et al. 2008a, b; Prado et al. 2010; Stoltzfus et al. 2001).

To date, most studies of language development in this region have clearly been motivated by linguistic theory. Many though have not extended their findings to applied outcomes or have examined language outcomes in an applied or intervention setting but have failed to take account of language theory or language differences. Several chapters in this volume and other papers (Baddeley et al. 1995; Greenfield 1997; Holding et al. 2004; Prado et al. 2010) have highlighted the dangers of insufficiently adapted or culturally inappropriate test instruments when examining nonverbal cognitive development. These dangers are even greater in the field of language development because the task that children have in learning their native language is radically different depending on the language itself.

Grammatical development appears to be particularly sensitive to differences between languages (Bates and MacWhinney 1987), but even small lexical differences can also have a great deal of influence on the results of research. For example, mistranslation or failure to consult authorities on children's native language can lead to invalid single test items, which in a small test battery can make a study far less sensitive. Stoltzfus et al. (2001) found that language and motor development were sensitive to iron supplementation and antiparasitic treatments in preschool children in Zanzibar. In this case, both aspects of children's development were assessed using short checklists intended for use with a wide range of ages. In such cases, the meaning of each single item is crucial given the relatively small number of items covering different developmental aspects and age ranges. Lack of reference to local linguistic authorities for these types of assessment approaches easily can lead to mistranslation of items. Reduced sensitivity of assessment measures or increased variability in solicited responses may affect findings, resulting in negative findings with respect to effects on language development. These issues can only be magnified as studies attempt to examine language development in a more sophisticated manner, in older children, and in more detail.

Given the paucity of research in language development in sub-Saharan Africa, it is worth briefly discussing what priorities are generally posed in the available research. Do researchers prioritize studying aspects of language development that are theoretically "interesting" or "rare," or do they contrast aspects of language development in the sub-Saharan region with those aspects within European languages? Are these approaches desirable or would it be preferable to examine development in the regional languages spoken by most people or in some of the fastest-growing languages? Are we yet at the stage where we can begin to compare similar languages in different areas of the sub-Saharan Africa region or provide a general overview of language development across the area?

8.2 Approaches to Reviewing the Data on Language Development in Sub-Saharan Africa

A number of possible approaches can be taken to review the data available on language development in sub-Saharan Africa. Two related approaches would be a geographic approach, treating each subregion separately, or a language family approach; the latter could be particularly interesting given the number of language families unique to sub-Saharan Africa. Unfortunately, both of these approaches still suffer from a paucity of studies, with data predominantly available from more wealthy and populous regions as compared to more rural or resource-poor settings, little or no research available from some regions or language families with large numbers of speakers, and a frequent reliance on studies with very small numbers of participants.

In identifying studies for inclusion in this review, two searches were carried out, in the databases PsycINFO and LLBA, including the terms "language development" or "language acquisition" and (1) the names of every sub-Saharan African country and (2) the names of every language spoken in sub-Saharan Africa by more than three million people. Some languages, however, for which studies were retrieved from the first search, were not represented in the second group. Likewise, no studies of language acquisition were published that were carried out in any Central African country—between Zambia in the South and Chad in the North.

Given the more functional approach taken by many researchers in child development in the region, data could also be classified according to the purpose for which they were collected—whether theoretical research on language development as part of larger studies of cognitive development, to examine provision or effectiveness of educational or therapeutic interventions, or in order to conduct studies of health or other influences on language development.

While some studies of language acquisition have been carried out for applied purposes or as outcome measures in studies of a variety of impacts on children's development, most have been carried out for "pure" theoretical reasons or in attempts to interlink cognitive and language development. This we feel is a useful distinction; we will first examine studies with a more theoretical motivation and add to this a brief review of applied studies where language development was a focus and which either specifically examine language delay or impairment to compare children subject to an impact or intervention on language outcomes or to advance methods of assessing language development.

Broadly, language development can be characterized as beginning with phonological development within the first year of life, continuing to the acquisition of a larger and larger lexicon as children enter the second year of life, and proceeding to word combinations and syntactic development later in the second year of life and beyond. Clearly, these periods of development overlap, with, for example, phonological development certainly not being completed by the time children start to grow their vocabulary. This chronological and linguistic typography is also a helpful classification for examining a very broad field of language development. Because some studies of one aspect of development have data from children outside the core age range typically studied for this area of development, we will not strictly apply age boundaries.

8.3 Very Early Development, Especially Phonological Development

8.3.1 Very Early Speech Development

Few studies of the onset of speech in Sub-Saharan Africa have been carried out, but Blount examined the early speech and language development of children in Kenya acquiring Luo. The children studied displayed babbling at around the same age and following the same pattern recorded in other cultures (Blount 1971, 1976).

8.3.2 Acquisition of Tone

Many languages in the region are tone languages. Researchers have taken advantage of this fact to examine a variety of aspects of tone. Tone acquisition in general, but with a wealth of data from the region, is well reviewed in Demuth (1995). Tone is used in languages to indicate lexical or grammatical distinctions—both types of usage are found in African languages.

Research from African languages elucidates a variety of aspects of the acquisition of tone. One study looked at the early perception of tone in Yoruba, a Nigerian language with lexical tone, examining head-turn preference among infants aged 6–8 months, growing up in London, and exposed or not exposed to Yoruba from their parents. At this age, infants hearing Yoruba pay more attention to pitch changes within words than infants hearing only English, but only when those pitch changes have lexical meaning. Both infants and adults were more sensitive to some tones than others, the same tones for both age groups (Harrison 2000).

Children learning Ga, spoken in Ghana, appear to gain control of suprasegmental information, including lexical tone, before fully controlling segmental output (Kirk 1973), meaning that they can accurately render the tonal changes in an utterance before they can produce all consonants and vowels accurately. Likewise, children learning Chichewa, spoken in Malawi, can produce tonal patterns before some segmental and morphemic patterns are produced accurately (Chimombo and Mtenje 1989). Lexical tone was also found to be acquired early in Zulu (Suzman 1991). More salient tones (in this case, the high tone) also appeared to be acquired earlier both in Chichewa and in Sesotho (Demuth 1989b, 1991; Suzman 1991).

Some aspects of tone, however, have been shown to be acquired later or are more problematic in acquisition. These may be aspects that require contextual use of tone. In Chichewa, tone changes occur along with morphosyntactic markers when utterances are negated, but these were not fully acquired by the children up to age 6 years in Chimombo and Mtenje's (1989) study. Suzman (1991) also found that children acquired the correct use of tone in grammatical constructions relatively late.

Demuth (1995) looked at tone marking on verbs in Sesotho in children aged 2–3 years. In Sesotho verb roots can have high, low, or no tone, though high tone is more frequent. In some contexts, verbs with no tone are realized as low and, in some contexts, as high. The study results demonstrated that children used high tones correctly earlier on verb roots, achieving 75% correct between 2 and 3 years of age, while low tones increased through this age group starting at 35% correct. However, some expected high tones were produced as low tones and some inconsistencies were still evident by the age of 3 years. More consistency was found in verb subject markers (in which persons one and two are marked with low tones and person three with high) though these were more frequent than individual verb roots, and marking was more consistent. Because of tone sandhi (contextual tone rules), the same verb root was more likely to be heard with different attached tones than were subject markers. In Sesotho, high tone could also "spread" through verb roots and subject markers. Children, however, appeared to find these contextual rules particularly difficult, both for verb roots and for verb subject markers, until they reached the age of about 3 years. Considering this study and all of the findings from different languages across the region, it seems clear that context-dependent tone is much more difficult for children than non-context-dependent tone, with frequency and consistency across linguistic segments playing a large part as well.

8.3.3 Acquisition of Clicks

As click consonants are almost uniquely found in Southern and Eastern African languages, data from the region are necessary to examine their acquisition. Surprisingly, there are very few studies related to this issue, with some available data collected to examine perception of nonnative sounds by children and adults outside the region. Best and McRoberts (2003) found that English-exposed infants and adults were able to distinguish Zulu clicks but that adults were not able to distinguish nonnative non-click sounds and concluded that the clicks are so different from native English phonemes that they are not assimilated to English phonemes (while the other nonnative phonemes are assimilated), so that as infants and children grow older, they do not lose the ability to distinguish the clicks.

Clicks also seem to be acquired slightly later than other native consonants in languages which have clicks. Naidoo (2003), working on Zulu, and Lewis and Roux (1996), working on Xhosa, found that clicks were produced accurately later than other consonants. Lewis and Roux noted that children aged 1.6–5.5 years, acquiring Xhosa as their first language, substituted clicks for other clicks, simplified clicks to become non-click consonants with the same place of articulation, or reduced clicks by removing an aspect of articulation such as nasalization. Likewise, Demuth (2007) noted that the only click in Sesotho was late acquired, with most children substituting a /k/ until around the age of 3 years.

8.3.4 General Acquisition of Phonology

As well as the tones and clicks found in languages in the region but not in all languages of the world, some other less usual aspects of phonology are found in some sub-Saharan African languages and have been the focus of study. Jakobson (1968) originally proposed that phonemes found in more languages will be acquired earlier than those rare phonemes found in few languages. Nwokah (1986) tested this proposal by studying a group of phonemes (especially doubly articulated consonants) found only in a few West African languages, examining their use by children aged 2–4 years acquiring Igbo, in Nigeria. The order of acquisition of these "hard" phonemes seemed to be predicted partly by rarity but more closely corresponded to the difficulty of articulating the phonemes, the frequency with which the phoneme occurs in the language, and the presence of parallel (e.g., voiced vs. unvoiced) forms of the phoneme. Likewise in Hausa, also in Nigeria, consonants that had been reported as late-learned in other languages (such as liquids) or those that had difficult articulation (the glottalized consonants) were also mastered later (Dresel 1977).

Mowrer and Burger (1991) examined the mastery of phonemes among Xhosa-speaking children aged 2–6 years, comparing them with English-speaking children, also from South Africa. Xhosa-speaking children made fewer errors at ages comparable with English-speaking children (and this difference was significant when comparing phonemes that exist in both languages), but the same phonemes (largely fricatives and liquids) were difficult to master for both groups. Naidoo (2003) also found that Zulu-speaking children aged 3–6 years produced longer and more accurate strings of syllables than their English-speaking peers. Both Xhosa and Zulu have more long, multisyllabic words, but with simpler syllabic structure within the syllables (fewer clusters and fewer closed syllables, ending in a consonant) than English. In line with the data from Xhosa and Zulu, Demuth (2007) found that accuracy for Sesotho segmental production was high at an early age. Similarly, this was attributed to simpler syllabic structure than in European languages. Nevertheless, some segments are commonly replaced with others (e.g., trilled /r/ replaced with a non-trilled consonant), consonant harmony has been observed (where articulation of one or more consonant changes so that more consonants in the word are articulated at the same place), and where syllables begin with a complex onset, part of this is sometimes deleted. These processes all resemble processes found in young children, at the stage where they cannot yet articulate all phonemes correctly, learning to speak other languages.

For the researchers studying the developmental neuropsychology of language, it is crucial to understand the typical course of language development—but this is rarely documented within the region. Wolf-Schein et al. (1995) comment that they developed a phonological assessment for two Zimbabwean languages (Ndebele and Shona) and suggested its use should be confined to children over 7 years of age, because typically developing children of this age are assumed to have acquired all the phonemes of their language. However, they note that developmental data have not been collected for these languages nor for other languages in the region.

8.4 Lexical Development and Language Development in Middle Infancy

The study of lexical development is a very useful tool in, for example, studies of general intellectual ability—examining vocabulary size is an often-used proxy for IQ (Kihara et al. 2009; Marchman and Fernald 2008). Many applied studies also investigate the rate of lexical development so this is potentially a very useful area of research.

Lexical development is of interest when addressing a variety of theoretical debates too, and this has been the motivation behind the majority of studies of lexical development in the region. Debates in the study of lexical development include the composition of early vocabulary, the reasons why some types of words might be learned earlier than others, and how different underlying cognitive concepts might be expressed differently in different languages.

8.4.1 Early Vocabulary and Related Skills

Two research groups have examined the composition of early vocabulary among children in sub-Saharan Africa, specifically children learning Kiswahili and Kigiriama in Kenya (Alcock et al. 2005) and Ngas in Nigeria (Childers et al. 2007). Typically nouns predominate in early production vocabulary, and this is true across many languages studied to date (Bornstein et al. 2004). Consistent with this general finding, Alcock and colleagues (2005) found that among Kenyan children, nouns predominated in production, while verb comprehension equaled noun comprehension. Childers et al. (2007), however, reported that among Nigerian children, verbs dominated in early vocabulary and suggested that linguistic features or cultural aspects of child-rearing in Nigeria may have led to this finding. Alternatively, differences in sensitivity of assessment measures for noun counts also could contribute to differences across these two studies, again emphasizing the need to develop assessments that take into account developmental differences in language development (e.g., a very frequent early type of label for objects as nouns may be sounds, rather than actual words).

Childers et al. (2007) also found that joint attention behaviors were just as closely linked to lexical development—both noun and verb comprehension and production—as in previous studies in developed regions. Although parent and caregiver joint attention behaviors may be different in this culture, this did not seem to affect the relationship between joint attention and vocabulary. Mastin and Vogt (2011a, b) also examined links between different types of joint attention and vocabulary development in rural and urban Mozambican families. While children in all families appeared to have similar relationships between joint attention abilities and vocabulary comprehension, relationships for early vocabulary comprehension did appear to differ between the two settings in Mozambique.

In four different areas of sub-Saharan Africa, a Communicative Development Inventory (CDI) method has been used for assessment of children's vocabulary development (Alcock et al. 2005; Childers et al. 2007; Mastin and Vogt 2011a, b; Prado et al. 2011). We discuss this under the heading of lexical development, because this is the main use of this type of assessment, but it is also used in studies of gesture and grammatical development. CDIs are parent-completed checklists which ask parents to report which of a list of gestures, words, and grammatical forms is closest to what their child produces and/or understands at that moment in time. They rely on parent knowledge of their child's current and emerging language and communication skills but do not rely on long-term memory of the child's behavior. Alcock and colleagues (2010a, b) have used CDIs successfully in more than one developing country setting with illiterate parents as informants and have adapted CDIs used in Kenya for related languages in Malawi, a neighboring country (Prado et al. 2011). The CDIs hold great promise for the assessment of language development in the region.

One criticism of CDIs is that children can only be reported to produce the classes of words that are included on the CDI, so that if a class of words is omitted, no related data will be collected. Although children may not produce a representative sample of their vocabulary during a session of recorded or transcribed spontaneous speech, spontaneous speech samples are a very helpful way to analyze children's early vocabulary, though these approaches cannot, of course, measure vocabulary comprehension. Blount (1969) summarized the early words spoken by four children learning Luo, in Kenya. First words seemed to start with caregivers' names and moved on to demands and words for food. Animals, body parts, and common household and environmental objects, all represented in most CDIs, were also found in early production vocabulary in Luo. A few verbs and function words were seen, but as in Kiswahili and Kigiriama, these were fewer than nouns in production.

8.4.2 Acquisition of Specific Classes of Vocabulary Items

Color terms: Because Berlin and Kay (1969) first noted a hierarchy of color terms, with some languages representing more basic color terms than others, researchers have been interested in how children acquire color terms. In Setswana, spoken in

Botswana, borrowed English color terms were noted to be replacing Bantu-origin color terms over time. This is notable particularly because Setswana has fewer basic color terms than English. Setswana roughly follows Berlin and Kay's original hierarchy but with a few exceptions. Older Setswana-speaking children (ages five through ten) were asked to name colors and to produce as many color terms as they could. Children used English terms for colors but the majority of color terms used were those within the Setswana repertoire of basic color terms. Even where English color terms were used, the gaps in the Setswana color vocabulary were not filled (Davies et al. 1994).

Odor terms: Mouele (1997) examined acquisition of olfactory terms by children learning the Wanzi language, a Bantu language spoken in Gabon. He suggested that like Berlin and Kay's hierarchy of color terms—basic color terms that do not refer to objects and higher-order terms that use an object name to indicate its color—there is also a hierarchy of odor terms. He noted that the odor terms he defined as "basic" can be heard in children's speech and songs.

Deixis: Abubakar (1986) examined the acquisition of deixis terms (terms that indicate directionality) among children 4 through 7 years of age learning Hausa. In Hausa, the preferred adult deixis terms for objects along an axis oriented in the direction speakers and listeners are facing are different than expected in western cultures. Objects further away are termed "in front," while those closer to the speaker being termed "in back." This is the opposite of situations in English where an object further away, but concealed by another object, is termed "in back." A greater proportion of Hausa-speaking children were observed to use mature deixis terms at a younger age than English-speaking children. It was suggested that the Hausa deixis system may be simpler to acquire than the English system, as it is consistent and does not require speakers to take into account interrelationships between objects—only the positioning of an object with respect to a speaker.

8.5 Syntactic Development

The study of syntactic development is highly divisive and theoretically polarized. We make no attempt to explain nuances of the various theories in this chapter, but will try to paint broad strokes and describe the results that have been found to date. It is rare in the study of child syntax in sub-Saharan Africa that one language has been studied by more than one research group. This pattern of data collection, together with differing aims and theoretical starting points, makes it hard to compare results from different research groups within the region. Nevertheless, the majority of studies have examined acquisition of Bantu languages, so we will also briefly address some relevant aspects of Bantu syntax. In addition, a small amount of comparable data from different research groups studying the same language is becoming available (notably from Zulu, Sesotho, and Kiswahili).

8.5.1 Acquisition of Noun Morphology

Several studies have examined the acquisition of Bantu noun morphology. In addition, Blount (1988) examined the development of plural morphology in Luo, the only non-Bantu language to be studied under this heading.

Bantu nouns largely carry morphology as prefixes, and in these languages, nouns are marked for noun class. Noun class is a system related to grammatical gender but with more possible categories. There are at least 10 classes in most languages, and there can be more than 20. This number of classes could be viewed as inflated, because singular and plural are counted separately (some noun classes have no plural, or the corresponding plural class varies between nouns or between languages.) In most Bantu languages, at least one or two noun classes have null prefixes on the noun. Typically, some semantic as well as phonological commonalities between members of a noun class exist (Contini-Morava 1996).

In early speech, children learning Bantu languages tend to omit noun class markers (Alcock et al. 2010b; Demuth and Ellis 2009). It is very rare for children to substitute an incorrect noun class marker, but in some contexts in some Bantu languages, omission from a noun that can take a marker can be grammatically correct. Demuth and Ellis (2009) found that children learning Sesotho (where prefix omission is allowed in some contexts) were more likely to omit noun class prefixes correctly than incorrectly (taking into account phonology and grammatical agreement), once they had reached the stage of mostly articulating the prefixes. They, however, also had a stronger tendency to omit prefixes when they were using nouns on which their caregiver also omitted prefixes.

Both Demuth and Ellis (2009) and Suzman (1996) found that phonological characteristics of words were important in predicting whether children would produce noun class prefixes or not. Demuth and Ellis noted that children were more likely to produce prefixes preceding a monosyllabic noun root (few Bantu words are monosyllabic), while Suzman examined acquisition in a variety of related languages and noted that, in Zulu and other Ngoni languages, prefixes always include an initial vowel and are multisyllabic, while in the Sotho languages they do not. Zulu-learning children include more noun class prefixes at an earlier age, possibly because the initial vowels are easier to pronounce but also because in sentence-medial positions, a word-initial vowel tends to be articulated while the word-final vowel of the previous word is dropped. Suzman contrasts 50% use of noun class prefixes at age two with Demuth's (1988) observation that noun class prefix use only starts at this age. Suzman and other writers on Zulu also observed use of partial prefixes (such as articulation of the initial vowel of a VCV prefix).

Blount's (1988) study of noun morphology acquisition in Luo also examines the role of phonology. Noun morphology is expressed in suffixes in this language; contextual phonological processes accompany these suffixes. Blount tested children aged 3–6 years with novel nouns and found that only by age six were children able to add suffixes with some degree of success to these novel nouns. He concluded that children seemed to be using a method of analogy to do this and that at younger ages they had not analyzed the relationship between the noun and its plural or possessive.

Of course, input patterns are important in examining children's learning of morphology. Ziesler and Demuth (1995) examined the pattern of noun class prefixes in child-directed Sesotho. It was found that prefixes were dropped in child-directed speech, and although many nouns were unprefixed due to being in a noun class that has zero prefixes, most nouns with prefixes that were genuinely omitted were not in contexts where this was grammatical. Older child and adult caregivers all dropped prefixes, although, as the sample size was limited to two children, it is difficult to draw firm conclusions about differences between children's output based on their input.

8.5.2 Acquisition of Verb Morphology

Although many areas of acquisition of syntax and morphology of verbs are of great interest, probably the area that has been most debated is the acquisition of tense and agreement markers on verbs. Children in many languages are observed to omit these markers and to produce a nonfinite verb form in place of finite, marked verbs. A variety of theoretical models seek to explain these omissions, and most relevant to data from the region is the Agreement/Tense Omission Model (Schutze and Wexler 1996) in which children are hypothesized to consider verb agreements to be optional in their productions.

Deen (2003) examined the acquisition of Nairobi Kiswahili. In Kiswahili, verb subject and tense morphemes are marked on verbs by prefixes (in that order). Deen suggested that initially children produce bare verb stems, followed by subject agreements without tense, then tense without subject, and finally full verb forms with both subject and tense agreements. It is not clear whether the two middle stages (subject without tense, tense without subject) are really distinct. Although Deen stated that the reduction in production of verbs with subject but without tense is significant across stages, it is not clear whether the decline is statistically significant (Deen 2001). Deen concluded that the data from acquisition of Nairobi Kiswahili cannot be explained by adult patterns or by prosodic features of verbs, but were compatible with the Agreement/Tense Omission Model. Additional data, however, from Coastal Kiswahili and a related language also spoken in Kenya, Kigiriama, combined with the Nairobi data, showed that individual adults vary as do the dialects of Kiswahili in how frequently they omit the subject and tense markers.

Alcock and coworkers (Alcock et al. 2004) found that children's production of zero, one, or two markers was significantly correlated with both linguistic maturity and the proportion of verbs they heard in the input that had a missing subject or tense marker. Children learning Nairobi Kiswahili heard more verbs with tense but no subject than children learning Coastal Kiswahili or Kigiriama, and they also produced more verbs with tense but no subject, while children learning Coastal Kiswahili or Kigiriama tended rather to produce verbs with subject but no tense. The latter are rare in these languages/dialects but might be produced by children based on metrical stress within the word (Demuth 1994), where a word with a strong-weak-strong-weak syllable pattern is reproduced as strong-strong-weak.

Gxilishe et al. (2007) also examined the acquisition of subject agreement in Xhosa, another Bantu language with similar verb structure, in South Africa. As in other such languages, not only must verbs carry a subject marker, but this must agree with the noun class of its referent. Use of subject markers increased between the ages of 12 and 39 months, and as in other languages (Connelly 1986; Demuth 1999), omissions rather than substitutions were responsible for the overwhelming majority of errors. Children's use of noun class markers on nouns was compared with their use of subject markers on verbs, and it was suggested that the differential word order found in combinations of noun and verb, whether neither, both, or one is marked, was significant and pointed to a generative explanation. Data for adult use of prefixes or of word order would help to clarify this case.

Chimombo (Chimombo and Mtenje 1989) examined the parallel development of tone and morphosyntax in Chichewa negatives. Children tended to overgeneralize a lexical negative ("I don't want," which is not appropriate in many contexts) in the same way that English-learning children use "no" in contexts such as "no Daddy" meaning "I don't want Daddy to do that." The three children studied varied in the order in which they acquired different types of negative markers and constructions, but as with acquisition of noun morphology in the Bantu languages, negative verb markers are prefixes and are largely omitted or reduced in immature language.

8.5.3 Acquisition of Verb Aspect, Voice, and Argument Structure

The acquisition of the passive voice, like the acquisition of verb tense, has been of intense interest to researchers examining crosslinguistic differences in language acquisition. Children's use of the passive is restricted in some languages, notably English, German, and Hebrew, before the age of about 6 years, and this late use has been attributed to a selective maturation of some types of passive structure (Borer and Wexler 1987).

Data from the region, from Sesotho (Demuth 1989a) and Kiswahili and Kigiriama (Alcock et al. 2012), suggest that full passives, including those with non-actional verbs, can be acquired much earlier in situations where the passive is heard frequently by children. Demuth (1989a) and Suzman (1987) have previously suggested that some additional features of passive use in Sesotho and

Zulu, respectively, might also increase the likelihood of children using the passive early. For example, in Sesotho, all questions that interrogate a patient are expressed using the passive, and in Zulu passives mainly occur in perceptually salient events where a physical action affects the patient. However, in Sesotho and in Kiswahili and Kigiriama, early use of the passive in non-actional contexts is widely seen—suggesting directly observable actions are not necessary for the early acquisition of the passive—and in Kiswahili and Kigiriama, these types of questions can appear in either active or passive. The common feature of the passive in Sesotho, Zulu, Kiswahili, and Kigiriama is that it is highly frequent in the input.

Crawford (2005) suggested that Sesotho passives are not truly productive passives but may be lexicalized, and hence, it is still possible to analyze the acquisition of Sesotho passives in terms of late maturation of productive passives. Alternatively, she analyzed Sesotho passives not as true passives but as applicatives or adversity constructions (neither of which would be subject to the maturational constraints she hypothesizes apply to passives). To test this, Crawford (2009) examined comprehension of passives in Sesotho-speaking children aged 5–6 years, looking at both "long" (similar to passives with a by-phrase) and "short" passives, and found that children's comprehension of long passives was not as good as their comprehension of actives or short passives. However, Demuth et al. (2010) tested 3-year-old Sesotho-speaking children on comprehension of actional and non-actional long passives and active sentences and found that comprehension of all types of sentences was equivalent, leaving the poor performance of older children in Crawford (2009) somewhat hard to explain.

Another marker of voice found in Bantu language verbs is the applicative. Applicative suffixes in Bantu languages work to change the argument structure of a verb either from transitive to ditransitive (e.g., changing the meaning from "Mama cooks food" to "Mama cooks food for the children") or from intransitive to a meaning similar to a locative or goal (from "The rain is falling" to "The rain is falling on the crops"). There are word order constraints on the applicative in Bantu languages (which vary between languages), and there are also argument structure implications (the number of arguments required by a verb being roughly equivalent to the number of nouns in the sentence). Demuth et al. (2003) examined children's learning of these constructions, finding that at 3 years of age, children produced correct word order at above-chance levels but that even by 8 years of age, children were not performing at adult levels. Analysis of adult speech found that these constructions are relatively rare in Sesotho, and Demuth et al. (2003) suggested that children may also be showing lexical construction effects in their learning of this construction.

As we suggested at the beginning of this section, the acquisition of syntax is a highly controversial area with many hotly defended viewpoints. It is fortunate that researchers from various theoretical positions are starting to research different but related languages (or in some cases the same language) although it would be useful to see more research in this area on non-Bantu languages.

8.6 Language Socialization

Schieffelin and Ochs (1986) define language socialization as both socialization of children through the use of language and socialization of children to use language. Under this category, researchers have been especially interested in how child-directed speech (CDS) differs from adult-directed speech and whether either the level of simplicity or the affective characteristics of CDS differ from the adult language. Sub-Saharan Africa, like many developing regions, has particular interest for those studying socialization partly due to widespread traditional child-rearing practices and beliefs and their difference from those in Europe and North America, where the majority of research in child development takes place, but also due to the higher number of daily caregivers which children in sub-Saharan Africa can have.

Researchers have taken advantage of caregiving both by paid caregivers and by older children to examine intra-cultural variation in language socialization. Nwokah (1987) examined the difference in child-directed speech by "maids" (older children aged 8–12; about two-thirds are girls. These are not children of the family, who care for an infant for around half of each day for their keep and a small amount of pay) versus mothers to 12-month-old infants in Igbo-speaking families in Nigeria. Both affective and linguistic characteristics of mother versus older child "maid" speech were different. Mothers spoke more, had longer MLUs, and used more declaratives and yes/no questions, while older children used more imperatives and Wh-questions. Affective characteristics differed less, but mothers used more teasing and older children more warnings and prohibitions. Several other categories of positive affect did not differ between caregivers. Mothers described children's activities and behavior more but in a neutral way.

Rabain-Jamin (2001) also examined mothers' and older children's speech in Wolof-speaking families with 2-year-old infants and older siblings (3–10 years old) in Senegal. Mothers' speech directed towards infants was predominantly either assertions or directives, and the younger group of siblings (3–4 years) also used a high proportion of directives in conversation with the infants.

These two studies examined interactions with children of different ages as well as from different language and cultural backgrounds. Blount (1971) examined longitudinally the progression of child-directed speech as infants get older in two Luo-speaking families in Kenya with infants who were initially 6 months old and continuing until the infants were 14 months of age. As the infants grew older, child-directed speech grew more frequent, with the biggest difference seen between the 6- to 11-month and the 12- to 14-month periods of age. Also in this latter period, adults changed their speech prosody from that of adult-directed speech more often than they did when the infants were younger. However, adults frequently used one-word utterances in their child-directed speech (percentages of utterances that were a single word ranging from 59 to 85% by child and age). Luo does not have many polysyllabic words and generally does not have single-word sentences in the way that Bantu languages tend to have, and the mean number of syllables per child-directed utterance (range 1.5–2.2) also suggests that adults are directing incomplete sentences to infants, although Blount does not give the MLU of child-directed utterances.

Geiger and Alant (2005) also examined qualitative differences in adults' speech to infants and young children and how it changed as children grew older in a village in Botswana. They concluded that much of the interaction and practice in prespeech skills came from infants' interactions with older children rather than adults, and those older children were also likely to be the ones to attempt to elicit speech from verbal infants through prompts and games. Interaction with preverbal infants was seen as eccentric.

Demuth (1986), however, observed that Sesotho-speaking adults frequently used prompts to teach children linguistic and social routines and found that parents held a very wide variety of views on the usefulness of verbal interactions with children and young infants. Some of the adults felt speaking to young infants was helpful, and learning to speak well was a valued part of learning Sesotho. Likewise, Rabain-Jamin (1998) also examined prompting and reported on speech in mothers of Wolof-learning infants, aged 16–28 months. Not only did mothers frequently use these language socialization strategies, but also they adapted their speech to the linguistic maturity of their child. Geiger and Alant (2005) warned researchers against applying findings from non-African settings to "African culture," but the differences between these studies highlight the fact that there is no one "African" set of parenting beliefs on language socialization.

8.7 Applied Studies of Language Development

If the study of typical language acquisition in sub-Saharan Africa is patchy, then the study of language impairment is almost nonexistent, as is provision for children with language impairments. This section is arranged thematically, starting by examining child language assessments that have been developed for the region, continuing by describing characterization and intervention for developmental language impairment, followed by a brief description of the situation on the ground for practicing speech and language therapists in East Africa.

8.7.1 Language Assessments

Direct assessment of language abilities in children in developing country situations is challenging, even with slightly older children with some experience of school or preschool, partly because children often are not accustomed to any kind of testing situation. Demuth et al. (2010) tested Sesotho-speaking 3-year-old children's comprehension and production of passives. Overall, they found that 44% of children either would not speak in an experimental situation or could not identify pictures during a warm-up task, even though all of the children were attending formal preschool. This finding highlights the need for language assessments that take into account children's unfamiliarity with the testing setting.

CDIs (Fenson et al. 1994) are one alternative means of assessing children's language development that do not rely on children's cooperation, as already noted, because they are parent-completed checklists. There are reports of CDIs for three language groups in the region—for Kiswahili and Kigiriama, related Bantu languages spoken in Kenya (Alcock et al. 2007); for Chichewa and Chiyao, Bantu languages related to each other (and also moderately closely related to Kiswahili and Kigiriama) spoken in Malawi (Prado et al. 2011); and for Ngas, spoken in Nigeria (Childers et al. 2007)—as well as a report of CDI use for unspecified language(s) in Mozambique (Mastin and Vogt 2011a, b). Childers et al. and Mastin and Vogt did not specify the specific CDI administration method used in their studies, though Alcock and colleagues (Alcock et al. 2007; Prado et al. 2011) were able to use an interview method to obtain data from largely illiterate parents in Kenya and Malawi. This method was found to be valid in Kenya and has also been used in other settings where many parents cannot read (Alcock et al. 2010b; Hamadani et al. 2010).

In multilingual clinic settings, and in particular in settings where the majority of children seen may have additional disabilities and moderate to severe impairments, a functional checklist of communicative behaviors may be helpful. Tuckley and Shah (2005) reported on a checklist which combined assessment with locally available materials, observation, and parent report that they have used successfully in Kenya.

For slightly older children, directly administered language assessments which avoid asking the child to speak may be possible to use with children unfamiliar with the testing setting. Picture Vocabulary Tests (PVTs) are widely used in Western settings (Dunn 1965, 1997), and children need only to respond by pointing to one picture of a selection of target and distractor pictures. Successful adaptations have been made into some African languages. Holding et al. (2004) constructed a PVT suitable for children aged 5–7 years speaking a small number of related languages in coastal Kenya. Nampijja et al. (2010) further adapted this assessment for Luganda-speaking children 5 years of age. In both cases, not only must the vocabulary items be adapted, but also the picture stimuli must be locally appropriate—Kenyan coastal stimuli proved not to be suitable for Ugandan lakeside communities. Alternative approaches to testing vocabulary suitable for primary school-age children (usually, in this setting, aged seven at minimum) include an odd-one-out task (Roller 1988) and a matching task (Alcock et al. 2010a). Both of these require a verbal response on the part of the child, but generally, it is only a one-word response, and they may be more suitable for assessment of complex, hard-to-depict, vocabulary.

Wolf-Schein et al. (1995) developed a phonological assessment for children 7 years of age and older speaking Shona or Ndebele in Zimbabwe. Naudé et al. (2007) suggested using elicited conversation to examine language development of children learning English in multilingual settings in preschools in South Africa, because they have observed that children's spontaneous conversations with each other are rarely in just one language. A highly targeted and comprehensive assessment of language abilities for children aged 8–9 years was developed by Carter and colleagues (Carter et al. 2003, 2005) for Kigiriama-speaking children in coastal Kenya. The assessment includes syntax, phonology, comprehension, and higher-level language.

8.7.2 Studies of Language Impairment in the Region

We will not extensively review studies examining effects on cognitive development of various biological insults, such as infection, brain injury, or malnutrition, that, as part of a larger test battery, studied language development. However, some researchers have examined language impairment as a primary outcome measure or as an idiopathic condition.

Carter et al. (2003, 2005) found that children who were hospitalized for severe malaria, on assessment between 2 and 6 years after discharge, were significantly poorer than control children on tests of most aspects of language ability—comprehension, syntax, semantics, and higher-level language (metalinguistic ability)—with the exception of pragmatic ability and phonology. Children with a history of infection were two standard deviations poorer than control children on language comprehension, syntax, and higher-level language. Law (2000) examined risk factors for language impairment among West African families living in London, where children of these families are at higher risk of referral for language impairment services. Parents and professionals had differing opinions and expectations on best parenting practices. Many parents were unsure of the value of talking to their preverbal babies and thought that they would disadvantage their child by speaking to them in their native language. Parents also were stressed by work and money pressures and felt strongly about the lack of the informal childcare structures that they would be accustomed to using in their countries of origin.

Demuth and Suzman (1997) analyzed the language development of a child learning Zulu who had been referred for delayed speech and who had been found to have no hearing difficulties and no other reason for developmental language impairment. He was compared with a control child and found to have impairments in phonology, morphology, and syntax, presenting a fairly common pattern for a child diagnosed with specific language impairment. He used far fewer noun and verb agreements, with his morphology not resembling use at a younger age by the control child.

8.7.3 Rehabilitation and Special Education Settings

Children in need of language rehabilitation and specialist assistance with spoken language are not just those with diagnosed speech and language difficulties. Many children, who are affected by HIV or AIDS, either themselves or through the loss of parents, are also in need of intervention. Levin and Haines (2007) examined the language input to children in a multilingual orphanage in Johannesburg, South Africa. In contrast to parental input in traditional settings in the region, as examined in the studies of language socialization referenced above, paid caregivers in the orphanage did not initiate or respond verbally to children except occasionally to use a child's name or give an instruction, and they did not respond verbally to children's vocalizations. In this setting, because of the ages of the children in the institution, there were no older children who could participate in language socialization.

One major issue in therapy settings in the region is the multilingual nature of many sub-Saharan African societies. Jordaan and Yelland (2003) surveyed speech and language therapists in South Africa where either children frequently are hearing multiple languages or the therapist and child do not share a common language or both. The most common home language in their sample was Zulu and the majority of children studied in English in preschool or primary school. They found that most therapists failed to deliver services in children's first language, mainly because parents requested therapy in English, despite current recommendations being that therapy should be provided in a child's first language. Parents appeared to wish to maintain children's bilingualism, but were not provided with advice on this from speech therapists. The authors noted that some children in their study were labeled as language impaired or delayed when their only language difference was poorer development in English (their second language) than monolingual English-speaking peers—a not very surprising finding in young bilinguals whose main exposure to English was at school. Naudé et al. (2007) emphasized the importance of assessing second language performance, though Jordaan and Yelland (2003) cautioned that second language delay, alone, may not be a language delay in the general sense in which that diagnosis is usually understood.

Issues of resources in rehabilitation and therapy in the region loom large. Researchers from outside the region may not have a clear view of the exact impact of these issues and what the picture is like for speech and language therapists in sub-Saharan Africa. It is for this reason that we now present an overview of pediatric speech and language therapy services in Kenya and, more broadly, in East Africa, contributed by the second author, who is a practicing speech and language therapist in this area.

The speech and language therapy service. The speech and language therapy service has existed in Kenya since the late 1960s. The country depends on expatriate therapists or Kenyans who have received training in Europe or the USA. Professional sustainability is a major issue in this context (Marshall 2005).

Currently nine speech and language therapists see children with communication disorders. They are located in the biggest cities of Nairobi and Mombasa. Access to the services is limited to the people living in the city or its outskirts. Sometimes wealthier East Africans who can afford travel and accommodation costs will travel from neighboring towns and countries to access the service.

Service locations and demand. The majority of the therapists are based in private hospitals, rehabilitation centers, mainstream, and special educational settings, including preschools, as well as domiciliary settings. Two of the nine therapists are Voluntary Service Overseas volunteers from the UK. These therapists are based in nongovernmental organizations and work predominantly alongside community-based rehabilitation or Educational Assessment Resource Centre workers. Most of the services in Kenya are private and users have to pay consultation fees. In Mombasa, an average of 84 children are treated in a year by each therapist. However, in a busier hospital setting, such as the one at Mulago Hospital (Uganda), around 200 children are seen between one speech and language therapist and one assistant (Jochmann 2005).

Referrals. The majority of the referrals in Mombasa are self-referrals or from pediatricians, general practitioners, special need teachers, class teachers, audiologists, or other speech and language therapists. Awareness of the service and its provisions seems to be increasing. In Mombasa, there is a 6-month waiting list for services. There is a need to generate awareness about the field, but that must go hand in hand with developing the services available to respond appropriately to the need.

Types of clients. A wide range of clients are seen including those with medical conditions associated with communication disorders—AIDS, cerebral malaria, epilepsy, encephalitis, infections with febrile convulsions, meningitis, otitis media, and pneumonia.

The children who have been diagnosed with a chromosomal syndrome associated with communication disorders include those with Down syndrome and fragile X syndrome. Other conditions include cerebral palsy, ADHD, autistic spectrum disorder, hearing impairment, cleft lip/palate and velopharyngeal anomalies, delayed speech and/or language development, speech and/or language disorders, voice disorders, stammering, traumatic head injury, general learning disabilities, dyslexia and other literacy disorders, and feeding and swallowing problems.

Types of services. Most of the therapy provided by therapists to children with communication disorders is on an individual basis, working closely with the parent or caregiver. A significant part of therapists' time also is taken up with training other professionals (medical, but mostly educational) in skills to enable them to facilitate the development of communication skills in the children with whom they work. There are forums where speech and language therapists meet with other professionals on a regular basis to provide knowledge and skills, and speech and language therapists also run parent support groups.

The recently formed ASLTEA (Association of Speech and Language Therapy, East Africa) holds a conference every 2 years. The primary aim is to provide continuing education for East African speech and language therapists by guest lecturers.

Challenges. Speech and language therapists face many challenges, including the following:

- Lack of research in the area of speech and language development, either in the Kenyan context or in local languages (e.g., Kiswahili).
- Lack of assessment and therapy tools (modified or otherwise) suitable to this context, though an articulation test is currently under development in Kiswahili.

- Lack of awareness of the profession among other professionals and the general population.
- Lack of opportunities for speech and language therapists to train locally in Kenya. Jochmann (2006) also summarized very similar issues facing speech and language therapists in Uganda. In 2008, however, VSO partnered with Makerere University in Uganda and established the first degree program in Speech and Language Therapy in East Africa.
- Lack of opportunities for continuing professional development. The courses available are difficult to access because of costs of travel, and speech and language therapists often have to rely on internet sources, journals, and occasional visiting lecturers.

8.8 Future Directions

This review of typical language development and applied studies of language development and disorders in the region leads to a number of conclusions about areas of research that are lacking. Geographically, the majority of research has been carried out in Southern Africa, in addition concentrating on a few of the Bantu languages spoken in that region. Research from elsewhere in Africa (primarily East Africa) also concentrates on Bantu languages; a small body of research from West Africa represents very poorly the large population and widely spoken languages of that subregion. Within the regions that are well represented, non-Bantu languages are poorly studied; a small amount of data are available from Luo in Kenya, a Nilo-Saharan language, but no data are from the southern African Khoisan languages or the East African Semitic or Cushitic languages, some of which have a few millions of speakers.

Another area of research that could be potentially very fruitful, and has to some extent begun in a modest way (Alcock et al. 2005, 2012; Suzman 1996), is the comparison between related but subtly different languages in the region. Languages of completely different classes have so many differences that comparisons can sometimes not be made in a valid way, but very closely related languages can have subtle differences that affect, or do not, the course of acquisition and can therefore teach us much about what influences the rate at which children acquire certain aspects of their native language.

Although some work has started in this area (Alcock et al. 2010b; Carter et al. 2003; Holding et al. 2004; Tuckley and Shah 2005), development of low-cost, appropriate, easy-to-administer language assessments for the region is crucial. Some of the assessments may be more suitable for research settings and some for clinical settings, but key features are adaptability and the existence of some kind of norms. Where two languages are closely related, we have found that it is not necessarily a great challenge to adapt an assessment from one language to another—initial adaptation to a new language family is the larger step (Alcock et al. 2007; Prado et al. 2011). Norming is another issue and is, unfortunately, highly resource intensive. In clinical settings, a less sensitive screening tool may have to be a compromise. Recent work on assessment of children in the sub-Saharan Africa region in a variety of more general areas of ability (Abubakar et al. 2007, 2008a, b; Alcock et al. 2008; Holding et al. 2004; Jukes and Grigorenko 2010; Nampijja et al. 2010) can also now be expanded to language assessments.

Finally and crucially, what we know about typical language development in the region needs to feed into speech-language therapy and educational services. Many of the publications in the field are conference proceedings, theses or dissertations or are otherwise difficult to obtain. We hope that this review will bring together some of the research and be a useful summary for applied practitioners in the region.

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Chapter 9
Psychosocial Aspects of Malnutrition Among African Children: Antecedents, Consequences, and Interventions

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9.1 Psychosocial Aspects of Malnutrition Among African Children: Antecedents, Consequences, and Interventions

Childhood malnutrition is a major public health problem worldwide, placing a heavy burden on already vulnerable communities by increasing the risk of mortality, morbidity, and cognitive and behavioural problems (de Onis and Blossner 2000; de Onis et al. 2004; Wachs 2008). Malnutrition can be characterized by either undernutrition (inadequate intake of calories or nutrients) or overnutrition (especially excess intake of calories). The current chapter critically evaluates the empirical evidence on the psychosocial factors that play a contributory role in the development of childhood malnutrition among children in Africa. Further, it discusses the evidence linking childhood malnutrition and adverse cognitive, social, emotional, and educational outcomes. Lastly, the chapter highlights psychosocial interventions currently in use to tackle this pandemic. The review of the existing empirical evidence is guided by the extended UNICEF food-health-care framework on malnutrition (Engle et al. 1999; UNICEF 1990) and Wachs systematic framework on multiple determinants of malnutrition (Wachs 2008).

9.2 Epidemiology of Malnutrition

Undernutrition is extremely prevalent in developing countries, affecting millions of children worldwide, especially in Africa and South Asia (Stephenson et al. 2000). Recent estimates indicate that more than 60 million children in Africa are stunted

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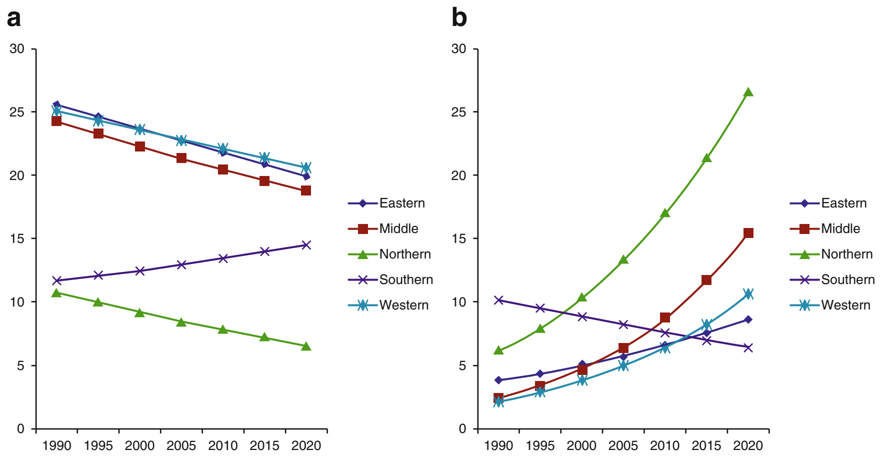

Fig. 9.1 Trends in the prevalence of over- and underweight in African regions for the period 1990–2020. These figures were generated based on the data from de Onis et al. (2010, 2011) (**a**) Underweight <2sd and (**b**) Obesity >2sd

(an indicator of chronic malnutrition) and these numbers are projected to rise to around 64 million children by 2020 (de Onis and Blossner 2000; de Onis et al. 2004). These figures indicate that Africa will not achieve the goals of halving the rates of malnutrition as set out in the millennium goals (de Onis et al. 2004). Millennium goals are a set of declarations adopted by 189 member states of the United Nation in 2000; the main goal of these declarations was to encourage government across the world to double their efforts towards freeing millions of people from poverty and deprivation. There are significant regional variations. Some regions of Africa, e.g. North Africa, show a steady decrease in the proportion of children who are undernourished, while in some regions, such as East Africa, the proportion of children who are undernourished seems to be decreasing much slower to have the expected impact by 2015 (de Onis et al. 2004). Figure 9.1a shows the trend in the prevalence of underweight children across different regions of Africa. Other than stunting and being underweight, millions of children in Africa suffer other forms of nutritional deficiencies, such as iron and vitamin deficiency. For instance, an estimated 93.2 million preschool children in Africa are anaemic (de Benoist et al. 2008), while 49.5 million children aged 6–12 years experience iodine deficiency (de Benoist et al. 2004). These micronutrient deficiencies further contribute to the burden of cognitive, social, and emotional impairments associated with poor nutritional status.

Driven by chronic poverty and food insecurity among other risk factors, undernutrition has traditionally been the main nutritional problem in Africa; on the other hand, overnutrition has predominantly been a problem of the more developed countries such as the USA. However, the prevalence of childhood overnutrition in developing countries is increasing at an alarming rate (de Onis and Blossner 2000). Recent estimates reveal that in 2010, 13 million preschool children in Africa were obese and overweight; these numbers are set to rise to 22 million by 2020 (de Onis et al. 2010). Figure 9.1b indicates the trends in obesity in the different regions of Africa. There are large regional differences to this trend. Obesity and overweight in childhood and young adulthood are often associated with the increased risk of metabolic syndrome and asymptomatic cardiovascular disease, and cognitive and emotional problems (Amuna and Zotor 2008). In understanding the ever-growing problem of overnutrition in Africa, the synergic effects of under- and overnutrition have to be taken into consideration. Research indicates that when children are undernourished prenatally or during the early postnatal years, their bodies become less likely to learn to use calories efficiently later in life (Delpeuch and Maire 1997). Consequently, they are at an elevated risk of retaining calories when they start consuming sufficient calories (Delpeuch and Maire 1997). Among African populations experiencing "nutritional transitions", overnutrition therefore has the potential of becoming a major pandemic if current trends are not halted or reversed.

9.3 Conceptual Framework: A Systematic Model to Understanding Antecedents of Malnutrition

The current review is guided by two conceptual models that view malnutrition as a condition resulting from the interaction of a complex set of causal factors at individual, familial, and community levels. The first model is the UNICEF extended framework on causes and consequences of malnutrition (Engle et al. 1999). The second is Wachs' systematic model of multiple determinants of malnutrition (Wachs 2008). The UNICEF model was first proposed in 1990 with the aim of providing stakeholders a set of guiding principles on one approach to intervention in the area of malnutrition (UNICEF 1990). According to the framework these causes can be stratified at three levels:

1. *Immediate causes* manifest themselves at the individual level. This level has two main factors: ill health and inadequate food intake. Ill health and undernutrition have a synergic effect on each other. Children who are unwell are likely to eat less, or their bodies are likely to be less efficient at using calories that have been consumed; therefore, these children become susceptible to being undernourished. On the other hand, undernourished children are more susceptible to ill health, especially due to infectious diseases.
2. *Underlying causes* manifest themselves at the household level. Three factors have been classified under this category: food security, inadequate care for mothers and children, and lack of access to an adequate and healthy environment. A healthy and hygienic environment protects children from acquiring infectious diseases that are likely to weaken their bodies, making it difficult for them to adequately use the nutrients they consume. Inadequate care for children refers to a set of factors directly related to parenting behaviour, and they include feeding habits and psychosocial and cognitive stimulation for children, among others

(Engle et al. 1999). However, for caregivers to provide optimum care for children, they require certain resources for themselves which include sufficient education, satisfactory nutritional status, mental health, and a manageable workload, among others. This set of factors is what is referred to as care for caregivers.

3. *Root causes* manifest themselves at the community and national level. Root causes of malnutrition largely involve issues related to access to potential resources. These causes include access to farm land and other resources that are essential for ensuring food security at the household level and adequate intake of nutrients at individual level.

Wachs extended the UNICEF model more recently (Wachs 2008). The new extension has two important features. First, the model points out the role of child characteristics (such as gender and temperament) in shaping nutritional outcomes. Second, the model specifies mediating and moderating links between the different elements of the extended care model. According to Wachs, unlike the UNICEF model, the revised framework explicitly states that the elements in the UNICEF model need to be seen as a system of linked influences, rather than as a collection of individual elements. The revised model shows:

> that the relation of the adequacy of child nutrition to family economic resources, caregiver resources and child characteristics is best described in system terms, where the influence of any one variable depends to some degree on the nature and level of other variables in the system. (Wachs 2008)

Moreover, Wachs highlights a similarity between the pathway to nutritional deficiencies and overnutrition. Wachs notes that factors such as family resources, caregiver resources, and child characteristics all seem to play a significant contributory role in shaping nutritional problems. Given this conceptual background, the rest of the chapter will present a critical review of the empirical evidence from Africa. The first section will address issues related to undernutrition, followed by a discussion of overnutrition, before providing a summary that ties these two concepts together within Africa.

9.4 Undernutrition

9.4.1 Psychosocial Antecedents of Undernutrition

9.4.1.1 Poverty

For children to be adequately nourished, they require sufficient intake of nutrients through well-balanced meals. One important cause of undernutrition is either the inadequate intake of food (being hungry) or consumption of a poor diet. A significant number of children in developing countries either take fewer calories than they require or largely depend on carbohydrate-rich food leading to macro- and micronutrient deficiencies. There are many underlying causes related to these concerns, but two of the most salient factors are inadequate finances and lack of resources. The literature links various forms of poverty to the increased risk of malnutrition among African children, including low parental educational levels (Bloss et al. 2004; Kikafunda et al. 1998b), poor occupational status (Vella et al. 1992), poor quality of housing (Abubakar et al. 2008; Wamani et al. 2006), low household income (Kogi-Makau 1992), and lack of access to basic resources (e.g. land, livestock, and poor harvest) (Haidar et al. 2005). Moreover, even among the poor, the more deprived families are, the higher the risk of malnutrition among their children. For instance, in a study in Tanzania, it was observed that among those living in poverty, families living below the fourth wealth quartile had more malnourished children than those in the first wealth quartile. In discussions with communities regarding their perceptions of sources of undernutrition, lack of finances is always reported as a major contributing factor to poor nutritional status (Abubakar et al. 2011).

9.4.1.2 Maternal Parenting Behaviour

Maternal caring behaviour has been observed to have a strong influence on a child's nutritional status in Africa. The term maternal caring behaviour encompasses a wide repertoire of behaviour, including responsivity to a child needs, mother-infant interaction, and the availability of play material that provides cognitive and social-emotional stimulation to the child. For instance, a study in Embu, Kenya, observed that toddlers (18–30 months of age) who experienced a less supportive home environment were frequently ill, which in turn led to poorer anthropometric outcomes (Sigman et al. 1989a). Follow-up data indicated that these effects were not transient; children who had poor outcomes at toddlerhood still had poorer cognitive outcomes at 5 years of age (Sigman et al. 1991; Whaley et al. 1998). These results are similar to what has been observed in Kilifi, Kenya (Abubakar 2008). In the Kilifi study, scores on a measure of quality and quantity of stimulation received at home (Bradley and Corwyn 1996; Caldwell and Bradley 2001) correlated with height for age (HAZ) and weight for age (WAZ). It was observed that children from homes with fewer learning materials and whose mothers did not provide sufficient stimulation were more likely to be malnourished compared with their peers. A longitudinal study in Egypt (Wachs et al. 1993) investigated if child-rearing factors moderated the nutrition-development relationship. The authors observed that parenting behaviours that provided stimulation and were responsive to a child's needs buffered the child against the effects of poor nutritional status.

9.4.1.3 Maternal Occupation

Traditionally, most African women worked in the farms; farm work was structured in a way that mothers were able to go to the farm with their children and continue with breastfeeding. Social changes have altered patterns of occupation, which, in turn, have an impact on child rearing, health, and nutrition. Maternal occupation and especially the degree to which the occupation takes the mother away from child rearing have been observed to impact nutritional status. For instance, in Tanzania, mothers who took their children to the farms had better nourished children compared with their counterparts who did not (Wandel and Holmboe-Ottesen 1992). In a Nigerian study involving more than 5,331 children aged 0–59 months, it was observed that the kind of work the mother engaged in (i.e. whether or not she took the child to work and whether or not the mother received a salary) influenced the child's nutritional outcome (Ukwuani and Suchindran 2003). As in the previous study, it was observed that mothers who went to work with their children had better nourished children compared with those who left them at home. The contributory role of maternal involvement in the work sphere on child's nutritional outcome is alluded to in discussions involving rural mothers. In focus group discussions both in Kenya and in the Gambia, rural mothers noted that combining several roles infringed on their time and ability to provide adequate care to their children and was a significant contributor to poor nutritional outcomes (Abubakar et al. 2011; Mwangome et al. 2010).

9.4.1.4 Maternal Mental Health

The link between maternal mental health and infant undernutrition has been clearly established by various studies in South Asia (Black et al. 2009; Black and Ramakrishnan 2009; Patel et al. 2003). However, the evidence linking maternal depression to infant nutritional status in Africa is less clear. While some studies report a link between maternal depression (mental health) (Adewuya et al. 2008) and nutritional outcomes, other studies do not observe this link (Harpham et al. 2005). Table 9.3 presents a summary of results from some recent African-based studies investigating the link between undernutrition and maternal mental health. Several potential factors may contribute to this observation. First, the problem may be with the measurement used. Most of the identified studies have applied brief screening tools, whereas it may have been necessary to use more extensive measures. Moreover, the extent to which these measures adequately assess maternal mental health in different subsamples in Africa has yet to be evaluated. Qualitative studies on antecedents and presentation of prenatal and postnatal mental health problems among African mothers have been limited. An exception is the study by Bass et al. (2008) which used mixed method approaches to check for the validity of the construct of postnatal depression and then adapted and validated measures of postnatal depression. However, there may be a need to go even further and investigate the sociocultural context in depth. Understanding the sociocultural factors linked to maternal mental health and the manner in which mental health problems are presented and dealt with in this population may be the key to better understanding the impact (or lack of impact) of maternal mental health in the African context. For instance in India, a detailed investigation into the cultural validity of the construct of postnatal depression and its sociocultural context highlighted both universal and context-specific issues relevant to understanding the effects of maternal mental health on children's nutritional status (Rodrigues et al. 2003). The investigators examined the illness narratives of mothers and observed that the symptoms reported by postnatally depressed mothers were similar to those recorded in studies with women in other cultures suggesting a universal clinical presentation of postnatal depression. However, they noted that, in their sample, a sociocultural approach rather than a biomedical psychiatric approach in dealing with emotional distress was needed. The authors suggested that within the Indian context, maternal emotional distress has to be understood against the background of social adversity, marital relationships, and cultural attitudes (Rodrigues et al. 2003). We still do not have such a detailed understanding of postnatal depression in the African context. Future research addressing this aspect is urgently needed to allow a proper interpretation of recent research findings. Moreover, African-based studies would benefit more from an evaluation of the effects of timing, severity, and chronicity of mental health problems on children's nutritional outcomes. (See Table 9.1 for a summary of studies on depression and nutritional outcomes in Africa.)

9.4.1.5 Maternal Intelligence

Several studies have reported a relationship between maternal scores on measures of intelligence such as Raven's Progressive Matrices and nutritional status of their children even after controlling for the potential effects of education and socioeconomic status. These findings have been attributed partly to dietary intake. Children of mothers who have higher scores on cognitive tests tend to have a better dietary intake compared with those whose mothers have low scores in cognitive tests. For instance, Bhargava and Fox-Kean (2003), working in Kenya, reported that maternal scores on Raven's Progressive Matrices were strong predictors of dietary intake, over and above maternal education, and other SES indicators. Similar results were reported from Egypt, where it was observed that maternal intelligence was a unique predictor of toddler dietary quality intake. However, in this same study, maternal educational level rather than maternal intelligence was found to be a better predictor of nutritional intake among school-aged children (Wachs et al. 2005).

9.4.1.6 Paternal Roles

Compared with maternal influences, paternal influences on child nutritional status have received little attention. Most studies investigating paternal influence have focussed on socioeconomic variables such as paternal education and occupation. This seems to be a major research gap given that women in affected communities mention that lack of involvement of men in intervention programmes may partially explain the lack of progress in reducing the rates of childhood malnutrition in these communities (Abubakar et al. 2011). Mothers from rural Kenya and Gambia

Table 9.1 A summary of studies on depression and nutritional outcomes in Africa

First author	Year	Sample	Design	Country	Results
Adewuya	2008	*N* = 242 *A* = 6w–9M	Longitudinal	Nigeria	Infants of depressed mother had poorer developmental outcomes compared with infants of nondepressed mothers at all the four time points measured
Avan	2010	*N* = 891 *A* = 6–24M	Longitudinal	South Africa	Children of depressed mothers at an increased risk of stunting compared with children of parents who are not depressed
Medhin	2010	*N* = 1065 *A* = prenatal–12M	Cross-sectional	Ethiopia	No relationship between maternal mental disorders and nutritional status of the children
Stewart	2008	*N* = 501 2–18M	Cross-sectional	Malawi	Maternal mental health problems associated with growth impairment
Harpham	2005	*N* = 2000 per country *A* = 6–18M	Cross-sectional	Ethiopia	In a four-country study, there was evidence of maternal depression impacting the child's nutritional status in Asian countries but not in Ethiopia
Tomlinson	2006	*N* = 147 *A* = 2–18M	Longitudinal	South Africa	No clear effect of depression on the child's weight
Ndokera	2011	*N* = 286 *A* = 2–12M	Cross-sectional	Zambia	Maternal depression related to reduced infant weight and height

N numbers, *A* age, *M* months, and *W* weeks

reported that their husbands made many of the decisions relating to use of family resources. These decisions affected expenditure on food, among other items. The mothers noted that since most fathers were not involved in nutritional counselling, it took a lot of persuasion to convince them to allocate extra finances to the purchase of nutritious foods.

9.4.1.7 Child Characteristics and Undernutrition

Taking a transactional approach, Wachs (2008) proposes the inclusion of child characteristics in the conceptual model on undernutrition. Four child characteristics (health, age, gender, and temperament) are proposed for inclusion in this model. An evaluation of African-based studies indicates that children's *health status* is strongly associated with compromised nutritional status. Illnesses such as HIV, malaria, parasitic infections, and diarrhoeal disease have all been associated with both growth restriction and micronutrient deficiencies (Abubakar et al. 2009; Nyakeriga et al. 2004; Olney et al. 2009; Stoltzfus et al. 1997). The relationship between ill health and poor anthropometric status is complex. Existing evidence points to the increased risk for growth failure being most common in childhood illnesses (e.g. malaria, HIV, and parasitic infections); however, it is difficult to ascertain a causal link. Poor health may lead to undernutrition because children may lose their appetite, thus affecting their nutrient intake.

Several studies have observed that a *child's age* is a significant predictor of nutritional status. Studies indicate that the prevalence of underweight and stunted children starts to dramatically increase at the age of 3–6 months (Bloss et al. 2004; Kwena et al. 2003; Stoltzfus et al. 1997) and seems to peak at between 12 and 24 months. This increase seems to coincide with weaning, as several studies report an association between some weaning practices and undernourishment (Schmutzhard et al. 1986; Walker 1990).

The role of *gender* as a potential risk factor for poor anthropometric status has been highlighted. A meta-analysis of studies from sub-Saharan Africa (Wamani et al. 2007) observed that boys were at a higher risk of stunting compared with girls, although the observed differences were relatively small. In this meta-analysis, the pooled estimates for mean *z*-scores were −1.59 for boys and −1.46 for girls. Moreover, the prevalence of stunting was higher among boys (40 %) compared with girls (36 %) in pooled data analysis; crude odds ratio is 1.16 (95 % CI 1.12–1.20). Within the African context therefore, the investigation of factors that predispose boys to a high risk of being undernourished is warranted.

Of the four proposed child characteristics likely to impact nutritional status, the least studied is *temperament*, though some early studies report the role of temperament in the growth and development of children in East Africa. These studies were carried out in the 1970s among the Maasai and Digos of Kenya (de Vries 1994, 1999). The studies observed that it was not the child's temperament that influenced nutritional outcomes, but how well the child fitted in the environment that ensured good health. For instance, among the Maasai, fussy children who called attention to themselves had better growth outcomes and survived longer, compared with those who were mostly quiet. It was hypothesized that in conditions of extreme poverty and need, fussy children forced caregivers to pay more attention to their needs, which increased and improved their chances for survival (de Vries 1994, 1999).

Table 9.2 A summary of studies on the influence of nutritional deficiencies on child development and cognitive outcomes in Africa

First author	Year	Country	Results
Aboud	1995	Ethiopia	Child's HAZ and WAZ influenced their performance on the measure of mental and motor development
Abubakar	2008	Kenya	HAZ and WAZ influenced performance on psycho-motor tasks
Abubakar	2010	Kenya	HAZ and WAZ affected motor, language, and social-emotional development at infancy
Aubuchon-Endsley	2011	Ethiopia	Haemoglobin and growth (HAZ and WAZ) were associated with attention levels among infants
Bogale	2009	Ethiopia	Iodine deficiency associated with impaired short-term memory in preschool children
Bangirana	2009	Uganda	WAZ influenced performance on tasks of visual spatial processing and spatial learning
Bhargava	2000	Kenya	Infants' arm circumference and calcium intake predicted performance on a psychomotor scale
Bhargava	2003	Tanzania	HAZ and haemoglobin concentration influenced scores on measures of educational achievement
Drewett	2001	Ethiopia	HAZ and WAZ influenced performance on both the motor and mental subscales of the Bayley Scales of Infant Development
Gewa	2009	Kenya	Iron supplementation led to a significant gain on scores of Raven's Coloured Progressive Matrices, while supplementation with Zinc, vitamin B_{12}, and riboflavin influenced performance on digit span
Kariger	2005	Zanzibar	HAZ and anaemia levels predicted age at which motor milestones, especially walking, were achieved
Keteme	2003	Ethiopia	HAZ influenced the performance of children and toddlers on the Bayley Infant Development Scales
Olney	2009	Zanzibar	HAZ predicted motor activity, motor development, and language development, while Hb levels predicted motor activity
Sigman	1989b	Kenya	Nutritional status predicted performance on measures of general IQ
Wachs	1993	Egypt	Children's mental competence was associated with fat intake, total calorie, and protein intake

HAZ height for age, *WAZ* weight for age

9.4.2 Psychosocial Consequences of Undernutrition

During infancy and toddlerhood, undernutrition contributes to developmental delay in areas such as language development and acquisition of motor skills (Abubakar et al. 2010). In a series of studies among children in Zanzibar, the contribution of anaemia and iron deficiency to delayed motors skills was demonstrated (Olney et al. 2007, 2009). Similarly, deficiencies of iron and vitamin B contributed to delayed milestones. Among school-going children, studies have shown that poor nutritional status contributes to poor performance across a range of cognitive abilities including global IQ, working memory, and attention (see Table 9.2 for a summary of studies reporting the effects of undernutrition on child development). Unfortunately, the effects of early childhood malnutrition are not transient; long-term effects have been reported. For instance, in a study investigating the effects of early childhood malnutrition on performance on cognitive tasks later in life, it was observed that anthropometric status at toddlerhood was significantly related to performance on cognitive tasks at both 30 and 60 months of age. Moreover, when the same sample of children was assessed at school age (7–8 years), their scores on the Raven's Standard Progressive Matrices were significantly related to SES and nutritional status during toddlerhood (Sigman et al. 1989b).

Additionally, children who are undernourished seemingly experience more behaviour and emotional problems compared with their well-nourished peers (Chang et al. 2002; Grantham-McGregor 1993; Liu and Raine 2006). For instance, in a large longitudinal birth cohort study involving more than 1,795 children in Mauritius, children who showed signs of malnourishment at age three were more aggressive or hyperactive at age 8 years, had more externalizing problems at age 11, and had greater conduct disorder and excessive motor activity at age 17 compared with their well-nourished peers (Liu et al. 2004). Furthermore, the study reported that there was a relationship between the degree of malnutrition and the severity of externalizing behaviour at ages 8 and 17. Moreover, low IQ mediated the link between malnutrition and externalizing behaviour at ages 8 and 11. The researchers concluded that their results:

> indicated that malnutrition predisposes to neurocognitive deficits, which in turn predispose to persistent externalizing behaviour problems throughout childhood and adolescence. (p. 161)

9.4.3 Interventions for Undernutrition

Interventions addressing undernutrition in Africa have largely taken three different approaches. The first sets of interventions have taken a biomedical approach with a strong focus on nutritional supplementation. Studies evaluating various forms of micronutrient supplementation in the African context have been widely reported. While these studies have shown significant effects in improving nutritional and health status, they have also pointed out the potential limitation of an approach that only uses nutritional supplementation. For instance, in Uganda, using a randomized, double-blind, placebo-controlled study, the benefits of zinc supplementation on growth and body composition of preschool children were investigated (Kikafunda et al. 1998a). The study observed that zinc supplementation may work only in subsamples of the population. Specifically, the study reported that zinc supplementation led to increased mid-upper arm circumference and greater weight gain in children from a school with parental SES in the medium range, but not among children in a low SES school (Kikafunda et al. 1998a). As noted by the investigators, these results point to the need for an evaluation of the benefits of zinc within the larger context of other risk factors.

Another set of interventions has looked at the problem of malnutrition as largely requiring community-based monitoring programmes that aim at enhancing caregivers' capacity to provide adequate nutrition. This set of programmes has shown promise in lowering the prevalence of undernourishment in the community. In Uganda, a large-scale programme aimed at enhancing child outcomes through improving parental skills, knowledge, and resources on child care was implemented (Alderman and Engle 2008). Project activities were divided into three broad categories: community-based interventions, parish-level activities, and support to national and district programmes. Caregivers were trained on relevant child care needs and resource mobilization for child growth promotion (Alderman and Engle 2008). This training included nutrition counselling, parenting skills, and aspects of psychosocial stimulation. Though minimal improvement in both nutrition and cognition was observed after an initial evaluation, improvement in parenting skills, knowledge, and behaviour makes it likely that in the longer run this intervention holds the promise of enhancing child outcomes (Alderman and Engle 2008).

A third set of interventions adopts a multidisciplinary approach to combat malnutrition. These interventions involve combining biomedical (nutritional supplementation and deworming) and psychosocial approaches (raising maternal awareness) to combat undernutrition. In Madagascar, a community-based programme which combined biomedical and psychosocial interventions recorded success in lowering rates of childhood undernutrition in participating villages (Galasso and Yau 2005; as cited by Alderman 2007). The programme focussed on mobilizing awareness of child care and hygiene through education sessions and demonstrations organized by trained community nutrition workers. These activities were complemented by micronutrient supplementation and administration of deworming medicines. In this project, the impact of the programme was evaluated through length of exposure to the programme and the number of children in the community who were malnourished. The results indicated that communities with an additional 2 years of exposure to the project had malnutrition rates 7–9 % points lower than communities with less time in treatment.

In appreciation of the fact that poor developmental and cognitive outcomes may become the most serious consequence of malnutrition, the WHO recommended the inclusion of play therapy as part of the integrated approach to the management of severe malnutrition among hospitalized children. The efficacy of psychosocial stimulation has not been evaluated in the African context. However, findings from other developing countries (e.g. Jamaica) show that psychosocial stimulation combined with nutritional intervention had long-term benefits on cognitive and behavioural outcomes in children who were undernourished (Gardner et al. 2005; Walker et al. 2011).

9.5 Overnutrition

Compared with undernutrition, relatively little research has been carried out on overnutrition in Africa. Given the scarcity of relevant data from Africa, this review also uses information from studies conducted elsewhere as a means of enhancing our understanding of the underlying issues and highlighting research gaps.

9.5.1 Psychosocial Antecedents of Overnutrition

Though not well understood, a mass of empirical evidence supports a genetic predisposition to overnutrition, especially in the case of obesity (Zhao and Grant 2011). Additionally, the literature indicates that this genetic predisposition works in synergy with environmental factors to contribute to the development of overnutrition (Xi et al. 2011). Not much research has been carried out in Africa to understand the psychosocial antecedents of overnutrition. Table 9.3 presents a summary of results of research on antecedents of obesity and overweight among African populations. These studies indicate that, among African children, parental characteristics, child characteristics, and sociocultural factors increase the risk of being overnourished. Specifically several studies report that children whose parents are highly educated are at an elevated risk of being overweight or obese (Kruger et al. 2005). High risk among those in the higher socioeconomic strata in Africa has been related to food choices such as the consumption of highly processed foods and soft drinks (Ben Slama et al. 2002). The risk of being overweight is higher among girls than among boys (Kruger et al. 2005; Mukuddem-Petersen and Kruger 2004), a finding that has partly been attributed to less involvement in physical activities as girls approach sexual maturation (Kruger et al. 2005).

The antecedents of overnutrition may differ as a function of area of residence. The diets of most poor/rural African populations mainly consist of carbohydrates, because of the prohibitively high cost of other foods, and this leads to a high prevalence of being overweight. Moreover, among urban populations in Africa (both rich and poor), new dietary patterns are one of the leading causes of overnutrition. The availability of processed and highly refined foods, sometimes at relatively low cost, is increasingly becoming a major contributing factor to the development of obesity.

9.5.2 Psychosocial Consequences of Overnutrition

Table 9.4 below presents a summary of key findings relating overnutrition to cognitive, educational, and psychosocial outcomes. Studies indicate that children who are obese or overweight are at a higher risk of exhibiting behavioural and emotional problems such as impulsivity, attention-deficit hyperactivity disorder, depression, anxiety, and uncontrolled eating behaviour. An alternative interpretation of these results is that the existence of these emotional and behavioural problems may lead to eating disorders which in turn may contribute to the development of obesity. Moreover, children who are overweight or obese have been observed to have poor school outcomes compared with their peers (Falkner et al. 2001; Galal and Hulett 2003). School problems indicated include absenteeism, poor peer relationships, low morale in class, and low academic self-concept. Some noteworthy points here are that the literature on childhood obesity is not very conclusive. Some studies indicate that on its own, obesity may not have adverse psychosocial effects if one controls

Table 9.3 Summary of some studies from Africa on the antecedents of overnutrition

First author	Year	Country	Prevalence	Factors associated with obesity/overweight
Adegok	2009	Nigeria	0.3 % obese 2.8 % overweight	Higher risk in girls Higher risk in high SES
Amstrong	2006	South Africa	4.9 % obese girls 3.2 % obese boys 17.9 % overweight girls 14.0 % overweight boys	Gender—higher risk in girls Sedentary lifestyles
Ben Slama	2002	Tunisia	3.7 % Obese	Parental obesity Food choices Length of sleep at night
Boukthir	2011	Tunisia	19.7 % overweight 5.7 % obese	Increased with higher SES Related to eating habits, e.g. high consumption of soft drinks
Gewa	2009	Kenya	17.7 % overweight 3.7 % obese 8.1 % both stunted and obese	Maternal overweight and obesity Higher levels of maternal education Being large at birth Age—older children more at risk Large households Being stunted
Kimani-Murage	2010	South Africa		Girls, especially as they start to mature sexually
Kruger	2005	South Africa	7.8 % overweight or obese	Female gender higher associated with inactivity especially among girls Higher among whites (who tend to be richer than black South Africans) Higher in urban dwellers Smaller households Increased with age
Monyeki	1999	South Africa	2.3 % boys overweight 0.0–4.3 % of girls overweight	Higher risk in girls
Mosha	2010	Tanzania	5.6 %–6.3 % overweight 4.2–8.6 % obese	Higher risk among girls Increases with age
Mukuddem-Petersen	2004	South Africa		Increased risk in rural areas Increased risk among girls
Nagwa	2011	Sudan	10.8 % overweight 9 % obese	Children from the higher SES more at risk, the prevalence rates high SES 56.8 %

(continued)

Table 9.3 (continued)

First author	Year	Country	Prevalence	Factors associated with obesity/overweight
Omigbodun	2010	Nigeria	2.3 % overweight	Higher in girls, especially post-pubertal
Omuemu	2010	Nigeria	5.7 % overweight	Food choices Physical inactivity Family health history
Senbanjo	2010	Nigeria	1.9 % overweight	Increased risk in families where parent had a high educational achievement
Senbanjo	2007	Nigeria	13.7 % overweight 5.2 % obese	Not associated with SES Associated with breastfeeding—risk of being overweight decreases with prolonged breastfeeding

Table 9.4 A summary of some of the cognitive and psychosocial consequences of being overweight or obese

Cognitive	Psychosocial	Educational
Cognitive flexibility	Lowered self-esteem	Low academic self-concept
Perception	Anxiety	School absenteeism
Memory	Eating disorders	Lower educational aspiration
Processing speed	Suicidal ideation	Lowered educational achievement

for mediating/confounding factors such as age, gender, and existence of other health problems. Moreover, it has been suggested that the effects of obesity may be strongly moderated by sociocultural factors. In westernized nations where there is generally a negative perception of overweight people, childhood obesity may have a more pronounced effect on psychological function. On the other hand, in the African context where being overweight is perceived as an indication of being "rich, fat and beautiful" (Renzaho 2004), the psychological implications of being overweight may be different. Studies to evaluate the consequences of overnutrition among African children are urgently needed.

9.5.3 Interventions for Overnutrition

While there are no studies to indicate the potential benefits of different intervention approaches in Africa, studies from other parts of the world indicate that the most effective approaches to dealing with the overnutrition epidemic are multidisciplinary interventions that include change of eating habits and levels of physical activity. For instance, a community-based project that used multimedia approaches to teach both adolescents and their parents on the need for increased activity levels and change of eating habits showed positive results, and participating adolescents were shown to have lowered BMIs (Bruss et al. 2010). This project encouraged the active participation of both adolescents and their parents. The inclusion of the whole family in obesity intervention programmes is an emerging approach that is gaining popularity (Davison et al. 2011). This approach aims at changing the family environment, which is considered to be a salient factor in the development of obesity. In developed countries, there have been calls to change what is referred to as the "obesogenic environment" (Burgoine et al. 2011; Giskes et al. 2011). Simply defined, obesogenic environments are settings that provide relatively cheap high-calorie foods with limited opportunities for movement and physical activities. Alongside raising awareness on good eating habits and encouraging physical activities, interventions aimed at the obesogenic environment campaign for more community playgrounds, active forms of transport such as bicycles, and fewer fast-food eating places must be included.

9.6 Future Directions

The current chapter presents a review of empirical evidence on the association between psychosocial antecedents and malnutrition in Africa. These findings help to understand the underlying mechanisms in the malnutrition epidemic, indicating some useful points of intervention. However, despite the obvious benefits of the work done so far, a lot still needs to be carried out. The most obvious gap is our insufficient knowledge of psychosocial antecedents, consequences, and interventions for obesity in the African context. Given the heavy burden of undernutrition, the limited interest in overnutrition is understandable; however, with the rapid development of overnutrition, more attention needs to be paid to this problem before it becomes a full-fledged epidemic.

Despite the large amount of empirical evidence in existence, knowledge gaps on psychosocial antecedents, consequences, and interventions for undernutrition are still major. Notable here is that, because of logistical limitations, most studies addressing potential psychosocial influences focus on one or two factors. Rarely do they take a comprehensive approach to address as many psychosocial antecedents as possible. This practice potentially limits the degree to which one can fully understand the mechanisms by which these factors relay risk for under- or overnutrition. In reality, several of these factors may interact to cause the observed adverse effects. Moreover, hardly any studies have investigated the potential effects of the larger setting (such as the village and other neighbourhoods); more multilevel studies that look at the interaction between individual, household, and community level factors in shaping the risk for undernutrition are needed.

9.7 Conclusion

The chapter highlights the salient role of psychosocial factors in shaping malnutrition, the adverse psychosocial effects of nutritional problems, and the potential role that psychosocial interventions can play in dealing with this public health problem. Empirical evidence from Africa indicates that a multidisciplinary approach is crucial to handling the problem of childhood malnutrition.

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Chapter 10
Assessing the Effects of Maternal Anemia on Child Development in Benin

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10.1 Background

10.1.1 Burden of Anemia in Pregnancy

In developing countries, over 50 % of pregnant women are anemic (WHO 1998). Thirty to fifty percent of these women have iron-deficiency anemia (IDA) compared with a much lower prevalence of IDA among pregnant women in developed countries where diets and iron supplementation are better (MMWR PiCD 1990). Maternal anemia as it affects child development is an excellent illustration of the interconnected feed-downward (culture- and context-driven) and feed-upward

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(neurobiology-driven) interactive processes and developmental plasticity that are at the core of the co-constructivist approach (Li 2003). In other words, the environmental/cultural context contributes to maternal anemia, subsequently shaping the child's brain/behavior development across the life-span (pre- and postnatally). Maternal anemia affects the child initially in terms of the gestational neurobiological environment for the child in utero, then in maternal health and quality of care giving in infancy and early childhood, and following into middle childhood through household nutritional and parasitic risk factors that contribute to the mother's chronic anemia, which extend to the child as he or she grows into adulthood. For women, these co-constructivist dynamics extend across generations as the developing girl, herself, later becomes a chronically anemic mother.

10.1.2 Physiopathology in Pregnancy

During pregnancy, the amount of iron required to increase the red cell mass, expand the plasma volume, and allow for the growth of the fetal-placental unit increases significantly. Oxygen-carrying capacity is proportional to the circulating hemoglobin concentration. From a physiologic perspective, the evidence is clear that moderate anemia is undesirable (Yip 2000).

10.1.3 Risk Factors for Anemia in Pregnancy

Malaria and iron deficiency are important and well-known risk factors for anemia during pregnancy. It is estimated that 26 % of severe anemia among pregnant women can be attributed to malaria and around 50 % to iron deficiency. The prevalence of fetal anemia at birth is high in malaria-endemic areas, and the risk is associated with the presence of high-density parasitemia in the mother at delivery. Other risk factors include helminth infections with hookworms and schistosomas, multiple pregnancy, urinary tract infection, sickle cell disease, micronutrients deficiency (folic acid), under nutrition, and poor antenatal care (Geelhoed et al. 2006). Our study in Benin, which is a small Francophone country in West Africa that is very impoverished, confirmed the role of these factors (Ouédraogo et al. 2012). Relationships between iron deficiency (ID) and infections are unclear, as is the role of specific infections (malaria, hookworm, urinary tract infection, bacterial vaginosis). The risk of iron-deficiency anemia is increased with parity: nearly threefold higher for women with 2–3 children and nearly fourfold greater for women with four or more children (Looker et al. 1997). The following genetic factors may be risk factors for anemia: hemoglobin C trait found in 10 % of Beninese people and sickle cell disease found in 4 % of Beninese newborns. The prevalence of sickle cell trait is 22 % in Cotonou in Benin (Latoundji et al. 1991).

10.1.4 Consequences of Anemia and ID in Pregnancy on the Outcomes in Children

10.1.4.1 Preterm Delivery and Low Birth Weight

Early anemia has been associated with an increased risk of preterm delivery (Xiong et al. 2000; Scanlon et al. 2000). Allen suggested three potential mechanisms whereby maternal IDA might give rise to preterm delivery: hypoxia, oxidative stress, and infection (Allen 2001). Chronic hypoxia from anemia could initiate a stress response, followed by the release of corticotropin-releasing hormone (CRH) by the placenta, increased production of cortisol by the fetus, and an early delivery. Some studies, including our study in Benin, have shown a link between anemia during pregnancy and preterm and low birth weight babies (Bodeau-Livinec et al. 2011; van den Broek 2003). No study, to our knowledge, however, has investigated the long-term outcomes of these children.

10.1.4.2 Anemia and ID in the Fetus

Results regarding maternal hemoglobin concentrations at or near term and cord blood hemoglobin concentrations are not consistent (Allen 2000; Brabin et al. 2004). Evidence, largely collected among infants aged 6–12 months, is accumulating that children born to anemic mothers have lower iron stores, even when they are born at term and with a normal birth weight (Strauss 1933; Colomer et al. 1990; Kilbride et al. 1999; Morton et al. 1988; Preziosi et al. 1997; Ahmad et al. 1983). It is known that iron is preferentially allotted to red blood cells. When iron supply is insufficient, the fetal brain may be at risk, even if the infant is not anemic (Lozoff and Georgieff 2006). In pre-anemic pregnant women, low ferritin concentrations also correlate with lower serum ferritin concentrations in the neonate (Lao et al. 1991). Iron deficiency can be remedied at any point; its consequences, however, cannot. According to Allen, more studies that assess the relationship between the iron status of pregnant women and the iron status of their infants postpartum are needed. Maternal anemia and subsequent infant health and development also deserve further study.

10.1.4.3 Cognitive Outcomes and Mental Health

In infants and preschool children, iron-deficiency anemia results in developmental delays and behavioral disturbances (decreased motor activity, social interaction, and attention to tasks) (Pollitt 1993; Idjradinata and Pollitt 1993). In South Africa, Perez et al. (2005) found that infants whose mothers were anemic in the early postpartum scored worse on developmental tests at 10 weeks and 9 months of age compared with infants whose mothers were not anemic. In the USA, Tamura et al. found an association between fetal iron status (umbilical cord serum ferritin concentrations) and lower scores on mental and psychomotor development test (Tamura et al 2002). Recent studies suggested a potential impact of maternal iron deficiency during pregnancy on a child's mental health and cognitive outcomes, but none showed an association (Insel et al. 2008; Hernandez-Martinez et al. 2011; Mihaila et al. 2011; Christian et al. 2010). To our knowledge, data related to maternal anemia and infant behavior is limited (Vaughn et al. 1986).

Given the potential huge impact of anemia and ID during pregnancy on childhood outcomes and the lack of data, we proposed our present developmental assessment research program. Our study in Benin follows children of 12 months of age in order to evaluate these relationships between maternal anemia, ID, and subsequent developmental outcomes for the children.

10.2 Hypothesis

The central hypothesis in our research program is that anemia in pregnancy and maternal iron deficiency are associated with adverse developmental outcomes and that the degree of anemia is associated with the degree of adverse outcomes. Possible mechanisms are decreased brain development due to iron deficiency, through the higher risk of low birth weight (LBW) and preterm births, through a higher risk of anemia and iron deficiency at birth linked to poorer developmental and mental health outcomes, or through hypoxia in pregnancy (severe and/or chronic).

10.3 Objectives

Our goal is to examine the cognitive function of children as a result of anemia in pregnancy. Lower scores on cognitive assessment are expected with decreasing levels of hemoglobin, adjusting for pre- and postnatal factors known to be associated with cognitive function in childhood.

10.4 Methods

10.4.1 Study Design

The study included a follow-up by 12 months of age of children born in Benin within a multi-country randomized controlled trial (RCT) funded by the European Commission (MiPPAD project). Offspring from the first 1,005 pregnant women enrolled in this RCT comparing mefloquine (MQ) and sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment for malaria during pregnancy (IPTp) are assessed.

10.4.2 MiPPAD Trial

The main outcome studied was low birth weight. The pregnant women were recruited from January 2010 to May 2011. All pregnant women who attended an antenatal care visit (ANC) during the second trimester of pregnancy were invited to participate. The exclusion criteria included psychiatric disease, neurological disease, or HIV infection. With informed consent, pregnant women were randomly assigned to either SP or MQ. If the gestational age at this visit coincided with the fundus being palpable (at least 13 weeks of gestation), the first dose of IPTp (either SP or MQ) was administered. The second dose of SP/MQ was administered coinciding with the next ANC visit at least 1 month after the previous dose. All IPTp doses were administered under supervision.

10.5 Variables

10.5.1 Variables Recorded in 1,005 Pregnant Women

At the time of recruitment, parity, maternal age, gestational age (date of last menstrual period and uterine height), gravidity, history of previous preterm birth, low birth weight, miscarriage, and stillbirth were recorded. Socioeconomic status including variables such as supplied latrines, supplied electricity, mother's education level, father's education level, marital status, and literacy (reading, writing) were recorded. The mothers were screened for sickle cell disease and hemoglobin C trait using electrophoresis. Three times during pregnancy (at the first IPTp administration, at the second IPTp administration, and at delivery), blood samples of the cohort women were evaluated for hemoglobin concentration (Hb), serum ferritin, C-reactive protein (CRP), folic acid, vitamin B_{12}, and malaria (parasite density and placental malaria). Anthropometric measurements for pregnant women were recorded at each visit: weight and height at first ANC to calculate the BMI, weight at each antenatal visit, and total weight gain during pregnancy. Helminths (ankylostomiasis, especially prevalent in Benin) were systematically searched with the KATO test. Other pregnancy complications recorded were mortality, urinary tract infection, hemorrhage during pregnancy, and other infections. The number of antenatal care visits was recorded. Anemia was defined as severe (Hb $<$ 80 g/l), moderate (Hb $\geq$ 80 and $<$100 g/l), mild (Hb $\geq$ 100 and $<$110 g/l), and no anemia (Hb $\geq$ 110 g/l).

10.5.2 Variables in Infants at Birth, 1, 9, and 12 Months in Offspring

At delivery, newborns were weighed and measured and their gestational age assessed by the Ballard score (Ballard et al. 1991). Birth defects and infant's gender were recorded.

Children follow-up is ongoing. Anthropometric measurements in infants are assessed at 1, 9, and 12 months, including child weight (measured in kg), length (measured in cm using a measuring board), mid-arm circumference, and head circumference (measured in cm using a measuring tape).

Blood samples in infants at birth, 1, 9, and 12 months of age are collected to assess Hb and malaria. Additional blood samples may be collected in case of emergency. Additional assessments of serum ferritin, CRP, and blood lead are performed at 12 months. Sickle cell disease and hemoglobin C are sought by electrophoresis. At 12 months of age, motor and cognitive functions are evaluated according to the Mullen Scales of Early Learning (MSEL). Mothers are asked about their child's potential deficiencies through the ten questions questionnaire (TQQ). Nutrition in infants, especially breastfeeding, is assessed through a questionnaire. At 1 year of age, anemia is defined as Hb concentration <110 g/l [34].

10.5.3 Variables in Mothers When Offspring is 1 Year of Age

Maternal depression is evaluated when offspring is 1 year of age through the Edinburgh Postnatal Depression Scale, which was already in use in Uganda (WHO/UNICEF/UNU 1997; Caldwell 2001). Maternal interaction with the child is evaluated through the use of the HOME inventory subscales (Caldwell 2001). Maternal nonverbal IQ is collected at 1 year postpartum through the Raven's Progressive Matrices Test.

10.6 Preliminary Findings

Our findings after the assessment of approximately 320 one-year-old children at the midway point of our follow-up data collection are very preliminary. However, we are seeing a clear and significant association between impaired development and both environmental and care giving quality risk factors. At this point maternal depression does not seem to be related to child Mullen outcomes at 1 year of age. This conclusion is based on a preliminary evaluation of overall child cognitive ability as measured by the Mullen Early Learning Scales composite score as it relates to maternal cognitive ability (Raven's Progressive Matrices Test), quality of care giving (Caldwell HOME scale), and SES (physical quality of the home).

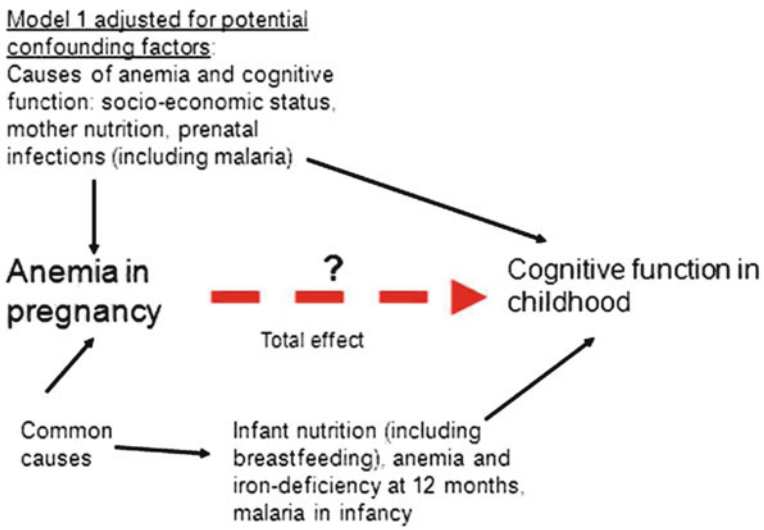

Fig. 10.1 DAG for the total effect of anemia in pregnancy on cognitive function in childhood

When all follow-up data has been completed, we will use the directed acyclic graph (DAGs) as developed by Hernan and others (Hernan et al. 2002). Within this strategy of analysis, causal diagrams will be used and will consider a priori causal knowledge. The role of each factor in relation to the exposure (anemia) and the outcome (cognitive function) will be considered according to a priori assumptions about the underlying biologic mechanisms. The role of covariates may include confounding, mediating, or effect modification. The analysis will be adapted accordingly as described below.

To study the total effect of anemia in pregnancy on cognitive development, we will take into account potential confounding factors [model 1 (Fig. 10.1)]. Important variables will be considered as adjustment factors (potential confounding) in the final analyses and will include lead exposure (found to be significant in a preliminary sample of our children); malaria during pregnancy; maternal malnutrition; micronutrient deficiencies (iron, vitamin B_{12}, folic acid); socioeconomic status; maternal age; gravidity; number of antenatal care visits; hemorrhage during pregnancy and other pregnancy complications; other infections in pregnancy, especially helminthes and urinary infections; nutrition in infancy (including breastfeeding); malaria during the first year of life; and iron deficiency at 12 months. Of note, the variables preterm birth, LBW, and anemia at birth and in infancy might be confounding factors as they may share common causes with anemia (Calis et al. 2008; Bodeau-Livinec et al. 2011; Berkowitz and Papiernik 1993; Siza 2008) during pregnancy and are risk factors for poor cognitive development (Walker et al. 2007). We will adjust for these common causes (socioeconomic malaria during pregnancy,

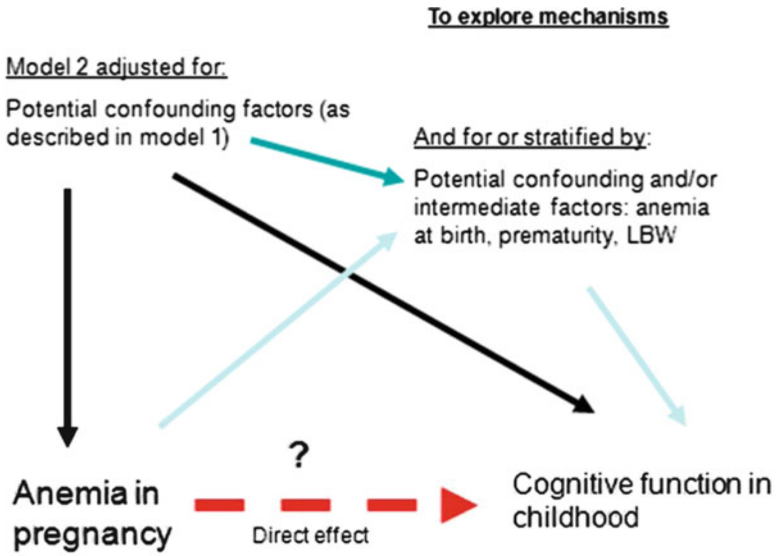

Fig. 10.2 DAG for the direct effect of anemia in pregnancy on cognitive function in childhood

maternal age, gravidity, number of antenatal care visits, maternal nutrition, maternal BMI), in order to remove possible confounding.

To study the direct effect of anemia in pregnancy on cognitive development, in addition to the variables adjusted for in model 1 (Fig. 10.1), we will take into account potential intermediate factors that may be in the causal pathway between anemia during pregnancy and cognitive outcome [model 2 (Fig. 10.2)]. The variables preterm births, LBW, and anemia at birth and in infancy may be intermediate factors, because they may be in the causal pathway between anemia during pregnancy and cognitive function later in childhood. Anemia during pregnancy may be a risk factor for preterm birth, LBW, and anemia at birth and in infancy (Colomer et al. 1990; Bodnar et al. 2005; Koura, personal communication). All of these factors are risk factors for poor development in childhood (Walker et al. 2007). If we find a relationship between these variables (anemia at birth and in infancy, preterm birth, low birth weight) and first, anemia during pregnancy and second, cognitive function, we will consider them as potential intermediate factors. Comparing models adjusting for preterm birth, LBW, and anemia in infancy to models excluding them will give us some insight into mechanisms. For instance, if estimates are different in the two models (model 1 in the DAG above adjusted for socioeconomic factors, malaria during pregnancy, maternal age, gravidity, number of antenatal care visits, maternal nutrition, BMI, prenatal infections and model 2 adjusted for the same factors and LBW that is assessing the direct effect of anemia during pregnancy on cognitive function in infancy), it could mean that LBW is an intermediate factor in the pathway between maternal anemia and cognitive outcome. If these estimates are not different in these two models, it could mean that LBW is not an intermediate factor (Bodnar et al. 2005). The same strategy applies to other potential intermediate factors.

We will also use another method to explore preterm births, LBW, and anemia at birth and in infancy as intermediate factors. We will apply model 1 in the following subpopulations: term babies weighing more than 2,500 g at birth, expected to be 82.7 % of our sample, and babies with anemia at birth, expected to be 61.1 % of our sample. This may provide information about the direct effect of anemia during pregnancy on cognitive function at 1 year of age in these populations. The same strategy will apply to study the association between iron-deficiency anemia and child development.

10.7 Possible Interventions and Conclusions

Various interventions have been proposed to improve early child development in low-income countries. The majority consist of parenting interventions in the postnatal preschool period that promote interactions between the children and their parents in the fields of education, learning, and feeding (Engle et al. 2011). Although the problems of intrauterine growth restriction (IUGR) and exposure to toxic agents (e.g., lead) and parasitic diseases (mainly malaria in endemic areas) have been identified as risk factors for impaired child development, very few interventions have been attempted involving pregnant women, and to our knowledge, none of these have specifically evaluated the impact of existing measures to prevent maternal anemia on child development.

Presently, following WHO recommendations (WHO 2001), a policy of micronutrient supplementation (iron and folic acid) is made available to all pregnant women in the majority of Sub-Saharan African countries. In Benin, as in most malaria-endemic areas, IPTp with sulfadoxine-pyrimethamine is also given twice in the course of pregnancy, along with the distribution of insecticide-treated bednets at the first antenatal visit. National guidelines also recommend that women should be systematically given an antihelminthic treatment with mebendazole at the same time as IPTp intakes. Such measures, if correctly implemented, should logically improve both the hematological status of the women and the cognitive development of their children. However, it is not clear if some of these interventions might be detrimental for child development. For example, supplementation of children with iron and folic acid has been shown to be detrimental in populations with high rates of malaria transmission, because iron given to non-anemic children may induce favorable conditions for the parasite multiplication and an increased risk of severe illness in supplemented children (Sazawal et al. 2006).

As a wide panel of prevention measures are already applied to pregnant women in low-income countries to decrease the burden of anemia, one of the main priorities for future research would be to evaluate carefully the effects of these interventions (both protective and potentially detrimental) in reducing developmental impairment in the children (Walker et al. 2011). It will then be the time to conclude on the role of maternal anemia (and specifically iron-deficiency anemia) on child development and to propose new interventions in pregnancy with broader objectives, including the prevention of IUGR.

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Chapter 11
The Assessment of Skill Learning in African Children

Esther Adi-Japha

11.1 Introduction: The Procedural Learning Memory Systems

Cognitive assessment of young African children is multifaceted and includes several core domains of cognitive development such as working memory and attention (Boivin and Giordani 2009). One of the tools used in these assessments is the Kaufman Assessment Battery for Children (K-ABC). In its recent form, the K-ABC-II (Kaufman and Kaufman 2004) includes a learning subscale with a list of items (or associations) to be learned and a test of their delayed recall (see also the Rey auditory–verbal learning test; Lezak et al. 2004; Rey 1958, which additionally provides a learning curve). These tests are suggested to be representative of daily learning and memory-related use.

Memory is thought to be organized into separate and distinct systems: a declarative system dealing with memory for facts ("what") and a procedural system dealing with memory for skills ("how to") (Cohen and Squire 1980). The term declarative memory refers to a flexible system responsible for the conscious retrieval of information (Cohen and Squire 1980). Learning tasks associated with this system are ones in which information is presented to the child and the task is to remember the information for later use. For example, immediate recall and delayed recall of a list of names for objects or paired associations (e.g., K-ABC-II). The term procedural memory refers to the long-term memory system subserving the acquisition and retention of skills and habits, specifically the repetition-dependent, implicit knowledge of the structure of recurring experiences (Brown and Robertson 2007;

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Cohen and Squire 1980). Laboratory tasks such as the pegboard or serial reaction time (Nissen and Bullemer 1987) are related to the procedural system, and it is on this memory system that the current chapter will focus.

Declarative and procedural memory processes normally closely interact during learning in everyday life (Born and Wagner 2004; Poldrack and Packard 2003). However, studies in patients with brain lesions and neuroimaging studies have provided support for the notion that declarative memory relies essentially on hippocampal function, whereas procedural memory relies on a dissociable system of brain structures, including primarily corticostriatal circuitry (e.g., Squire et al. 2004; Reber and Squire 1998).

During childhood, procedural memory formation appears to be of much greater relevance than in adulthood because of the acquisition of many new motor skills (e.g., handwriting, biking, swimming). Motor skill acquisition is typically cited to demonstrate learning that is supported by the procedural memory system. Ullman (2004), however, highlighted the fact that the procedural memory system is involved in the acquisition of language skills and habits, such as the implicit knowledge of language rules, in addition to the acquisition of new motor skills. In spite of the fundamental role of the procedural memory system in development, tasks related to the procedural system, specifically the acquisition of new skills, are not commonly studied as part of a cognitive assessment. This may be due to the fact that the assessment of skill acquisition requires a retention test, which as we shall see should be taken several hours (e.g., 24 h) following the learning of a novel skill. The current chapter emphasizes the relevance of assessing skill acquisition as part of the assessment of cognitive development in young children and puts forward some examples of skill acquisition testing.

11.2 Forming Long-Term Memories

Procedural memories are those that deal with memories for skills. We can be aware of acquiring a new skill, for example, learning to ride a bike (explicit procedural acquisition), but it is also possible to be unaware of acquiring a new skill, as occurs for grammatical rules (implicit procedural acquisition) (Robertson 2009). In this section the process of memory formation will be reviewed with emphasis on two forms of skill acquisition that have been extensively studied: explicit motor skill acquisition (e.g., Dorfberger et al. 2007; Korman et al. 2003) and the implicit acquisition of sequences (e.g., Nissen and Bullemer 1987; Song et al. 2007).

A memory passes through at least three key milestones in its development: initially it is encoded, then it is consolidated, and finally it is retrieved. During consolidation, a memory can undergo both quantitative and qualitative changes. A memory may be enhanced, demonstrated by a quantitative increase in performance, or it may be stabilized, demonstrated by becoming quantitatively less susceptible to interference. A memory can also undergo qualitative changes: there can be a shift in the strategy used to solve a problem or the emergence of awareness for what had earlier been learned. Although there is a rich diversity in the behavioral expression of consolidation, each of these examples may rely upon the same underlying mechanism. Contrasting performance at retesting against the end of training performance provides a direct measure of "off-line" performance changes that occur during consolidation (Robertson 2009; Doyon et al. 2009).

Consolidation processes can depend on the type of task, the course of practice, the time to retesting, and the presence or absence of sleep. Motor memory consolidation possibly begins as early as after a few practice trials, and thus after the brain has been exposed to sufficient relevant behavioral experience. Yet experimentally, this memory process has been defined when the emergence of delayed, off-line, gains in performance or a diminished susceptibility to interference by a subsequent experience is observed in the post-training phase (Doyon et al. 2009). Off-line improvements in the ability to perform a finger opposition task, for instance, are dependent on a plateau phase reached at the end of training following a fast learning phase (Hauptmann et al. 2005). Off-line improvements in a motor sequence learning task are sleep dependent when individuals are aware of the underlying sequence. However, when individuals have little awareness for the sequence, off-line improvements are able to develop over waking or over a night sleep. Potentially, the effect of individuals' awareness on off-line learning is mediated by their declarative knowledge for the sequence: disrupting declarative knowledge for the sequence can induce improvements over wake periods (Reis et al. 2008; Robertson 2009).

It is helpful to distinguish between processes of acquisition, consolidation, and long-term stability (also referred to as retention) of a new motor skill from adaptation, that is, the return to baseline levels of performance in response to external perturbations. An example of adaptation to an external perturbation is the response to directional errors in visually guided reaching movement caused by prism glasses. With practice, performance returns to the "baseline" level (Reis et al. 2008). Whereas motor skill acquisition is a naturally occurring experience for young children, motor adaptation refers more to laboratory tasks and will not be discussed here.

Acquisition of a new motor skill involves the acquisition of new movement qualities and/or muscle synergies that enhance performance beyond preexisting levels. Skills may take long to acquire. Enhancement of skills due to consolidation processes ("off-line" learning) can appear hours after the termination of the process (e.g., 24 h post-training). Complex skills are learned over long periods (i.e., learning to play piano or basketball) and sometimes do not reach plateau levels after years of practice. It should be kept in mind that in the process of acquisition an overlap of reward and error-based learning is possible.

It has been shown that the structure of motor practice has a strong influence on motor skill retention. Task practice structure can be characterized as a continuum with a simple structure, such as constant practice, on one end and a more complex structure, such as variable practice, on the other. A constant practice structure is drill-like, with multiple repetitions of the same task in a row, whereas variable practice structure is one in which a motor task can be randomly interleaved with trials of other motor tasks. Compared with constant practice, strong evidence exists that variable practice enhances long-term retention of a motor skill, although it may not show any performance benefits during or at the end of the practice phase. For example, Ste-Marie and colleagues (2004) studied handwriting acquisition in children under two conditions—practicing the letters either in blocks of each letter or in random sequences of all the letters. Acquisition of handwriting skill was slower under the random-order condition, but once acquired, the skill was better retained. Also, those who had practiced writing letters in a randomly given order were quicker when tested on writing out full words. These authors emphasized the fact that random practice is likely to produce more effortful processing during acquisition, and the recruitment of cognitive resources involved produces deeper learning. The implications for handwriting practice in schools are obvious. Practice is important for learning, but it should be practice without monotonous repetition. Kantak and colleagues (2010) applied a 1 Hz repetitive transcranial magnetic stimulation (rTMS) to different brain areas, immediately following constant or variable motor practice of a goal-directed arm-movement task. Their findings provide evidence in support of the stronger involvement of effortful control areas in a variable practice. These authors reported that interference to dorsolateral-prefrontal cortex (DLPFC), but not to primary motor cortex (M1), after variable practice attenuated motor skill retention, whereas interference to M1, but not to DLPFC, after constant practice attenuated motor skill retention. It should be noted that the DLPC was associated with the encoding of the goal of the motor movement, while M1 (and the striatum) was found to be involved in encoding the sequence of movements (Robertson 2009).

While several lines of evidence indicate that declarative memory undergoes substantial maturation during the preadolescent years, it is commonly assumed that procedural memory in children is as effective as (Reber 1993) or even superior to that of adults (Drummey and Newcombe 1995; Fischer et al. 2007). The latter results were related to the notion of sensitive ("critical") periods, positing that early in childhood there are periods of increased brain plasticity wherein the brain's capacity to respond to instructive experience is often enhanced, i.e., maturational windows of opportunity in which neuronal properties are particularly susceptible to shaping by experience (Keuroghlian and Knudsen 2007). Human developmental studies suggest that while in some domains (e.g., explicit motor skill acquisition, Dorfberger et al. 2007) a similar pattern of skill acquisition can be shown (see also: Meulemans et al. 1998; Murphy et al. 2003; Savion-Lemieux et al. 2009; Thomas and Nelson 2001; Vinter and Perruchet 2000), in other domains children lag behind (implicit sequence learning: Thomas et al. 2004; artificial language rules: Ferman and Karni 2010), and in others children fail to fully learn (e.g., temporal interval discrimination task using the auditory domain, Huyck and Wright 2011) or consolidate (implicit sequence learning, Fischer et al. 2007). It was suggested that learning effects are particularly sensitive to preexisting bases of knowledge and strategies (Birdsong 2006; Murphy et al. 2003; Watanabe et al. 2007; Thomas et al. 2004).

Studies of motor skill acquisition show a similar pattern of acquisition in children and adults (Dorfberger et al. 2007), including robust consolidation gains (Dorfberger et al. 2007; Savion-Lemieux et al. 2009). However, the role of sleep in consolidation processes may be age dependent. While adults' learning in a computerized version of a sequence finger-tapping task was enhanced following sleep, learning in children was not (Wilhelm et al. 2008). The authors suggested that this change may stem from a greater hippocampal competition in children in whom hippocampal-mediated consolidation of explicit declarative knowledge of the sequence structure may have interfered with consolidation of procedural learning. The hippocampus is a brain area frequently implicated in sleep-dependent processing for both the declarative and the procedural memory systems. While adults learn the explicit aspects of the sequence structure before they actually performed the finger-tapping task, and hence had no competition, 6-year-old children had difficulty remembering it.

Only one study tested susceptibility to interference in skill learning in children. Dorfberger and colleagues (2007) studied the time course of acquisition of a finger opposition sequence (FOS) task, a task that has been extensively used as a model task for procedural learning in adults. In the FOS, a 5-element finger-to-thumb movement sequence, which is fully available to the participants in an explicit manner from the first recorded trial, is repeatedly performed. In adults, the retention of training-dependent performance gains in the motor domain may be lost or markedly reduced by the introduction of a subsequent training experience if the latter occurs within a time window of up to a few hours (4–6 h for the FOS task) after the termination of training on the former task. Dorfberger and colleagues (2007) showed that the learning of the 9 and 12-year-olds, in contrast to that of the 17-year-olds, and young adults (e.g., Korman et al. 2007) was not susceptible to interference at 2 h post-training. Children, in contrast to adults, showed significant consolidation in the presence of interference, supporting the notion that the maturational differences in skill acquisition may reflect differences in the consolidation process.

The implicit acquisition of a sequence is often studied using a serial reaction time task (SRTT, Nissen and Bullemer 1987). The SRTT is a paradigm that has been widely used to assess implicit memory function in adults (e.g., Song et al. 2007; Thomas et al. 2004; Meulemans et al. 1998). It is basically a choice reaction time task that requires the subject to react as fast and accurately as possible to a visual cue appearing on a screen at one of several possible positions within a horizontal array. Unknown to the subject, the sequence of target positions is not randomly determined but follows a set of rules (e.g., a predefined sequence) that can be either deterministic (Nissen and Bullemer 1987) or include probabilistic elements (e.g., Song et al. 2007). Despite remaining unaware of these rules, subjects typically develop implicit knowledge about the spatiotemporal constraints of the underlying structure as a consequence of prolonged training. This is reflected by increased response times to sudden violations of the rules. Using a deterministic grammar, Meulemans et al. (1998) compared SRTT performance between children aged 6–7 years, children aged 10–11 years, and adults. Although response times generally decreased with age, implicit learning, measured as the difference in response time to a structured sequence as compared with a random sequence of the target stimulus, was closely comparable in the three groups. This finding indicating that young children can implicitly acquire the structure of the sequence as well as adults has been subsequently confirmed in another study in children down to 4 years (Thomas and Nelson 2001). Studies of implicit sequence learning have shown robust structure learning in a spatial location task in 2-year-olds (Bremner et al. 2007), and even preverbal 12-month-old infants learned the structure of a trisyllabic speech item (Kovacs and Mehler 2009).

As noted earlier, finger-tapping tasks with explicit knowledge of the trained sequence (e.g., the FOS task) show sleep-dependent consolidation gain (Korman et al. 2003, 2007). Song and colleagues (2007) used a probabilistic variant of the SRTT, termed ASRT (alternating SRT, i.e., where random elements are imbedded within a sequence at fixed positions), featuring probabilistic sequences to investigate off-line consolidation. Probabilistic sequences confer the advantage that spontaneous explicit awareness does not occur. These authors found that neither sleep nor time during the day enhanced sequence-specific knowledge (assessed as difference in performance between random and rule-based elements), supporting the association between goal-directed explicit knowledge and sleep-dependent consolidation gains (Robertson 2009).

Recent studies on children with developmental disabilities suggest that cognitive and motor impairments tend to co-occur (Nicolson and Fawcett 2007). This issue will be reviewed in the next sections.

11.3 Motor Skills, Procedural Learning, and Their Relation to Cognitive Development

The relationship between global aspects of cognitive and motor performance was first discussed many centuries ago by Descartes (1596–1650), who stated that cognitive processes are entirely different from motor processes (Hatfield 2003). More recently, Piaget argued that cognitive and motor processes cannot be seen as separate entities because cognitive development relies totally on motor functioning (Piaget and Inhelder 1966). Yet, one of the major criticisms on Piaget's theory of cognitive development is that he gave too little consideration to the motor possibilities and impossibilities of the young child (Berger 1988). Adolph (2005, 2008; Adolph and Berger 2006) suggested that researchers' views of motor development have been naïve, because they have not recognized the complexity of cognitive tasks demanded of infants. Adolph proposed that infants are learning to learn as they master locomotion and subsequent gross and fine motor skills. Infants and young children continually have to solve complex problems in adapting and changing each movement in response to their perception of the current, but ever changing, environment; their changing constraints on physical movement, because of physical growth of arms, limbs, and other body parts; and their current levels of neural maturation and motor capability.

Both areas of motor and cognition seem to follow a similar developmental timetable with an accelerated developmental progression between 5 and 10 years of age (Roebers and Kauer 2008; Wassenberg et al. 2005) and a protracted development into adolescence (Diamond 2000). Several studies that tested the direct relationship between global aspects of cognitive and motor performance found only weak associations. Wassenberg and colleagues (2005) studied the relationship between cognitive and motor performance, statistically correcting for attention, in a large cross-sectional sample drawn from a population of 5- to 6-year-old children attending normal kindergarten. The relationships found were rather small. When cognitive tasks without a motor component were included in the estimate of cognitive performance, no significant association with overall motor performance was found. Instead, a more specific association was supported. It was shown that performance on several specific cognitive tests (i.e., working memory and verbal fluency) was modestly related to motor performance, independently of attention. All relations were positive; lower performance on the abovementioned cognitive tests indicated a lower performance on the motor test. Similar findings were reported by Roebers and Kauer (2008) who studied the association between motor and cognitive control in 7-year-olds. Controlling for age, their findings suggested that only some aspects of cognitive and motor control are significantly interrelated. These findings argue against a global relation between cognitive and motor performance. Thus, the theoretical assumption, raised by influential researchers such as Piaget, of a direct linkage between global aspects of cognitive and motor behavior, could not be supported. Instead, specific (rather than general) associations were highlighted.

Using co-occurrence of effects from brain damage or brain abnormalities and correlations between deficits in motor and cognitive skills in developmental disorders, Diamond (2000) summarized the links between motor and cognitive skills. He reported significant evidence for specific motor–cognition associations in each of the two areas. Diamond's neuroimaging evidence suggested that some of the primary brain regions previously thought to be involved only in motor activities (e.g., cerebellum and basal ganglia) or cognitive activities (e.g., prefrontal cortex) are coactivated when doing certain motor or cognitive tasks. From these lines of research, it appears that individuals' ability to plan, monitor, and control motor and cognitive activities may lead to similar normative developmental pathways and to comorbidities in cognitive and motor deficits.

The development of early motor and cognitive skills lays the path for later developmental achievements. At preschool, children acquire a variety of motor skills which are important for their physical, social, and academic development (Riethmuller et al. 2009). Traditionally, motor skills are subdivided into gross and fine motor skills. Recently, fine motor skills in preschoolers were shown to predict later achievements in reading and math and proved useful in identifying children at risk for school achievements (Grissmer et al. 2010; Pianta and McCoy 1997; Son and Meisels 2006). Surprisingly, one of the most predicting measures was a visual–motor skill task (copy five designs).

In view of association between specific subdomains of motor and cognitive development, two areas of cognitive development have been more closely studied in relation to the developments of the motor system. These subdomains are language and executive functioning.

11.4 Motor Skills, Procedural Memory, and Their Relation to Language Development

For many years, prominent language researchers argued that language development was not related to motor maturation. Lenneberg (1967) pointed out in a classic work that major speech milestones are reached in a fixed sequence and at relatively constant chronological ages suggesting "a remarkable synchronization of speech milestones with motor-developmental milestones" (p. 127). For example, at 6 months, infants begin to sit independently and are able to lean forward and reach unilaterally while sitting. Cooing changes into babbling that resembles single-syllable utterances, but neither vowels nor consonants have fixed recurrences. Although examples such as these might appear to provide evidence of links between motor and language development, Lenneberg (1967) used them as a means for making a strong argument against this view, claiming not only that "the onset of language is not simply the consequence of motor control" (p. 127) but that there is "independence of language development from motor coordination" (p. 131). Bates et al. (1979, Chap. 2) included an 11-item locomotor development scale in a 3-year longitudinal study of 25 infants followed from 9 months to a year. Their findings indicated that locomotion correlated positively and significantly with the gestural measures in only 4 out of 200 possible relationships, or 2% of the matrix (p. 94), supporting the hypothesis of no simple link between language development and neuromotor maturation. In line with Bates et al. (1979), Bloom (1993) reported no relation between onset of walking and production of first word and between block building and language and play development.

However, researchers who studied classic sensorimotor behaviors of the sort described by Piaget (1952) came to a different conclusion concerning the relation between motor and language development. It is important to note that sensorimotor behaviors are indices of underlying cognitive change, but they are also *motor* behaviors, behaviors that represent advances in the infant's capacity for action. Thelen (1979) reported a striking peak in frequency of rhythmic arm movements (e.g., shaking, swinging, banging) at around 28 weeks of age. This is also the age at which many infants begin to produce reduplicated babble, vocalizations in which well-formed syllables are organized into a regularly timed, rhythmically organized sequence (e.g., [bababa]; Koopmans-van Beinum and van der Stelt 1986; Oller and Eilers 1988). Iverson (2010), who reviewed the literature concerning the link between motor and language development during the first 18 months of life, suggests that as infants perform rhythmic arm movements, they have the opportunity to practice a skill—production of rhythmically organized, tightly timed actions—that is a central characteristic of reduplicated babble.

According to Iverson (2010), changes in motor skills (i.e., achievements and advances in posture, independent locomotion, and object manipulation) provide infants with a broader and more diverse set of opportunities for acting in the world. These opportunities provide contexts for acquiring, practicing, and refining skills that contribute, both directly and indirectly, to the development of communication and language. An indirect link between movements and language development was suggested above. A direct link between emerging locomotion and communication skills was suggested by Campos et al. (2000) who proposed that the emergence of ability to follow eye gaze and pointing directed toward distal objects—a major milestone in the development of joint attention—may be related to crawling experience. Similarly, Karasik et al. (2011) suggest that walkers are more likely to locomote toward their mothers and then hold out the object for her inspection than crawlers.

The evidence reviewed here, regarding direct and indirect links between motor development and the development of communication and language, does not imply that motor advances are necessary for language development (Campos et al. 2000; Iverson 2010); rather this evidence supports a role for motor development in language acquisition that might be best labeled "normally participatory." All other things being equal, and given a typically developing child in a typical environment, motor development is a key participant in the process of language acquisition.

It may be the case that some of the indirect evidence results from an underlying mechanism common for the development of specific motor and language skills. The link suggested by Thelen (1979) between rhythmic arm movements and reduplicated babble may be explained by an underlying procedural functioning of acquisition and retention of repetition-dependent skills in the two separate domains: rhythmic arm movements and reduplicated babble. It may be hypothesized that the procedural system is shaped (wired) during the acquisition and retention of repetition-dependent motor skills as rhythmic arm movements, where *implicit knowledge of the structure of recurring experiences is built*. This same system may be later used for acquiring grammatical language rules.

Imaging studies of motor skill acquisition over the period from minutes to days (Doyon and Benali 2005; Karni et al. 1995) have led to propose that there are two distinct motor learning circuits, a corticostriatal system and a cortico-cerebellar system. The corticostriatal system is particularly involved in learning sequences of movements, whereas the cortico-cerebellar system is particularly involved in adapting to environmental perturbations. However, all three brain regions—motor cortex, basal ganglia, and cerebellum (and also the frontal cortex for explicit skill monitoring in the early stages)—are involved in the initial stage of motor skill acquisition, whereas the roles of the corticostriatal and cortico-cerebellar systems diverge as practice continues. Ullman (2004) highlighted the fact that in addition to the well-known procedural learning motor system (for motor skills) there is also a procedural learning system for language skills and habits, such as our implicit knowledge of language rules. It comprises the basal ganglia; frontal cortex, in particular Broca's area and premotor regions; parietal cortex; superior temporal cortex; and the cerebellum. The system has clear commonalities with the corticostriatal and cortico-cerebellar motor learning systems, the difference being that the language-based system interacts with the language-based regions of the frontal lobe, whereas the motor skill system interacts with primary motor cortex. Both systems include premotor regions. It may be that the commonality between functions is even further enhanced. Seger (2006) suggested that two important common functions utilizing the basal ganglia and shared by some motor and cognitive tasks are performing a sequential, coordinated series of events over time and complex categorization. The sequential events could be performing a coordinated motor movement, organizing grammatical elements in language, or sequencing subgoals in complex reasoning.

The notion of an interrelation between motor and language development is further supported by evidence from studies of individuals with deficits in either domain that will be reviewed later on.

11.5 The Relation Between Motor Skills, Procedural Learning, and Executive Functioning in Children

In the cognitive literature, the term executive function (EF), executive control, or cognitive control is used for any activity that involves high demands for the individual. These activities may involve a high level of difficulty (because of complexity or novelty); continuously changing conditions (requiring selective, sustained attention) and time constraints (need for speeded responses); and/or a strong emphasis on accuracy (Hughes and Graham 2002). Empirical studies on the factorial structure of executive functions revealed three distinguishable dimensions (1) shifting/switching between different tasks; (2) monitoring and updating, including dynamically manipulating and/or temporally sequencing information in short-term memory; and (3) deliberately inhibiting dominant, automatic, or prepotent responses (Miyake et al. 2000). These three aspects of executive functioning, however, have also been shown to be significantly intercorrelated, suggesting both unity and diversity of executive control skills.

Numerous studies have demonstrated the importance of executive functions in school and life (e.g., Duncan et al. 2007). However, it is not clear how skill learning and EF are interrelated. Current literature on motor skill learning divides learning into two components: one encodes the spatial goal of the movement, and the other encodes the movements needed to achieve that goal. The goal component is related to awareness. Recent functional imaging work has shown that the primary motor cortex (M1) is associated with movement-based processing and that communication across a large circuit, including the parietal and prefrontal cortices, is associated with goal-based processing. These data suggest that EF may be related to the goal components and will be more pronounced during the fast learning phase (initial phase of practice). Imaging studies reveal that movement and goal-based components are both activated after motor skill teaching (Robertson 2009), but their activation may depend on the structure of practice and acquisition rate which may alter the relative proportions of the motor skill components.

Roebers and Kauer (2008) studied the relationship between cognitive and motor control by correlating individual performance on a variety of motor and EF tasks in a normative sample of 100 seven-year-olds. Similar to other studies on the relationship between motor and cognitive development, only low to medium correlations emerged between the two domains, interpreted by the authors as related to the speed and accuracy demands of all tasks and indicating shared dimensions of executive functioning across the cognitive and motor domains. On most of the tasks, Roebers and Kauer used two trials per task. The authors note that when partial correlations (controlling for age) were computed for the composite scores of cognitive and motor control in trials one and two, separately, a significant association between the two domains was found for trial one but not for trial two, supporting the claim that the impact of executive functioning is more pronounced when tasks are novel. This finding is consistent with the notion that the involvement of executive functions is strongest when tasks are novel.

11.6 Procedural Memory Formation in Children with Developmental Disorders

Motor skills and skill learning were mostly studied in disorders associated with learning disabilities as dyslexia, dysgraphia, attention deficit/hyperactivity disorder (ADHD), language impairment (LI), and developmental coordination disorder (DCD) but also in other, less common, developmental disorders (e.g., children with mental retardation, Down syndrome, and autism). While motor and skill learning deficits have been reported in the former groups of deficits, in other developmental disorders, procedural skills were found to be relatively preserved.

Dyslexia is a disorder in children who, despite conventional classroom experience, "fail to attain the language skills of reading, writing and spelling commensurate with their intellectual abilities" (World Federation of Neurology 1968). Children with dyslexia were reported to have deficits in gross motor skills, such as difficulties in swimming and riding a bike and throwing and catching a ball, as well as in fine motor skills such as poor handwriting and difficulties in tying shoelaces. These children were also reported to demonstrate "soft neurological signs," including deficits in speed of tapping, rapid successive finger opposition, heel–toe placement, and accuracy in copying (for a review see Nicolson and Fawcett 2011). Evidence in support of the view of procedural skill deficits in DD was suggested by Nicolson, Fawcett, and colleagues who reported impaired performance of individuals with dyslexia in motor sequence learning (Nicolson et al. 1999), in eye blink conditioning (Nicolson et al. 2002), and in overall learning rates for procedural skills (Nicolson and Fawcett 2000).

Vicari et al. (2005) tested motor skill learning in 16 school-age children with DD and matched typical readers on the SRTT and on the mirror-drawing tasks. The mirror-drawing task is a procedural learning task that requires the establishment of fast and repetitive production of visuospatial stimuli but no acquisition of sequences. The participant is asked to repetitively trace a shape (e.g., star) through a mirror that inverts the image. Participants were trained on the mirror-drawing task, and memory consolidation was tested 24 h post-training session. Vicari et al. (2005) demonstrated that children with DD have lower accuracy and slower performance on the

SRTT. Furthermore, although these children performed similarly to normal readers on the training phase of the mirror-drawing task, they performed significantly less well on the retention of task, suggesting impaired consolidation of newly acquired motor skills.

Dysgraphia is the more familiar component of what is known as disorder of written expression. Disorders of written expression are defined as a combination of difficulties in an individual's ability to compose written text that are manifested by illegible handwriting, letter shape distortions, dysfluent writing, spelling errors, and difficulty in written expression of ideas that cannot be attributed to disabilities in reading or oral expression (DSM-IV—American Psychiatric Association 1994). The term dysgraphia commonly refers to a combination of illegible handwriting and spelling errors (Adi-Japha et al. 2007). To date, there is no study available of skill learning in children with dysgraphia. Studies concerning the locus of the deficit (Adi-Japha et al. 2007; Mather 2003; Smits Engelsman and Van Galen 1997) concluded that dysgraphia was associated with poor motor control, compromising greater "noise" in movement production, rather than poor letter knowledge. Given that handwriting is acquired by the procedural system, it may be expected that children with dysgraphia would show a procedural deficit (Nicolson and Fawcett 2011).

The core symptoms of the neurobehavioral syndrome attention deficit/hyperactivity disorder (ADHD) as defined by the DSM-IV (American Psychiatric Association 1994) are inattention, impulsivity, and hyperactivity. However, additional concerns have been raised by evidence of difficulties in skilled motor performance in these children. For example, deficits in tasks such as buttoning clothes, tying shoe laces, and writing or printing letters have been described (Adi-Japha et al. 2007, 2011a; Karatekin et al. 2003). Children with ADHD are often impaired in the performance of repetitive motor tasks (Barnes et al. 2010; Mostofsky et al. 2006), and these impairments are taken as evidence for procedural memory deficits (Barnes et al. 2010). Adi-Japha et al. (2011a) studied 32 adult female participants, 16 with ADHD, who were trained on a sequence of finger movements (the FOS task) and tested before training and, immediately, 24 h and 2 weeks after training. Both groups showed similar within-session gains in speed. Additional delayed consolidation gains were found at 24 h, but less robustly in the ADHD group, and, again, at 2 weeks post-training. However, while controls showed significant delayed gains in accuracy at 24 h and 2 weeks post-training, accuracy deteriorated in ADHD from pre-training to 24 h post-training and was only at pre-training levels by 2 weeks post-training. These results demonstrated that both the acquisition and memory consolidation of motor skills are atypical in ADHD.

The incidence of primary (specific) language impairment (LI) among kindergarten children is estimated to be 7% (Tomblin et al. 1997). Children with LI present delayed or disordered language acquisition that is not secondary to conditions such as hearing loss, developmental delay, neurological insult, or environmental deprivation. Although language performance is, by definition, the central impairment in these children, deficits seem not to be limited (or specific) to language and to include weaknesses in basic nonlinguistic processing skills (Ullman and Pierpont 2005; Windsor et al. 2008). Within the nonlinguistic domain, there is considerable evidence that the performance of children with LI on a variety of motor tasks is slower and is more vulnerable to the effect of cumulative experience (e.g., Bishop 2002; Estil et al. 2003; Hill 2001). For example, LI groups show deficits in fine and gross motor tasks, such as peg moving, bead threading, ball rolling, and tapping (Bishop and Edmundson 1987; Corriveau and Goswami 2009; Miller et al. 2001; Powell and Bishop 1992). Adi-Japha et al. (2011b) studied 32 five-year-old children, 16 with language impairment (LI) matched to controls for age and visual–motor integration skills. The children practiced the production of a new graphic symbol and were tested 24 h and 2 weeks post-practice day. Differences in performance speed emerged between the groups: children with LI showed a later onset of rapid learning in the practice phase (replicating a similar finding reported by Tomblin et al. 2007), and only the comparison group exhibited delayed, consolidation, gains 24 h post-training. At 2 weeks post-training, children with LI improved, closing the gap in performance speed. Speed–accuracy trade-off was characteristic of speed improvements in LI. These results indicate atypical and delayed acquisition in children with LI and support the view that deficient skill acquisition in LI goes beyond the language system.

The Procedural Deficit Hypothesis (PDH, Ullman 2004) posits that specific language impairments (SLI) can be largely explained by abnormalities of brain structures that subserve procedural memory. The PDH predicts that impairments of procedural memory underlie the grammatical deficits observed in the disorder. Hedenius et al. (2011) studied children with SLI and controls using the ASRT task (the alternating SRTT, mentioned in Sect. 11.2). These authors found that although both groups showed evidence of initial sequence learning, only the TD children showed clear signs of consolidation. When the children were recategorized on the basis of grammar deficits rather than broader language deficits, a clearer pattern emerged. Whereas both the grammar impaired and normal grammar groups showed evidence of initial sequence learning, only those with normal grammar showed consolidation and longer-term learning. This study suggests that consolidation and longer-term procedural learning are impaired in SLI but that these impairments are specifically tied to the grammatical deficits in the disorder.

Developmental coordination disorder (DCD) is a condition characterized by marked impairment of motor coordination that significantly interferes with an individual's academic achievement and/or activities of daily living (American Psychiatric Association (APA) 2000). Children with DCD experience numerous functional challenges secondary to their motor impairment, including difficulty with dressing, tying shoelaces, handwriting, and playing sports (Missiuna et al. 2006; Polatajko and Cantin 2005). Gheysen et al. (2011) studied the SRTT in 18 children with DCD and 20 matched typically developing children. Overall, DCD children demonstrated general learning of visuomotor task demands comparable to that of typically developing children but failed to learn the visuomotor sequence.

There is a considerable overlap between different developmental disorders associated with learning disabilities, with an apparent comorbidity between most (for a review see Nicolson and Fawcett 2007, 2011). This led Nicolson and Fawcett (2007) to hypothesize that impairment in any one brain region—cerebellum, motor cortex, or basal ganglia—would lead to an impaired ability to initially acquire the skills associated with that region. Because there is an overlap in brain regions involved in these developmental disorders, this would lead to comorbidity in symptoms. For example, comorbidity of motor and phonological problems suggests that both language and motor components of the cortico-cerebellar procedural learning system are affected, whereas intact motor skill suggests that only the language-related components are affected. Nicolson and Fawcett (2011) suggested that the strong implication of this framework is that the neural systems level of description provides an under-explored classificatory system that complements, or may even replace, the current DSM-IV symptom-based diagnostic system.

Not all developmental disabilities are associated with impaired skill learning. The literature suggests that children with autism as well as those with mental retardation have relatively preserved implicit skill learning skills. Nemeth and colleagues (2010) studied the ASRT task in children with autism and found that ASD children showed general skill learning and implicit learning of probabilistic sequences similar to that of two groups of controls, one matched in IQ and the other in age (Barnes et al. 2008). In addition, the groups did not differ in consolidation. The authors suggested that learning mechanisms associated with frontal–striatal–cerebellar anatomy are partly intact in ASD.

Difficulties that individuals with intellectual disabilities encounter in any task requiring effortful or intentional information processing are well documented in the literature (e.g., Bebko and Luhaorg 1998; Bray 1979; Brown 1974). It has been reported, however, that these individuals, including those with Down syndrome, have a relatively preserved implicit skill learning (e.g., Vicari et al. 2000; Vicari 2006; Vinter and Detable 2003, 2008).

The findings discussed above suggest impaired procedural learning in developmental disorders associated with learning disabilities, but not in all developmental disorders. These results highlight the need to include measures of skill learning in the diagnostic process.

11.7 The Assessment of African Children

As shown earlier in this chapter, skill learning is a basic underlying brain mechanism involved in several key developmental domains as motor skills, language, and academic achievements. Impairment in the functioning of this mechanism was strongly associated with developmental disorders that are related to learning disabilities. It was suggested that the neural systems level description of procedural memory provides an under-explored classificatory system that complements, or may even replace, the current DSM-IV symptom-based diagnostic system (Nicolson and Fawcett 2011).

Studies of African children at risk from diseases affecting the brain such as cerebral malaria, sickle-cell disease, and HIV provide evidence of consistent deficit patterns in attention, working memory, and learning. These patterns of deficits are common in children with developmental disorders related to learning disabilities. Currently available assessment batteries of cognitive development include tests of working memory, of executive functioning, and of declarative memory (e.g., KABC). To have the full picture, however, procedural memory assessment should be included.

For school-age children, available tools for the assessment of procedural memory are the mirror-drawing task (Vicari et al. 2005) for the assessment of declarative motor skill learning, the FOS task (Dorfberger et al. 2007) and its computerized version (Fischer et al. 2007) that combines explicit motor and sequence learning, and the ASRT task (Hedenius et al. 2011; Nemeth et al. 2010) for studying implicit sequence-specific effects. For kindergarten children, available tools include the invented letter task (Adi-Japha et al. 2011b) to assess (visual–) motor components and the SRTT evaluating sequence learning (Thomas and Nelson 2001). Both tasks could be used for assessing older children as well as adults, although for the SRTT the length of the sequence changes from 10 (in children) to 12 (in adults). The SRTT has several early childhood variants (Bremner et al. 2007; Kovacs and Mehler 2009) for children younger than 4 years of age, as well.

Recently, Ruel et al. (2012) used the Test of Variables of Attention (TOVA); the Kaufman Assessment Battery for Children, second edition (KABC-2); and the Bruininks–Oseretsky Test of Motor Proficiency, second edition (BOT-2) to assess the neurocognitive and motor deficits in HIV-infected Ugandan children. The BOT-2 is a comprehensive assessment of motor function that generates scores in different domains of movement and coordination. HIV-infected children demonstrated significantly lower motor proficiency, as assessed by the BOT-2. However, from these results, it is not clear whether children with HIV are impaired at their motor skills or whether their ability to acquire new motor behaviors and retain them is impaired as well. A simple task as the invented letter task (Adi-Japha et al. 2011b), which is a repeated production of simple dot-to-dot task composed of three dots, could inform whether this is the case. Our pilot data suggest that this task measures effectively skill learning in kindergarten and primary school children, as well as in adults.

Central to the assessment of procedural skills is the assessment of consolidation processes: enhancement and susceptibility to interference. In the assessment of susceptibility to interference (e.g., in the FOS task), the training session is doubled in length to allow the practice of two different stimuli. In adults, enhancement of skills develops in the hours that follow the training session and, in some cases, is sleep dependent. This makes the assessment of procedural memory more complex. One solution is to assess only the learning process (the training session). Several studies in individuals with developmental disabilities suggest that impaired acquisition precedes impaired consolidation processes (Adi-Japha et al. 2011a, b). In this case, the assessment process should include several blocks, so that the shape of the learning curve could be evaluated (see Adi-Japha et al. 2011b for the invented letter task and Tomblin et al. 2007 for the SRTT). Several lines of evidence suggest that consolidation in children has different time scales, is not sleep dependent (Fischer et al. 2007), and may take place a few hours following the training sleep. Direct studies of this issue are yet missing. Another solution is to test the child a few weeks later to assess retention. Studies of skill acquisition suggest that the enhanced performance level remains stable for weeks and months following the training session. Future studies in African children should therefore include measures of skill learning to provide a comprehensive evaluation that is in line with current knowledge of the underlying neural mechanisms involved in development.

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Chapter 12
The Assessment of Neuropsychological Outcomes in Pediatric Severe Malaria

Penny Holding and Michael J. Boivin

12.1 Introduction

Malaria remains one of the most widespread infections in the world, with about 75% of the two billion exposed annually residing in Sub-Saharan Africa (Snow et al. 2005). The consequence of exposure goes beyond the infection itself (Holding and Snow 2001). At the societal or macro-level, also referred to as the exosystem (Bronfenbrenner and Morris 1998), infection has been associated with a significant negative impact upon economic growth (WHO 2000). This impact is both through the diversion of scarce resources for treatment and direct effect upon the development of human potential (Breman et al. 2004).

At the micro (individual) level, the effect of malaria can manifest as a loss of function, dampening educational achievement and occupational attainment. The well-being of families is affected by both the need to provide for a sick or disabled member and the loss of potential income. In Sub-Saharan Africa it is the children that are most affected by the disease (Carneiro et al. 2010). Therefore, the consequences of infection may begin early in life and continue long after disease exposure. The need to reduce risk, promote resilience, and remediate poor outcomes renders an understanding of the "neuropsychology of malaria" at the microlevel as

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a major contributor to the ability to reduce the potential burden of the disease on the mesosystem (family) and exosystem (community) levels.

In the early 1990s, research in cerebral malaria involved only a small group of individuals and was carried out in a context where issues of mortality were paramount. The quality of life of survivors was accorded relatively minimal attention. A more sensitive and sophisticated approach to understanding malaria has developed (Breman 2001; Breman et al. 2001), and, as research has expanded in breadth and depth, a number of salient lessons have been learned that have important implications both for the understanding of malaria and for the investigation of the brain/behavior impact of other diseases. These lessons include test selection, the definition of disease exposure, and the importance of measuring and accounting for a range of background factors. These issues are the focus of the present chapter.

12.2 Measuring Health Effects: Describing the Impact upon Development

The history of psychological assessment in Sub-Saharan Africa is little older than the literature here reviewed, with most tests used having been introduced by researchers trained in the European/North American approach to assessment. This approach has, for the most part, guided test selection as mitigated by proposed sensitivity to the brain/behavior effects of that particular disease. The result is batteries of tests that, in the main, have been adapted from material not necessarily familiar within an African setting. The consequence is potential compromise in test reliability and unknown implications for test validity. The implications associated with moving tests across and between cultural and linguistic contexts have been addressed in detail elsewhere (Holding et al. 2010; Malda et al. 2010; Brouwers et al. 2009; Alcock et al. 2008; Sternberg et al. 2001; Sternberg and Grigorenko 2004). The intention of this chapter is to discuss these issues as they relate to understanding the pediatric neuropsychological effects of severe malaria. To do so we will evaluate the evidence across multiple contexts and develop a meaningful conceptual analysis and estimation of disease brain/behavior effects.

Some contend that results between sites can be combined only if the same test is used to gauge neurocognitive outcomes. This assumption has driven such initiatives as the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI), which is a structured interview designed to assess ICD-10 and/or DSM-IV mental disorders (WHO 1997). However, this approach ignores the richness of the effect of cultural and linguistic diversity on assessment, amply demonstrated in the work of Vygotsky and Luria (Ratner 1991). When this diversity is ignored, problems in administration and interpretation follow. To illustrate, the CIDI depression subscale was designed to take 8 min to administer. When used with nonliterate respondents and those who use languages do not have specific vocabulary to describe the mental health issues being addressed, it requires about 45 min.

Other problems come from the inclusion/exclusion of appropriate or relevant material. Serpell (1979) comparing performance between children in Africa and Europe clearly demonstrated how functional outcomes are misrepresented when unfamiliar material is used. For example, is it appropriate to classify a North American student as having a neurodevelopmental dysfunction because she fails to correctly label a picture of zebu cattle as a cow, being unfamiliar with the hump in the middle of the back? Similarly, by using pictorial material in Africa that uses European images, or tasks that stress speed as a measure of intelligence, assessments of disease effects within the African context will be prone to limitations of interpretation. Using one cultural source to dictate appropriate test content also limits the validity of the picture of development that emerges. Obedience is a characteristic of behavior highly valued in Africa. Therefore, an assessment schedule that does not include obedience as an integral part of intelligent functioning is not sampling appropriate neurocognitive outcomes in the region.

Cultural differences should neither constrain our investigations nor should they be minimized or avoided. They should be acknowledged and addressed by paying careful attention to the way in which tools are selected, developed, and applied to the reporting of performance scores (Durlak 2009). Clearly cultural universalities in human functioning allow comparison of outcomes from testing and also at the functional level (Poortinga 1999). In this chapter we will attempt to combine results across studies of severe malaria, not only to draw conclusions about the effects of disease exposure but also to explore the methodological strengths and limitations of the assessments undertaken. The first step is to identify which aspects of development are likely to be affected by disease exposure.

12.3 Health Burden of Malarial Disease: Pathogenesis and Potential Sequelae

Between 20 and 70% of children living in malaria endemic areas will, at any one point in time, carry malaria parasites in their blood stream. The density of these infections will depend upon the level of endemicity for that parasite (Snow et al. 2003). Malaria disease is responsible for 50% of pediatric hospital admissions in endemic malarial areas and accounts for 20% of deaths in children under 5 years of age in Africa (DCPP 2005; WHO 2005). The most severe form of the disease, cerebral malaria, develops in approximately 8% of all *Plasmodium falciparum* cases in children (Marsh et al. 1995; Newton and Krishna 1998). Mortality rates for cerebral malaria are as high as 20–40%, even with aggressive treatment (Enwere 2005; Maitland et al. 2004; Snow et al. 2003; Turner 1997). There are three other parasites (ovale, vivax, and malariae) and while associated with both morbidity and to a lesser extent mortality, they have not been associated with neurological complications in children to the same degree. *Plasmodium knowlesi* is a zoonotic species that causes malaria in macaques, but can also infect humans and cause a deadly form of the disease.

Cerebral malaria (CM) is a severe form of the disease defined by coma not due to other CNS infections, the presence of *P. falciparum* parasites. This is the most common acute non-traumatic encephalopathy in children in Africa and possibly in the world (Molyneux 1990). In addition to deep and prolonged coma, signs and symptoms can include hypoglycemia, hyperpyrexia, respiratory distress (associated with metabolic acidosis), and the occurrence of multiple and prolonged seizures (Bondi 1992; Brewster et al. 1990; Crawley et al. 1996; Molyneux et al. 1989). As these signs and symptoms are associated with other encephalopathies and those living in malaria endemic areas will often host parasites at subclinical levels, a definitive diagnosis is significantly improved through the confirmation of malaria-specific retinopathy (Taylor et al. 2004; Birbeck et al. 2009).

Among survivors, neurological studies have reported sequelae that include sensory impairment (visual, auditory, tactile), hemiparesis and quadriparesis, and other movement disorders, epilepsy, mood disorder, and intellectual impairment (Bondi 1992; Brewster et al. 1990; Carme et al. 1993; Meremikwu et al. 1997; van Hensbroek et al. 1997). The proportion of child survivors of malaria with impaired consciousness left with long-term neurologic sequelae is estimated at between 5 and 20% (van Hensbroek et al. 1997; Newton 2001; Mung'ala Odera et al. 2004; Idro et al. 2007) and with neurocognitive sequelae at approximately 20% (Holding and Snow 2001; Holding and Wekulo 2004; Carter et al. 2005a, b; Kihara et al. 2006). Overall this translates to approximately 3/1000 children in a malaria endemic area who will develop long-term impairments because of severe malarial disease (Holding and Snow 2001), a significant burden in a resource poor setting.

12.4 Overview of Pathophysiologic Mechanism of Brain Injury in Cerebral Malaria

The complexity of mechanisms involved in severe disease suggests that there are potentially multiple mechanisms for brain damage. Several pathogenic mechanisms have been proposed to explain the onset of coma in cerebral malaria. Some involve a compromised blood flow and others an excitation of a proinflammatory response.

(a) The histopathological hallmark of cerebral malaria is engorgement of cerebral capillaries and post-capillary venules with infected erythrocytes, through a process known as sequestration (Newton et al. 2000; Taylor et al. 2004). In the microvasculature of the brain, infected erythrocytes adhere to endothelial cells of cerebral blood vessels and bind to other erythrocytes. The net effect of these two processes is a degree of microvasculature blockage and a reduction in substrate supply of glucose and oxygen for brain metabolism (Dondorp et al. 2004). These effects may be worsened by anemia, states of ischemia like shock, respiratory distress, lactic acidosis, or when there is increased metabolic need such as during seizures. Relative cerebral anoxia may result and is likely to affect a number of brain regions, although damage to the deep white matter structure served by watershed regions may be most evident. Watershed areas in the parietal–temporal region are thought to be the most vulnerable, leading to lesions that may compromise neurological and neuropsychological integrity (Crawley et al. 1996). Two other regions vulnerable to hypoxia are the hippocampus and the basal ganglia, both associated, though not exclusively, with memory function (Caine and Watson 2000; Knowlton 2002).

Another possible candidate route is white matter damage of the periventricular regions, associated with visual–spatial difficulties, tactile perceptual skills, visual–motor integration, social perception, emotional functioning, and nonverbal problem solving (Rourke 1987; Woods et al. 2000). Neural networks in brain regions mediating attention and memory are also especially vulnerable to hypoglycemic coma, blood–brain barrier compromise, immunoreactive pathogenesis, and hypoxic–ischemic crisis (Jung et al. 2005; Krishnamoorthy et al. 2000; Yamamoto et al. 2002). These various pathways suggest specific functional vulnerabilities.

(b) Microvascular sequestration in tissue with high metabolic demands (retina and brain) leads to impaired blood flow, tissue hypoxia, and cellular swelling (oncosis). This typically leads to hyperlactatemia, which is characteristic of the children with CM confirmed by retinal findings (Lewallen et al. 2008). These processes may also lead to cerebral edema and subsequent raised intracranial pressure. Endothelial cell-wall damage and blood–brain barrier compromise could lead to the immunoreactive proinflammatory components of CM brain pathogenesis as proposed by Boivin and others (Boivin 2002; John et al. 2006; Turner 1997). Microvascular sequestration and the subsequent metabolic challenges associated with sequestration, especially when it leads to seizures and further focal metabolic disruption in the brain, may be related to neurological disability and/or neurocognitive and psychosocial difficulties commonly associated with an epileptic profile (Birbeck et al. 2010; Opoka, et al. 2009).

(c) There is also ample evidence to suggest an immunologically based trigger for coma in both human subjects and animal models of cerebral malaria (Lou et al. 2001) perhaps mediated by cytokine-based endothelial activation and disruption of the blood–brain barrier (Brown et al. 1999). Cytotoxic damage may result. Another pathology observed is cerebral edema (Taylor et al. 2004), and brain swelling is demonstrable on computerized tomography scans (Newton et al. 1994). This could result from any of the potential mechanisms described above and could be considered the most extreme outcome. Diffuse encephalopathy associated with this outcome might produce a variety of neuropsychological effects or lead to global impairment.

(d) Another consequence of the proinflammatory response is the release of mediators such as nitric oxide levels in the brain (Levesque et al. 1999; Dobbie et al. 2000). The consequences of this mechanism would, in contrast, be transient.

(e) There may also be indirect pathways to functional impairment. It may be that a principal deleterious effect of cerebral malaria is to disrupt the normal maturation of neural networks. The frontal and parietal neocortices continue to myelinate throughout childhood and into adulthood (Paus et al. 1999; Sowell et al. 2003). The degree of myelination and axonal thickness in the left frontal and parietal cortices has been positively correlated with working memory capacity in children between the ages of 8 and 18 years (Nagy et al. 2004; Olesen et al. 2003). If cerebral malaria disrupts the process of myelination in these important regions, then impairment of intellectual functioning may become apparent over the longer term.

12.5 Overview of Neuropathogenic Mechanisms of Brain Injury in Severe Malaria

Cerebral malaria in adults tends to be part of a multi-organ disease with more focal encephalopathy characterized by symmetrical upper-neuron lesions and cortical infarcts (Vokaer et al. 2004); (Kampfl et al. 1993; Millan et al. 1993; Cordoliani et al. 1998; Sakai and Barest 2005). These events seem to be related to cerebral venous thrombosis, or dural sinus thrombosis (Krishnan et al. 2004). In contrast, CM in children tends to be accompanied by more extensive and diffuse CNS involvement. This often includes seizures and brainstem signs (Idro et al. 2005b, c). CT scans of CM children have revealed infarction of the right frontal and parietal regions (Idro et al. 2005b; Mohanty, et al. 2003). A single MRI pediatric CM case study (13-year-old girl) in the medical literature showed acute findings of bilateral symmetric hyperintensities on T2-weighted and FLAIR sequences involving the centrum semiovale white matter, suggesting cytotoxic edema (Gamanagatti and Kandpal 2006).

Significant in light of the involvement of the centrum semiovale white matter in the pediatric MRI cerebral malaria case study noted above is the observation of newly emerging ADHD symptoms in CM surviving children in Malawi (Birbeck et al. 2007). Functional magnetic resonance brain imaging (fMRI) studies with medication-naïve ADHD children have also observed hypofrontality and temporoparietal brain region abnormalities. Neural networks in these brain regions mediate executive processes (learning, memory, attention). These functions are especially vulnerable to hypoglycemic coma, blood–brain barrier compromise and cerebral immunopathogenesis, and hypoxic–ischemic crisis in children (Rubia et al. 2007; Smith et al. 2006; Banaschewski et al. 2005; Jung et al. 2005; Yamamoto et al. 2002; Krishnamoorthy et al. 2000). When these regions are metabolically injured, the behavioral impact is often most clearly expressed in the form of ADHD-type symptoms. We propose that these pathophysiological processes during CM can destabilize or injure these neural networks and induce ADHD-type symptoms.

The pathogenic pathways of severe malaria are multiple and complex, with a range of potential consequences on functional development. One potential pathway is therefore disruption to metabolic processes in the CNS, which may potentially be associated with white matter damage in a number of regions. These are in turn associated with specific functional outcomes that include visual–spatial and visual–motor skills, social functioning, and memory deficits. Possible disruption to the process of myelination may also lead to impairments in working memory capacity that might be expected to increase with age. Other processes suggest more global consequences on development, such as cytotoxic damage. In contrast the release of nitric oxide, through the proinflammatory response, may manifest in functional impairments that are transient.

12.6 Method for a Systematic Review of the Neuropsychology of Pediatric Cerebral Malaria

The evidence of the effects of malarial disease upon development provided in the literature will be summarized both by study and by functional outcome. Searches were carried out in 2011 using multiple databases: PubMed, Google Scholar, Questia, Scopus, ISI Web of Knowledge, and EBSCO. The search terms included a combination of "child development," "cognition," "Africa," and "malaria." Additionally, we administered the ancestry method (i.e., using the references cited in identified articles) to identify other articles. References to texts and thesis were followed up by direct contact with authors where possible. The online abstracts of studies identified from the database search were reviewed if they met the following criteria:

1. Location: conducted in Sub-Saharan Africa (SSA).
2. A psychological/developmental variable was a main outcome measure.
3. Study population of children younger than 18 years.
4. Information provided on the psychological tools used.
5. From a pediatric population exposed to severe malarial disease (*P. falciparum* in the peripheral blood stream, in the presence of impaired consciousness, seizures, severe anemia, or respiratory distress).
6. Inclusion of a control population.

Nine cohorts of children were found in the literature describing the long-term neuropsychological sequelae of severe malarial disease in African children, henceforward referred to as CM (cerebral malaria). One other prospective cohort was identified (Abubakar et al. 2007), which investigated children up to one-year post-discharge, but was excluded from the summary analysis as the study measured treatment effects in a randomized trial investigating seizure control, and did not therefore include a control group to evaluate disease effect.

There was variability between these studies in the disease definition used as the inclusion criteria. In 3 of the studies, disease exposure was defined as a score of 2 or less on the Blantyre coma scale, peripheral parasitemia, and the exclusion of other causes of encephalopathy (Newton et al. 1997), although one study also included children who had had impaired consciousness (coma scale of 4 or less). In 2, duration rather than depth of coma was used (>6 h Ghana and >12 h Senegal) as medical records did not provide a systematic record of coma depth. In further three studies, a combination of three diagnostic categories was used as the inclusion criteria (coma, impaired consciousness (coma scale scores equivalent to Blantyre 3/4 or prostration), and malaria with seizures). Only in the Malawi study was the diagnosis of cerebral malaria verified by the use of retinopathy (Taylor et al. 2004; Boivin 2002).

Six studies investigated the association of severe disease with generalized neuropsychological impairment, while the others were designed to test a specific brain–behavior-related hypothesis. The Senegal study focussed on the relationship of cerebrovascular damage to neuropsychological sequelae; the Kenya 2 study focused on the specific vulnerability of the temporal lobe and/or hippocampal function; and the Ghana study focused on the presence of interhemispheric transfer inefficiencies.

Each study also administered a different combination of neuropsychological assessments, although tasks from, or similar to, the Kaufman Assessment Battery for Children (KABC) were used in four. While all studies reported having piloted the tests used in the study population prior to administration to the study sample, publication of data that allows for the evaluation of the psychometric properties of the tests applied is not available for half of the published studies. Details of the studies and tests used are presented in chronological order of publication, with sample characteristics summarized in Table 12.1.

12.6.1 Making Comparisons Across Sites and Between Tests, the Rubric Used

The results for each study are described below and summarized in the Appendix on a test-by-test basis, focusing upon effect sizes by functional area of the difference between the CM children and their controls.

Instead of attempting to directly combine results, we are interested in comparing outcomes derived from multiple tests to identify consistent patterns and draw meaningful conclusions. This is obviously the more appropriate approach where performance scores are necessarily derived from different test versions, different tests, or where different administration procedures were used. Three factors need to be addressed in order to make meaningful comparisons between sites and between tests. The first is an understanding of what the test is measuring, the second of how the test functions within that population, and finally an understanding of the potential sources of variability in performance achieved.

To be able to compare across studies, the current analysis attempted to summarize individual test results, wherever possible, within a framework of common functional concepts. Each test was categorized according to the neuropsychological function assessed and the modalities used to present material and/or elicit a response. To attribute functional areas we were guided by the authors or, where necessary, descriptions of the named or similar tests in Lezak (1995) and Spreen and Strauss (1991). Given the paucity of literature validating, in the cultural context in which they were applied, the underlying neuropsychological skills of each test presented, it was not possible to evaluate the appropriateness of these attributions.

Table 12.1 Cohort descriptions

Country, year of first publication	Definition of cases	No. of study pairs—boys/girls	Age at assessment (in years)	Mean age at admission (in years)	Time to assessment (in years)	Controls: source/matching criteria	No. of years in school
1. Ghana urban, 1995	Coma + parasites (mean length 9 h SD 2.27)	7/13	7–16	7.3 SD 2.18	Mean: 3.9 SD 1.2	One school/age, gender, years in school, hand dominance	2–11
2. Gambia urban and rural, 1996	Cerebral malaria (no neurological impairments on discharge)	21/15	5.5–8.5	3.5 range 0.8–6.5	Mean: 3.4 SD 1.3	Neighborhood/age, gender, SES, school	Not reported
3. Kenya 1 Rural, 1998	Impaired consciousness (Blantyre score 3–4)	50/37	6	2.2 range 0.8–3.5	Minimum 3.5	Community database/ age, gender, SES, nutrition, health	0–2
4. Senegal urban and rural,2002	Coma: mean length 1.8 days range 0.5–5 days	17/11	5–12	3.4 range 1–10	Mean 6	Clinic records: age, education level, nutritional status	0–5
5. Kenya 2 rural, 2005	Cerebral malaria Seizures, no coma Mild malaria Coma: mean length 1.4 days	77/75 72/84 93/86 30/14	6–12	2.3 1.9 n.a.	Median 5.3 Median 5.9 n.a.	Demographic surveillance System/random sample community	0–5
6. Uganda 1 urban, 2007	Cerebral malaria Seizures, no coma Mild malaria Coma: mean length 1.4 days	54 87	5–12	7.4 range 5–12	0, 3, 6 months and 2 years post-discharge	Outpatients clinic/ neighborhood Approximate age	0–6
7. Kenya 3 rural, 2010	Severe malaria[a] Community controls	23/27 38/39	6–7	Data not supplied approx. 3–5	Data not supplied approx. 2–3 years	Demographic surveillance system	Data not supplied (approx. 33% in school)
8. Malawi Residence not described, 2011	Cerebral malaria + retinopathy Non-malarial admissions	41–42 49–46	3–5	Data not supplied <5	(1–40 months) mean 1.43 sd 0.98 1.19 sd 0.078	Hospital records/age	Preschool era
9. Uganda 2 Urban, 2011	Severe malaria (seizures/coma/ impaired consciousness) Community controls	37/25/31	5–16	6.97	3 months	Neighborhood/age	Data not supplied approx. 1–4

A comparison was then made of differences in effect size observed for different functions, by which the relative sensitivity of different neural structures or neural networks can be estimated. The effect size of disease exposure on each test was reported using means and standard deviations, where provided, to calculate Cohen's d (Cohen 1992). Where this information was not available, odds ratios, or eta squared, were converted to the d statistic (De Coster 2009; Chinn 2000; Rosnow and Rosenthal 1988; Thalheimer and Cook 2002). Some studies reported only estimated mean differences, for which no method for conversion was found in the literature. The results of these studies only allowed a comparison of trends in effect.

Conversion to the d statistic was derived from the calculator provided by the links: http://www.uccs.edu/~faculty/lbecker/es.htm and http://www.uccs.edu/~faculty/lbecker/index.html (downloaded 28/11/2005 10:19:5). Given the importance of School exposure accounted for variability in test performance after adjusting for school attendance and other social factors (Holding et al. 2004; Alcock et al. 2008), where possible test scores were corrected for school attendance, analysis also accounted for the influence of other significant background factors wherever data allowed.

Those tests where there was also a significant difference between group means are reported in the tables included in the appendix, **italicized and in bold**. The range of effect sizes found in any functional area was used to estimate the level of impairment observed using Cohen's interpretation (0.2–0.49 mild, 0.5–0.8 moderate, and greater than 0.8 severe problem).

12.7 Studies Included in a Review of the Neuropsychology of Pediatric Cerebral Malaria

12.7.1 Neuropsychology of Cerebral Malaria in Ghana

The investigators examined the vulnerability of specific neuropsychological functions as a consequence of white matter damage and integrity of the corpus callosum (Dugbartey 1995; Dugbartey et al. 1998). Measures of these functions included speed of information processing, tactile interhemispheric transfer, attention, language function, memory, and bilateral motor and sensory–perceptual functions. The neuropsychological tests administered were selected from a range of sources and administered to school children (mean attendance 6 years), though tests were employed without major modifications.

Despite the small sample size, a number of effect sizes are considered large, suggesting a clinically significant difference in observable performance between the cerebral malaria survivors and the control group children, even where a statistical significance was not found. The pattern of deficits observed is suggestive of cerebrovascular damage, with larger effects on tasks that might be considered more complex and cognitively demanding (e.g., trail B vs. A, Corsi block vs. digit span) or that include a delay interval (delayed recall vs. immediate recall).

Another interesting observation is that of larger effect sizes on tasks that involve the right hand or right ear, the side where nonexposed populations normally display a relative advantage. Small effect sizes were observed in short-term memory and tasks that emphasized processing speed. The authors also reported that poorer performance was related to a longer period of coma. This study suggests vulnerability in survivors of CM in a variety of functional outcomes, though not a generalized cognitive disadvantage. As children in this study attended mainstream school, there is also evidence of schooling as contributing towards resilience for these children.

12.7.2 Neuropsychology of Cerebral Malaria in the Gambia

The authors examined whether the presence of cognitive impairment would be present in the absence of neurological impairment in children with CM (Muntendam et al. 1996). Neuropsychological tests were selected to sample aspects of general intellectual development and sensory motor function, with a focus on nonverbal aspects of development. Tests were piloted on the study population to ensure they were understood by the children to be tested.

Not only did the CM children not display any functional impairments as compared to controls, but the mean test scores of the CM children were actually higher than those of the controls in all the intellectual development tests and in finger tapping, although not significantly so. The exception to this general pattern was the Balance Test, where the children were timed standing on one leg. The effect size here can be considered medium to large, in favor of a superior performance among the control group children as compared to CM children.

The results of this study are in direct contrast to those of all other studies. The authors suggested that the lack of observable deficits for the CM children may be due to the exclusion of the CM children with signs of neurological sequelae or impairment. It also is possible that the simplicity of the tests, created to ensure the acceptability of the material to local children, including the ability to administer tests without using oral instructions, contributed to the lack of test sensitivity. In the Ghanaian study discussed in the previous section, simpler tasks were also found to be less sensitive to disease effects, perhaps because of a performance ceiling effect. The trend for more complex tasks to be more sensitive is common to other studies, which also indicate that other features of disease and the potential influence of other coexisting risks or environmental factors, rather than the presence or absence of neurological sequelae, appear to better predict the course and nature of cognitive outcome.

12.7.3 The Presence of Cognitive Impairment in Kenya

The main question concerned the identification of cognitive impairment in CM and of clinical risk factors for impaired outcome (Holding 1998; Holding et al. 1999, 2004).

The core of the tests administered came from an adaptation of subtests from the Kaufman Assessment Battery for Children 1st Edition (Kaufman and Kaufman 1983). Content and administration techniques were altered in order to take into account local linguistic and cultural experiences and psychometric properties evaluated. Reported here is a summary of performances on two mental processing composite scores. Other results report performance on locally developed tests administered to expand the range functions assessed to include attention, language, motor dexterity, and behavior problems.

The neuropsychological effects of clinical severity of symptoms during the acute phase of illness were also evaluated. These included coma duration prior to and following admission and number of seizures. Initial analyses that were completed relied on a very tight matching of cases and controls in order to focus on disease effects (Holding et al. 1999). However, later reanalyses revealed the importance of other background factors that had not initially been included in the matching, primarily related to schooling, in accounting for variability in outcome (Holding et al. 2004).

Despite a trend towards poorer performance among the children who had severe malaria, the relatively small effect sizes were indicative of a significant level of resilience among survivors. The majority performed on most of the tests presented at a level indistinguishable from their peers. The CM group was, however, characterized by a wider variability in performance outcome than the community controls as well as a significantly greater proportion of children with impaired performance in one or more functional areas. Some children showed severe generalized impairment (about 3%), and others had mild-to-moderate impairment in specific areas (about 11%), primarily in language, adaptive behavior, and attention. Functional areas significantly affected by exposure to severe disease varied by the severity of symptoms, with the largest effect sizes, and widest range of problems, observable in children with deep coma, hypoglycemia, and a failure to mount a high fever. The reanalysis of the data highlighted the importance of taking into account the interaction between disease exposure and other health and environmental conditions in isolating the direct contribution of the proximal effects of the disease, to variability in performance (see Appendix).

12.7.4 Neuropsychology of Cerebral Malaria in Senegal

This retrospective study was designed to test the hypothesis that the consequences of severe malaria would be felt primarily through those brain systems most vulnerable to cerebrovascular crises: attention, memory, and executive function (Boivin 2002). The test battery consisted of the KABC administered in the local language of Wolof and the Test of Variables of Attention (TOVA; Dupuy and Greenberg 1993/2005). The TOVA is a computerized measure of sustained vigilance and impulsivity that involves responding to a target stimulus (i.e., smaller square within the upper half of a larger square) and not responding to a nontarget (i.e., smaller square within the lower half of a larger square). Educational information was not detailed but was made available by the author (MB) for reanalysis for this chapter. Adjusted and unadjusted effect sizes are both reported in the appendix. Longer coma during acute illness was again found to be an important indicator of problems measured later at school age. Significant neuropsychological deficits were reported in KABC subtests involving visual–spatial analysis (simultaneous processing), KABC memory (sequential processing), and TOVA attention (omission errors).

While both this and the Kenyan study used the KABC-1, there is a large difference in effect sizes found, which might be explained by the difference in approach taken to preparing the subtests for use. The process of adaptation used in Kenya appears to result in a factor structure that more closely resembles the original (Holding 1998). The process of translation, followed in the Senegal study, while not overly compromising the factor structure, exposes the children to unfamiliar material, thus providing them with more complex challenges. The difference in effect sizes between the two studies might therefore be attributable to the relative vulnerability of more complex psychological functions, and thus supporting the study hypothesis.

This study also highlighted the multiple risks faced by children exposed to malaria infection, providing an exploratory model that illustrates the importance of accounting for the major contributors to variability in cognitive performance. In addition to health history, the model included socioeconomic indicators such as parental education and nutritional resources.

12.7.5 Language Impairment and Temporal Lobe Dysfunction in Kenya

This study primarily investigated the relationship between seizure activity associated with malarial disease, temporal lobe epilepsy, and language impairment (Carter 2002; Carter et al. 2003, 2005a, b, 2006; Kihara et al. 2009). Assessments were therefore selected to test the hypothesis that the principal functional areas at risk would be language and memory (episodic and semantic). The cognitive test battery consisted of local adaptations of a selection of tests, some of which had previously been used within the local population (Holding et al. 2004). The language measures were also adaptations of techniques used in other contexts, but necessarily required modification of content to address the language of the children being studied. Performance outcome was not reported using means or standard deviations, but with estimated mean differences and odds ratios for impaired performance. Much of the data provided therefore did not allow for test performance to be converted to Cohen's d and are therefore directly comparable neither to other data within the same study nor to those from other studies.

The sensitivity of language development to the effects of severe malaria was supported although the hypothesis that impaired outcome was associated primarily with temporal lobe dysfunction was not. The evidence provided here is that functional areas sensitive to malarial exposure varied by the nature of that symptomatology, highlighting the importance of clarifying disease symptomatology as part of the prognostic profile. Again, larger effect sizes were observed in what appear to be, given the level of information provided on test content, more complex functions.

12.7.6 Neuropsychology of Cerebral Malaria in Uganda

In this set of studies (Boivin et al. 2007; John et al. 2008a, b), the authors prospectively studied the neuropsychological effects of cerebral malaria using the same tests as those used by Boivin (2002) in his retrospective study of CM in Senegal. Published data focused on the proportion of children with impaired performance. Descriptive tables provided by the authors of results at 3 and 6 months and 2 years post-discharge were used to calculate effect sizes of unadjusted group means (reported in the Appendix in brackets). Effect sizes of scores adjusted for school exposure, provided by the authors, are also reported.

Effect sizes ranged from small to large depending upon the time since discharge, the functional area (see Appendices—Uganda studies), and whether or not the performance measure accounted for background factors such as schooling and socio-economic indicators. The most consistent functional area affected appears to be attention, followed by working memory (KABC sequential processing). While effect sizes showed a trend towards increasing with time since discharge, the reduction in the numbers reported with impairments at six months may reflect the clinical observation that some neurological sequelae resolve over the first year following illness.

The prospective, longitudinal nature of the study enabled a demonstration of the long-term nature of deficit development. At two years following illness, the proportion of children who displayed impairment was significantly greater than the control population, although overall mean differences were only observed in the attention measure. The pattern observed is consistent with the picture that emerged from other studies, emphasizing the importance of attention, the long-term nature of the deficits, and the variability in outcome between survivors of CM.

This study was also the first to document that CSF TNF production is associated with neurologic and cognitive sequelae (John et al. 2008b). Elevated CSF TNF-alpha levels on admission were associated with an increased risk of neurologic deficits 3 months later. TNF-alpha was also negatively correlated with age-adjusted scores for TOVA attention and KABC working memory 6 months later. In a subsequent structural equation modeling analysis with this Ugandan CM cohort, Boivin evaluated the extent to which immunological indicators of severity of malaria illness at hospital admission predicted attention and memory performance measures two years following acute illness. The immunological measures were CSF TNF, RANTES, and granulocyte levels, which were found to be predictive of severity of malarial illness in previous published work with this cohort (John et al. 2006, 2008b). The occurrence of EEG diffuse slow brain wave abnormality at 72 h post-admission to hospital during acute illness was also entered into the model. Using SPSS AMOS structural equation modeling, TOVA attention, TPT memory scores for drawn geometric shapes following the tactile learning trials, and KABC sequential processing score was predicted by the immunological and EEG measures of severity of CM illness (see Fig. 12.1). The CMIN value was 17.0 with a corresponding probability of 0.32, indicating that the data fit the model initially presented by Boivin (2002) in his Senegal findings.

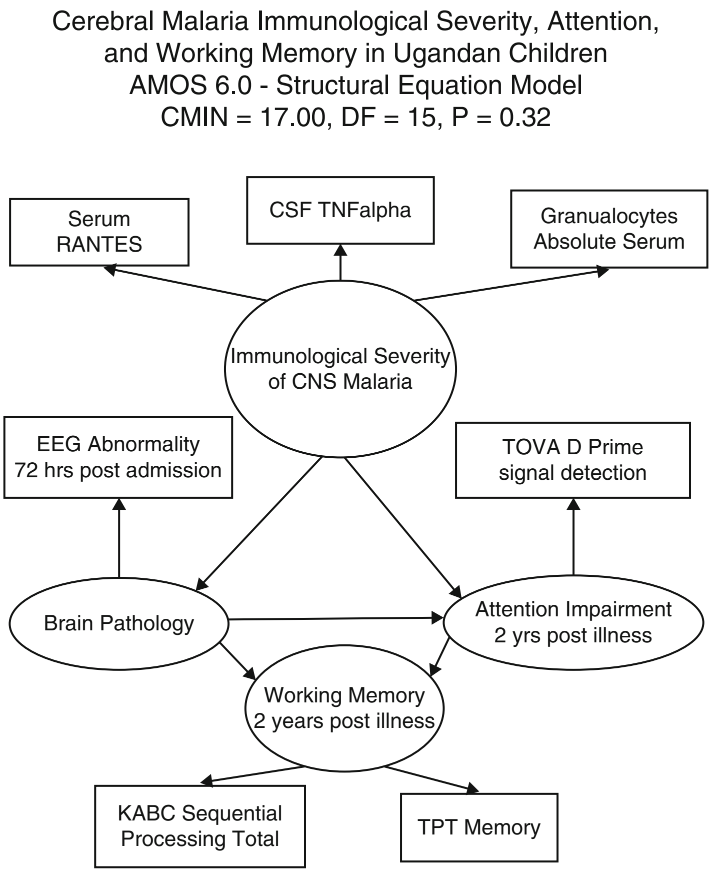

Fig. 12.1 *2-Year SEM memory model*. Using SPSS AMOS 6.0, this is the schema for a structural equation model of the immunological and neurological factors of clinical severity of cerebral malaria (CM), as they relate to neuropsychological outcomes. These models were based on the cohort of 44 CM children (Boivin et al. 2007) at 2-year follow-up of neuropsychological assessment following hospital discharge (John et al. 2008a). The neuropsychological measures in the model are from the Test of Variables of Attention (TOVA) visual test D prime signal detection score for overall attention performance, the Kaufman Assessment Battery for Children (KABC, first edition) sequential processing (memory) global score, and the Tactual Performance Test (TPT) total time per block across all three trials. The serum RANTES, CSF TNF-*alpha*, and serum absolute granulocytes measures were based on specimens drawn at hospital admission during acute illness. EEG was done at 72 h posthospital admission and abnormality was defined as diffuse slow brain wave or ictal brain wave abnormality. The SEM CMIN was 17.00 (DF = 15), $P = 0.32$. Lack of statistical significance indicates that the data fit this model

12.7.7 Novelty Detection: An EEG Evoked Potential Study of Severe Malaria in Kenya

The focus of this study was to examine the use of evoked-related potentials (ERPs), an assessment format that does not require an active response from the child. This enables the same protocol to be applied to a variety of ages and across contexts. ERPs measure brain functions through the size of amplitude of the orientating response to novelty detection, generally considered a measure of attention. In order to maintain acceptable variation in the orientation response, the visual paradigm required the authors to substitute photographs of faces from the local population for the original foreign faces. The auditory stimuli provided from the UK appeared to be sufficiently familiar to engage the respondents. This provides clear documentation that despite using measurement techniques that purportedly provide more consistency between different cultural and linguistic groups, there may still be the need to adapt the stimulus materials to be used, particularly in the visual paradigm.

Significant differences in ERP latency and amplitude responses between controls and both severe malaria and CM survivors were observed in both auditory and visual modalities.

The data supplied did not allow for the calculation of effect size; however, in Chapter 14 of this volume, Michael Kihara presents a detailed methodological overview on the measurement of cognitive outcomes of at-risk children using novelty processing as measured by ERP.

12.7.8 Neurodevelopmental Effects of Cerebral Malaria in Malawi

This study (Boivin et al. 2011) investigated much younger children than in previous studies, using a developmental screening instrument developed within the target population (the Malawi Developmental Assessment Tool (MDAT); Gladstone et al. 2010). To measure behavioral impairments, the Achenbach Child Behavior Checklist (CBCL) was translated and back-translated into the local language of Chichewa so as to provide a parent-rated measure of internalizing and externalizing symptoms.

This is the first study that measured disease effects on neurodevelopmental in younger children (2–5 years of age), closer to the time of the illness (the median age for cerebral malaria in this region is 3–4 years of age). This was also the first study of the neurocognitive effects of cerebral malaria to incorporate malaria-specific retinopathy during acute illness as a diagnostic criterion for children admitted into the study. The significant differences found in global intellectual development and in language suggest that differences can be identified early with less specific measures of neurocognitive function. The reason for a lack of effect on behavioral development, observed in other studies, needs clarification and may have been related to the sensitivity of the tool selected or the age of the children at illness.

12.7.9 The Effect of Severe Malaria on Achievement Uganda

A subsequent study by Bangirana et al. (2011) investigated the effect of malaria with neurological involvement on cognitive ability, behavior, and academic achievement. It also investigated whether cognitive ability predicted academic achievement in children after malaria infection (Bangirana et al. 2011). Test scores between both groups were compared using analysis of covariance with age, sex, level of education, nutritional status, and quality of the home environment as covariates. This provides us with a clearer picture of disease-specific issues. However, the authors report only estimated mean differences; consequently these results are not directly comparable between tests within this study, or across other studies, using the effect size rubric. Children in the malaria group had lower attention scores and more behavioral problems than the community controls using the CBCL internalizing symptoms measure. No significant differences were observed in other cognitive abilities and academic achievement scores between the two groups. The authors consider the attribution of the lack of effect to the short-time interval between illness and assessment (3 months), citing previous evidence from their study group that deficits are more evident in the longer term. Indeed smaller effect sizes characterized the differences observed in other functional areas close to the illness episode. Other potential explanations for a lack of effect could be attributable to the inclusion of children with a wide range of symptom severity that may have diluted the observable disease effect. Another possibility is that previously acquired knowledge may be relatively spared, while children may fall further behind their peers in learning new information or skills. This suggestion is consistent with Bangirana and colleagues conclusion that severe malaria with neurological involvement affects attention and behavior, but may not affect academic achievement at three months post-discharge.

The process of test construction and validation that accompanied this study (Bangirana et al. 2009a, b, c) highlights challenges that can occur in transferring tests between contexts. While showing similar factor constructs to the original KABC-II, the derived factor structure also indicated significant cross-loadings, as well as the failure of some KABC subtests to relate to other tests in the battery in the way originally intended (an example is the number recall test). What this work does clearly highlight is the danger in assuming that children from different cultural or educational exposures will necessarily solve similar tasks with identical strategies and thus the need to explore both the statistical and conceptual relationships between tests in different populations. Furthermore, given the differences in the underlying factor structures, then we should also expect the subscale scores derived for this new population to reflect an approximation of the original conceptual framework and not its direct representation.

12.8 A Summary of the Evidence: Prognostic Indicators, Functional Outcomes, and Other Sources of Variability in Outcome

12.8.1 Prognostic Indicators

Evident from the studies reviewed is the association between increased severity of symptoms, as indicated primarily by depth and duration of coma (Idro et al. 2005a) and more generalized and severe levels of cognitive impairment. The functions that had the strongest relationship to coma were tactile discrimination, memory (block tapping, digits, complex figure), and aspects of attention (coding, scanning errors) (Dugbartey 1995; Holding et al. 1999; Boivin 2002; Boivin et al. 2007; John et al. 2008a, b; Bangirana et al. 2011).

Other important prognostic indicators of later neurodevelopmental impairment include hypoglycemia, clinical features of intracranial hypertension, and the failure to mount a high fever and seizures (Murphy and Breman 2001; Holding et al. 1999; Idro et al. 2005a). The least consistent of these associations is with seizures. Thus, an intervention targeted at seizure control showed no protective efficacy with regard to cognitive sequelae (Abubakar et al. 2007). Furthermore, seizures in the absence of deep coma were associated with less severe impairment (Carter et al. 2005a, b; Kihara et al. 2009). Nonetheless, an episode of acute illness characterized by multiple or prolonged seizures (Carter et al. 2003, 2005a, b; Idro et al. 2005a) is likely to be associated with impairment, although of a different pattern to that characterized by "deep coma" (Blantyre coma score of zero) (Boivin et al. 2007; Idro et al. 2005a). The functions that had the strongest association with seizures were higher-level language function and adaptive behavior (Carter et al. 2005a, b; Idro et al. 2005a). Persistence of seizure activity after hospitalization was also associated with differences in outcome. When exposure to disease was associated with active epilepsy at follow-up, then affected children were at risk of general cognitive impairment across several functional areas including motor skills, attention, behavior, everyday memory, and language (Carter et al. 2005a, b; Idro et al. 2005a).

The differing pattern of outcomes observed supports the clinical picture of malaria as a syndrome. The data implicates a variety of pathological pathways, supporting the involvement of each of the potential pathways outlined in Section 1 above. Whether it is malaria being studied, or any other disease, differing symptomatology, severity, and pre- and post-disease exposure all need to be taken into account in adequately understanding the pathways to risk and resilience.

12.8.2 Functional Outcomes

12.8.2.1 Global Intellectual Function

Common to most studies was a consistently poorer performance, though not necessarily statistically significant or with a large effect size, of the exposed children across the majority of tasks. Group mean scores in measures employed to represent global functioning, such as the KABC processing composite scores and the MDAT total score in younger children, showed significantly poorer performance levels in survivors of cerebral malaria (Boivin 2002; Boivin et al. 2007; John et al. 2008a, b; Boivin et al. 2011). In contrast small to negligible effect sizes were observed using different versions of similar tests, as well as with another proxy measure of global functioning, Raven's matrices (Raven 1947); (Dugbartey 1995).

In summary only a small number of children appear to be left with global intellectual impairment that is suggestive of diffuse damage, perhaps related to cerebral edema, cytotoxic damage, or the development of an epileptic syndrome. Our review also provides support for the contention that, although some functions appear to be relatively more sensitive than others, the effects of severe malaria may vary between children. Differences between studies in the pattern of effect sizes, and subtle differences in outcome from similar batteries, provide us with the opportunity to define more precisely which aspects of development might be most disrupted.

12.8.2.2 Memory

In adults cerebral malaria appears to be associated with white matter damage, epilepsy, and specific memory deficits (Carlill 1917; Richardson et al. 1994, 1997; Varney et al. 1997). In one case study, severe deficits in delayed memory and naming ability were observed 10 years after the patient contracted cerebral malaria, consistent with temporal lobe/hippocampal dysfunction (Grote et al. 1997). Memory deficits are therefore characteristic of the sequelae of the disease in adults, while in children results indicate that simple short-term memory or memory span are not vulnerable.

Memory deficits associated with specific temporal lobe damage were also not generally supported by the data. However, there is evidence to suggest differential effects of different disease courses. For example, performance across a range of tasks of everyday memory, both recall and recognition were impaired in children with cerebral malaria, but not in those who survived malaria with seizures (Kihara et al. 2009).

Working memory performance, particularly the visual–spatial scratch pad, however, was more consistently vulnerable. To illustrate this, the only verbal memory task reported to show a significant effect of disease status (Boivin's translation of the KABC Word Order) contained an interference task. The same task without the interference section, and thus a reduced working memory component, was not sensitive to disease exposure (Holding et al. 2004). Attention is another important component of working memory capacity, and when changes in procedure were made to reduce the sustained attention component of the hand movements task (memory for a motor sequence), a differential sensitivity to disease was observed (Boivin 2002 versus Holding et al. 2004).

12.8.2.3 Attention

Attention is particularly vulnerable to global insults to the central nervous system (Connolly and Kvalsvig 1993), and problems in attention capacity and vigilance can be manifested even where IQ deficits and neurological soft signs cannot be clearly documented (Boivin and Giordani 1993). Significant differences in performance were recorded across all studies, with effect sizes ranging from mild to severe, the size of the effect differing by test and time since discharge. In line with expectations, therefore, deficits of attention were widely found, although not consistently with the largest effect sizes. The most sensitive aspect of attention investigated was sustained attention, manifested in errors of detection in visual scanning tasks. The time component of attention tasks was the least sensitive measure, although speed, measured through reaction time/processing speed, was impaired in more complex tasks. The one investigation of auditory responses (Kihara et al. 2010) also suggested sensitivity of attention in other modalities.

Attention is also a component of activities designed to measure other functional areas, as evidenced in the discussion on working memory. To understand the contribution that impairments of attention have in the development of other cognitive skills and achievement, a more experimental paradigm, partialing out different components of performance, would be needed. An analysis of this paradigm is elaborated in the section below.

12.8.2.4 Conceptual Reasoning/Visual-Perceptual Functions

Again effect sizes varied depending upon the modality used and with increasing complexity of the task. Perceptual organization, measured by block-design-type tasks, discriminated the disease groups in the Senegal and Kenyan studies, but not in the Ghanaian study, neither through copying by drawing nor block design. As performance on these tasks improves significantly with school experience, the survivors of cerebral malaria in the last of these studies may have shown in their performance the benefits of their more lengthy school exposure (Holding et al. 2004).

Two of the discrimination tasks in which effect size was indicative of a more severe impairment involved interhemispheric transfer of information (bimanual tactile discrimination and dichotic listening—Dugbartey 1995). This is consistent with deficits found in adults suggesting possible periventricular lesions, white matter damage, and/or compromised development of commissural structures (Richardson et al. 1994).

12.8.2.5 Executive Functions

We can say little about the effect on tasks specifically designed to measure executive functions (e.g., planning and problem solving) as these were directly measured in only one study and there in only eight pairs of children, although the effect size was the largest calculated (Dugbartey 1995; Dugbartey et al. 1998). However, the strength of the association between impaired executive functions and other health risks experienced early in life suggests that this area of development is worthy of a detailed evaluation (Taylor 1987; Espy et al. 1999; Garon et al. 2008). Supportive of this hypothesis is the observation of an increase in effect size associated with increasing task complexity, as illustrated in the memory tasks.

12.8.2.6 Language Functions

Tests of language functions are the most difficult to transfer across cultural and linguistic groups. There was therefore little overlap between the language assessments used in different studies, with a wide range of tests employed across four of the five studies. Effect sizes ranged from mild to severe. Results suggest that different components of language, both receptive and expressive, are sensitive to different symptom patterns within the spectrum of severe disease. Again cerebral malaria affects a wider range of language skills than less severe disease. Most sensitive were measures of expressive language and higher-order more complex language functions (Carter et al. 2005a, b; Holding et al. 1999, 2004). The disruption of language development, therefore, does not appear to be necessarily associated with temporal lobe dysfunction.

12.8.2.7 Sensory Motor, Tactile Discrimination, and Motor Dexterity

Performance on motor tasks showed sensitivity, though inconsistent, to disease status. Effect sizes in motor speed were negligible to mild, suggestive of some motor slowing, but not the severe impairments that might be expected from the data on neurological sequelae following CM (van Hensbroek et al. 1997). This may of course have been an artifact of how subjects for these follow-up studies were selected. For studies that were primarily cognitive in focus, those unable to manipulate the materials provided may have been excluded.

While motor dexterity and fine motor skills appear to show some sensitivity to disease exposure, larger effect sizes were found in those tasks involving tactile discrimination. Here performance may have been affected both by compromised perceptual function and motor coordination. An interesting observation was that the right side superiority over left side performance, anticipated at the population level, was not as clearly observable in the CM groups. While the left side effect sizes were negligible to small, larger effect sizes were observed in right side performance.

12.8.2.8 Behavior/Psychological/Intrapersonal Functions

Anecdotal reports from parents describe both internalizing and externalizing symptoms (Dugbartey 1995). However, evidence for more extreme behaviors, such as aggression and "running away," is limited to the period closer to the time of the illness. These externalizing symptoms therefore appear to be transient in nature. Other transient sequelae reported in other literature include visual impairment, lending support to the suggestion that some aspects of the proinflammatory response may result in acute but temporary impairment.

The results of standardized approaches to the assessment of behavior problems show an inconsistent picture. One measure, assessing adaptive behavior, was sensitive to more persistent effects of disease exposure, especially among those children who developed epilepsy. Results indicated that cerebral malaria is associated with functional immaturity (items reflecting self care and independence) rather than psychopathology (Holding et al. 1999; Carter et al. 2005a, b). The use of the CBCL also identified internalizing and not externalizing behaviors as an issue in school-age children, but not in younger children (Bangirana et al. 2011; Boivin et al. 2011). Given the pattern of results in other functional areas, this inconsistency in reports may reflect the lack of sensitivity of the tools, rather than the lack of an effect of this area of functioning. Questions concerning behavioral organization and planning, not yet explored, may also prove to be more sensitive to longer-term effects.

12.8.2.9 Academic Achievement

Little is known about applied outcomes such as school-based skills, with only two studies incorporating achievement measures. Effect sizes ranged from negligible to large. However, the study with the largest battery of outcomes reported on children only 3 months post-discharge. Achievement may be most susceptible to cumulative effects of loss of cognitive skills on learning, and thus, a longer-term follow-up would be needed to observe a significant effect.

12.8.2.10 Task Complexity

Even within the heterogeneity of the results observed, certain common patterns could be distinguished across the different studies. From among the neuropsychological functions assessed, those that most often showed a significant effect of disease were more complex tasks. Functions showing large effect sizes included attention, tactile discrimination, language, working memory, and adaptive behavior, whereas simple reaction times, processing speed, and simple memory functions showed negligible effects across all studies. The outcomes reported, both in terms of functional area and level of impairment, varied by disease course, highlighting the need for a range of measures to monitor different aspects of cognition.

The process of cultural adaptation followed in the KABC-based battery used in Kenya did apparently maintain construct validity, as evidenced by a factor structure close to that of the original KABC (Holding 1998). Performance on this version of the battery suggested that general intellectual ability maybe the least vulnerable of the developmental areas (Holding et al. 2004). In contrast, the version applied in the Boivin studies appeared to be more sensitive to disease effects. This version translated the material and maintained content and procedures closer to the original standardization, but with minimal cultural adaptation (Giordani et al. 1996). Thus, the differential sensitivity to disease effects of these ostensibly similar measures of global functioning is perhaps because, as the differential factor structures suggest, the two versions are measuring subtly different sets of skills. Consistent with this, as we described above, is the observation that across all measures, larger effect sizes were found in more complex tasks, suggesting a relative sensitivity of higher-order functions.

The greater complexities of the translated, as opposed to adapted, subtests can, however, have its own inherent limitations, when material presented is too unfamiliar. For example, in two subtests photo series and Gestalt closure, the use of images unfamiliar to the target population was felt by the authors to be among the most difficult subtests. The lack of sensitivity of these subtests could stem from the ceiling effect/constrained variance created by material strange to all children, regardless of disease exposure. Similarly the relative unfamiliarity of the materials used of Raven's matrices test, abstract designs, and the type of problem to solve, visual analogies, may also have resulted in constricting performance levels across groups, making it possibly an inappropriate test to use rural African cultures (Wober 1975).

12.8.3 Other Sources of Variability in Outcome-Exploring Background Factors

The Gambian study was the only study that consistently found no disease effects. Their results may be attributable to factors such as sample size and the properties of the tests administered. It is also possible that a contributory factor could be differences between study populations in the patterns of confounding factors such as sociocultural status, quality of home environment, and immediate health history characteristics (e.g., intestinal parasite infection, incidence of anemia, history of malnutrition).

12.8.3.1 Age at Admission

While none of the studies reviewed set out to investigate this directly, there is other published evidence that children admitted with severe malaria younger than three years of age are at greater risk for persisting cognitive impairment than those over three years of age (Idro et al. 2005a). This is consistent with other health-related vulnerabilities and certainly suggests the need to take age at exposure into account.

12.8.3.2 Age at Assessment

This too varied between studies, with children seen for follow-up at ages ranging from 3 to 16 years. Those studies that included older children all showed a trend towards larger effects of disease exposure on performance, an observation consistent with our conclusion that disease effects are more apparent in more complex tasks. The one prospective cohort also found increasing effect size with age (John et al. 2008a, b). Age at assessment therefore appears to contribute to variability, possibly through a combination of differences in the level of task complexity that can be administered, and the cumulative effect of the process of myelination.

12.8.3.3 Contextual Characteristics

All the studies reviewed in this chapter were completed in resource poor settings in which children live in conditions of poverty. However, the potential contribution of poverty or poverty-related factors to increases in the risk of exposure and disease effects (Worrall et al. 2005) has not yet been widely evaluated. Whether the outcomes observed were primarily attributable to disease exposure or as a consequence of the synergistic effect of multiple exposures was difficult to address given the study designs, which limited variability by using matched samples. However, using structural equation modeling (SEM) techniques, Boivin and colleagues concluded that cognitive outcome cannot be explained by malarial status alone (Boivin 2002). Although both the cross-sectional and retrospective nature of data collection make it difficult to determine the direction of causation, the analyses suggest that factors underlying cognitive impairment are likely to be entangled within a host of other health and environmental factors that constitute a complex web of poverty.

Educational level, for example, may have obscured the relationship between malarial history and a range of functional skills in children, perhaps accounting, in part, for the significant interaction effects reported (Holding et al. 2004). The most severely affected children may not be sent to school at all, such that their poor scores result from both underlying brain damage and a lack of exposure to test materials and procedures. Once above a functional threshold that ensures a child attends school, further development may then be more closely related to the extent and type of schooling, with test performance reflecting the degree to which schooling fosters literacy skills and test-taking strategies.

In addition parental literacy, occupational status, father presence, and nutritional resources have been also shown to have a significant effect on performance on selected cognitive tasks. Having fewer siblings (siblings play an important caretaking role in rural homes) has been associated with poorer outcome in one study (Holding 1998) and rural residence (perhaps a proxy for a lack of health and educational resources) in another (Boivin 2002). The studies reviewed also reported that children exposed to severe disease were at greater risk of intestinal parasite infection, were more likely to have had severe diarrhea in the year prior to assessment, and had lower school attendance rates (Boivin and Giordani 1993; Holding et al. 2004; Carter et al. 2003).

The complexity of relationships between risk factors is further illustrated by the tangled relationship between malnutrition and cerebral malaria and the uncertainties that remain concerning the possible protection afforded by nutritional status (see summary in Holding and Kitsao-Wekulo 2004). Although Idro et al. (2005a) noted that severe malnutrition was associated with significantly greater likelihood of impairment in surviving children, none of the studies are able to provide data that helps to clarify the relationship between nutritional status, severe malarial disease, and cognitive outcome.

12.9 Neuropsychology of Severe Malaria Within a Co-constructivist Framework

A co-constructivist framework considers the effects of a disease such as severe malaria, on the developmental trajectory across the life span, encompassing multiple levels (i.e., neurobiological, cognitive, behavioral, and sociocultural) in understanding the effects of disease on neuropsychological outcomes (Li 2003). A cohesive interpretive framework like this is important, given the broad variability in settings, disease, and environmental factors that are experienced. Framing the factors contributing to risk and resilience for children facing any disease can guide the interpretation of findings and provide a reasonable starting point for modeling these relationships.

Our review of studies on severe malaria in African children illustrates the breadth and depth of information that can be elicited even with a lack of uniformity between studies. We have applied a number of techniques to detail the complex picture that emerges of the relationship between disease exposure and functional outcome. Firstly, we have carried out an analytic description of each of the studies, identifying the strengths and weaknesses of the assessment batteries used, and summarized into themes the pattern of functional impairments that emerge. We have extended this analysis through the calculation of effect sizes, to better understand the strength of the relationships that are then observed.

Below we illustrate how the application of statistical modeling techniques can be used to effectively dissociate the neurocognitive disability directly caused by CNS malaria (proximal factors) from that of more sociocultural (distal) factors. The studies included in this exercise explored common concepts, even though they may have used different measures, with the focus of the analysis being to evaluate the fit of a single explanatory model. Model components were derived through an exploration of the potential relationship between attention and working memory, suggested by the retrospective study of the neurocognitive effects of cerebral malaria in Senegalese children (Boivin 2002). The analysis investigated the association between performance on KABC subtests, as measures of cognitive function, and the TOVA D prime as a measure of visual attention. The results for three comparison groups from Boivin et al. (2007) (cerebral malaria, uncomplicated malaria, non-malarial groups) are provided in Fig. 12.2.

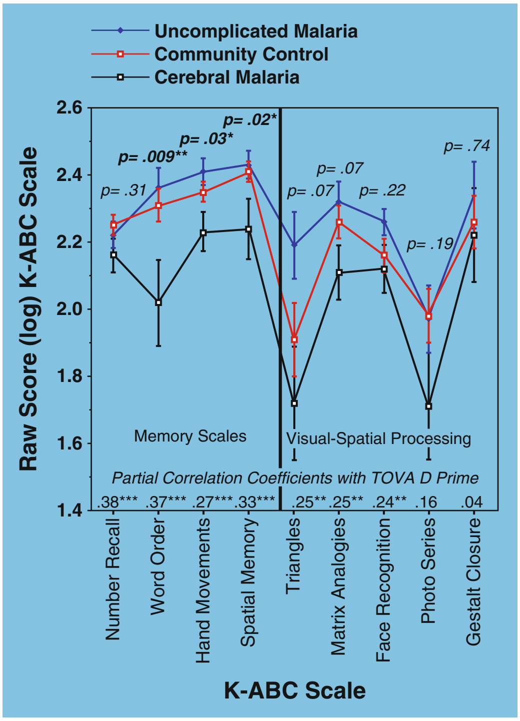

Fig. 12.2 *KABC subtests memory attention*. The means and standard errors are plotted for the three groups (uncomplicated malaria, community controls, and cerebral malaria) of children at 6-month posthospital discharge neuropsychological assessment follow-up for children in the Boivin et al. (2007) study. The log-converted raw score means of the subtests from the Kaufman Assessment Battery for Children (KABC, first edition) are adjusted for age and education level. The KABC subtest plots are ordered *left* to *right* on this graph, in terms of those subtests having the strongest correlation (for all three groups combined) with the Test of Variables of Attention (TOVA) visual test D prime signal detection score of overall attention performance. The Pearson product–moment correlation coefficients between the KABC subtest and the TOVA D prime scores are denoted along the *horizontal* axis (***$P<0.001$, **$P<0.01$, *$P<0.05$). The KABC subtests measuring memory had the strongest correlations with TOVA D prime (*left side* of graph) and also had the greatest overall between-group differences, with the cerebral malaria children doing more poorly compared to the uncomplicated malaria and community control groups. The ANOVA between-group P values for this comparison is located above the plots on the graph itself (***$P<0.001$, **$P<0.01$, *$P<0.05$)

The subtests are plotted from left to right in order of the overall strength of the correlation between each subtest and the TOVA. In this graph there is a trend for memory subtests to have a stronger relationship with attention than the visual–spatial processing subtests. The visual memory measures were found to have the greatest deficits for the cerebral malaria children. The tests with the lowest correlation with attention were, however, also those whose design was most unfamiliar to the study population and may therefore have been the least reliable of the measures. The data displayed provides the suggestion that visual–spatial working memory deficits seen in CM survivors may partly be due to attention problems (Boivin et al.

2007; John et al. 2008a). The evidence from ERP data (Kihara et al. 2010) suggests that a more detailed investigation of the same relationship with a wider range of auditory memory tests might also yield informative data.

The model developed then tested the relationship between biological risk (disease severity, brain pathogenesis), environmental risk (home quality), and cognitive function (attention, working memory, etc.). Data was derived from four studies with African children that used similar assessment data: Senegal (Boivin 2002), Uganda (Boivin et al. 2007), Kenya (Holding et al. 2004), and Malawi (Boivin et al. 2011). Cognitive ability was represented by performance on KABC sequential and simultaneous global processing scales. Attention was represented in three of the four studies by the TOVA visual test, while the remaining study used a paper and pencil measure of visual scanning and attention (Holding et al. 1999).

The SEM analyses depicted in Fig. 12.3 are important in that they are the first to use multiple studies in multiple African countries using similar (but not identical) outcome measures in order to document the potential of statistically dissociating the impact of CNS injury (cerebral malaria) from the more long-term effects of poverty in determining cognitive ability in at-risk children.

The SEM model was found to fit the assessment data for all four studies in that the CMIN value is not statistically significant ($P > .05$). Occurrence (Malawi) or severity of CM illness (e.g., length of coma, seizure occurrence: Uganda, Senegal, Kenya) was significantly predictive of lower attention performance, which was subsequently predictive of both KABC sequential and simultaneous processing. Furthermore, in all four studies various indicators of quality of home environment (e.g., SES indicators of material possessions, nutritional status, parental literacy) were also independently predictive of KABC performance.

Figure 12.4 uses a more detailed analysis of the neuropsychological assessment of Ugandan CM children (3 mo follow-up) to illustrate the analytical strategy for dissociating more proximal factors of cerebral malaria illness from the more distal factors of the poverty. Moving from the top of the figure downward in this SEM analysis, severity of malarial illness (granulocytes, ESR, parasite density) is predictive of degree of brain pathogenesis (EEG diffuse slow wave abnormality, coma duration at admission). This in turn is predictive of TOVA attention ability (D prime, correct response time variability). Attention is predictive of working memory (KABC sequential processing, TPT memory score), which is subsequently predictive of KABC simultaneous processing and overall TPT time-per-block performance across all three trials (preferred hand, non-preferred hand, both hands). At the same time the quality of home environment, measured by nutritional status, HOME score, parental education level, and SES material possessions score, is predictive of overall cognitive ability.

These models provide preliminary support for the suggestion that attention may be the most universal and sensitive area of functioning through which we can estimate disease effects. They also strongly support the need to address the pattern of disease symptomatology in understanding outcome. And finally they highlight the contention that the effects of malarial disease cannot be understood independently of the experience of poverty, characteristic of the context in which the majority of affected children grow up.

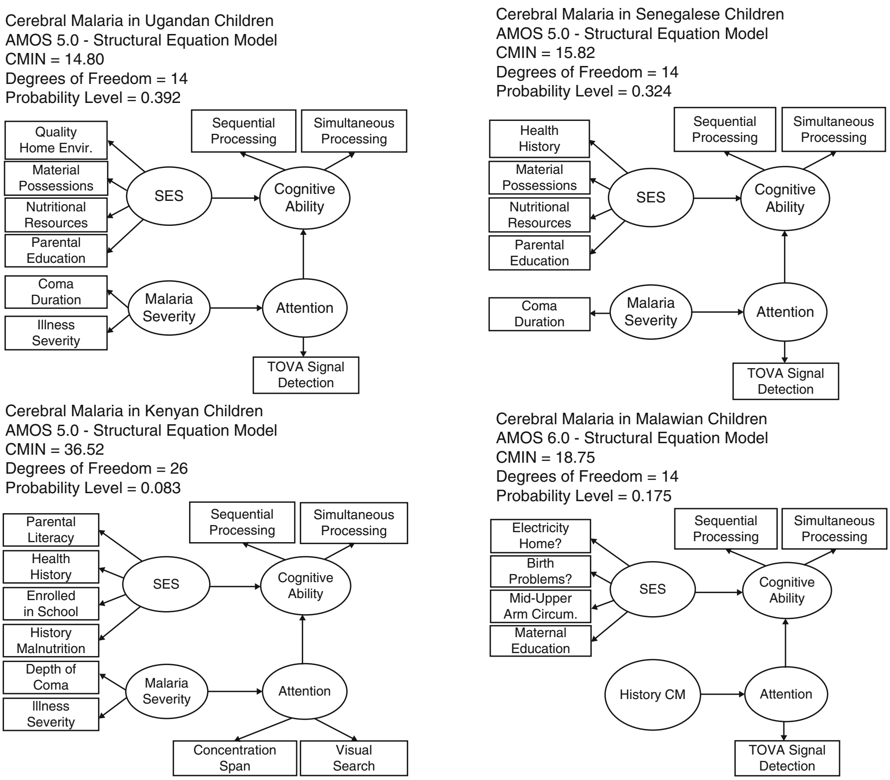

Fig. 12.3 *Four country SEM TOVA SES*. Using SPSS AMOS 5.0 structural equation modeling, the relationship between quality of home environment, severity of cerebral malaria illness, and overall cognitive outcomes is evaluated in a similar manner across four different cerebral malaria studies (Uganda in the *upper left*, Boivin et al. 2007; Senegal in the *upper right*, Boivin 2002; Kenya in the *lower left*, Holding et al. 1999; and Malawi in the *lower right*, Boivin et al. 2011). For each of the four SEM country graphs, the SEM schema depicts quality of home environment indicators on the *left side*, as they relate to cognitive ability. Severity of cerebral malaria (CM) illness (e.g., depth of coma or occurrence of seizures) is in the lower portion of each of the graphs and is predictive of measures of attention (e.g., TOVA D prime signal detection or visual search/scanning). The measures of attention are then predictive of overall cognitive ability as measures by the KABC sequential and simultaneous processing global scores. Lack of statistical significance for each of the CMIN scores ($P > 0.05$) indicates that the data fit each of the models

Fig. 12.4 (continued) The KABC subtest plots are ordered *left* to *right* on this graph, in terms of those subtests having the strongest correlation (for all three groups combined) with the Test of Variables of Attention (TOVA) visual test D prime signal detection score of overall attention performance. The Pearson product–moment correlation coefficients between the KABC subtest and the TOVA D prime scores are denoted along the *horizontal* axis (***$P < 0.001$, **$P < 0.01$, *$P < 0.05$). The KABC subtests measuring memory had the strongest correlations with TOVA D prime (*left side* of graph) and also had the greatest overall between-group differences, with the cerebral malaria children doing more poorly compared to the uncomplicated malaria and community control groups. The ANOVA between-group P values for this comparison is located above the plots on the graph itself (***$P < 0.001$, **$P < 0.01$, *$P < 0.05$)

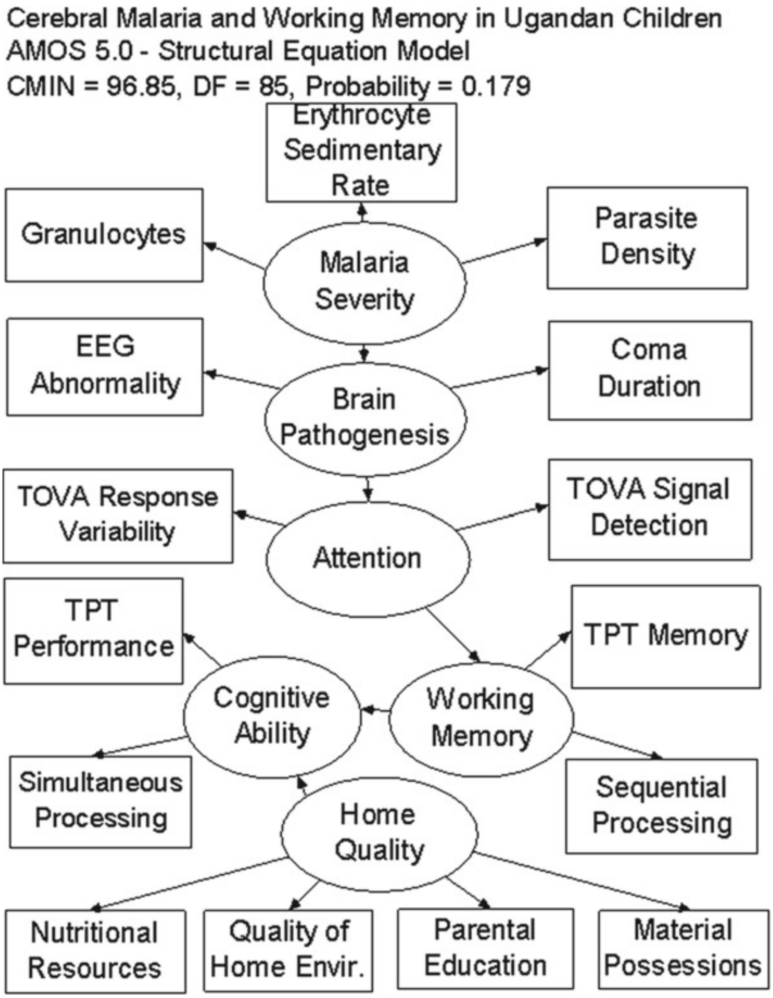

Fig. 12.4 *Uganda CM work mem SEM*. This is a more elaborate model than that contained in Fig. 12.1, in that it incorporates quality of home environment (distal) measures along with the more proximal disease severity and brain pathogenesis measures to predict neuropsychological outcomes in Ugandan CM survivors. This model uses SPSS AMOS structural equation modeling for the CM children at 3-month posthospital discharge follow-up evaluation from the Boivin et al. (2007) study. Severity of illness at hospitalization (granulocytes, erythrocytes, and *P. falciparum* parasite density) was predictive of coma duration and EEG abnormality at 72 h post-admission (diffuse slow wave form abnormality). These were then predictive of TOVA attention measures at 3-month post-discharge, which were in turn related to TPT and KABC memory (sequential processing) performance. Working memory, along with quality of home environment (material possessions SES, parental education level, Caldwell HOME score, and nutritional resources), was predictive of overall cognitive ability as measured by KABC simultaneous processing and TPT performance. The CMIN value of 96.85 (DF = 85), $P = 0.179$ indicates that the data fit this model. Figure 12.3 KABC subtests memory attention. The means and standard errors are plotted for the three groups (uncomplicated malaria, community controls, and cerebral malaria) of children at 6-month posthospital discharge neuropsychological assessment follow-up for children in the Boivin et al. (2007) study. The log-converted raw score means of the subtests from the Kaufman Assessment Battery for Children (KABC, first edition) are adjusted for age and education level.

12.10 Conclusions

Given the variability observed in outcome within the CM groups, the proportion of children with impairments in one or more cognitive function appears to be the most sensitive global indicator of disease burden (Dugbartey 1995; Holding et al. 1999; Carter et al. 2005a, b; Boivin et al. 2007; John et al. 2008a, b). The cumulative evidence suggests that a significant proportion of survivors, estimated at around 14–20%, display impaired performance in at least one functional area two years or more after their illness episode. The functional areas most vulnerable to significant impairment appear to be more complex tasks, particularly those that involve components of attention. Furthermore, the nature of the impairments observed has implications for the development of the individual (microsystem), family (mesosystem), as well as the community itself (exosystem).

Developing a single model and testing its fit across different sites and with different combinations of assessments have allowed us to evaluate the robustness of the theory underlying that model. What is clearly illustrated by this exercise is the need to address multiple influences on development if the effects of individual risk factors are to be adequately understood. SEM, and similar modeling techniques, provides a sensitive methodology for exploring the complex interaction factors affecting risk and resilience. With the foundation of knowledge that now exists with regard to the specific effects of malarial disease, it was possible to draw up an initial model to guide the selection of appropriate test material for the future exploration of disease effects.

A Lurian approach to neuropsychological assessment has unraveled the complexity of malaria disease effects (Luria 1973). This approach requires multiple sources to develop and explore influences upon neuropsychological functioning. One universal standard approach cannot measure all the possible influences without burdening the participants with an enormous battery of tests. Furthermore, given the subtlety of cultural influences on the development of psychological skills, developing an extensive battery of tests also puts an enormous burden on the researchers. As we have demonstrated the application of different measures across different studies does not preclude the ability to summarize results in a meaningful and informative way. In combining the results across the different studies, it is not the lack of consistency in test selection that was the most difficult barrier to overcome. Indeed, had all studies used a single, restricted, test paradigm, then the richness of the information that has emerged would have been lost, limiting the ability to account for variability in outcome.

The difficulty here experienced arose more out of the variability in statistical approaches used and the differences in the level of detail at which data was reported. Summarizing across data extraction processes would have been achieved much more simply had studies, for example, consistently provided means and standard deviations, enabling a standardized method of calculating effect sizes.

Furthermore, as different linguistic and cultural influences make it unrealistic to assume that identical measures can be used across multiple sites to measure exactly the same cognitive functions, we advocate the need to include measures that have been standardized and validated *in situ*, to ensure sensitivity to true population differences, and to understand the extent to which tests used are measuring similar constructs across studies. Another significant limitation of the studies available is the largely retrospective nature of study design. While addressing the long-term effects, retrospective studies do not allow for a characterization of the progression in, and development of, neurodevelopmental consequences that would be helpful in supporting families in managing their children and their own anxieties. Retrospective studies also do not provide any information on the possibility of transient damage in cognitive functions following a proinflammatory response, as has been reported in sensory motor functions (van Hensbroek et al. 1997). The stories associated with the recovery pattern of individual children suggest case studies as a rich source of clinical knowledge, with larger prospective studies providing a means of validating the extent to which the issues reported might affect the wider community.

Thus:

- To guide future investigations we propose a model whereby the severity of disease is related to the level and type of brain insult, the development of specific functions, such as attention and language, and the corresponding effects on more general cognitive ability and achievement.
- Assessment tools need to address specific cultural and linguistic demands and have proven reliability and validity *in situ*.
- Investigations should take into account the interrelationships between disease exposure, health/nutritional status, the quality of the environment, and subsequent cognitive outcome.
- To allow comparability across and between studies, adequate test descriptions should be provided and data reported in a more standardized manner.
- Using malaria retinopathy will improve the classification of children with cerebral malaria in the manner described by Taylor and colleagues (Lewallen et al. 2008) and allow a clearer understanding of the neurological features that characterize CM.

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Appendix

Table 12.2 Performance differences as effect size—Ghana (Dugbartey 1995)

Functional area	Test name—effect size *d*					
Global cognitive functions	Raven's progressive matrices	0.32				
Conceptual/visual perceptual	***Categories test***	***2.41***	Block design	1.07		
Attention	Coding	0.45	***D2 cancellation*** total ***errors***	0.28 ***1.05***		
Memory	Digit span	0.46	***Corsi block***	***1.22***	***Rey–Osterrieth*** immediate ***delayed***	*0.76* ***1.22***
Language	Word fluency	0.63	***Dichotic listening*** left ***right***	0.59 ***1.05***		
Speed of processing	Trail making A B	0.37 **0.85**	Visual reaction time left *right*	0.08 0.27	Auditory reaction time	No data
Motor/sensory motor	***Finger tapping*** left ***right***	0.68 ***1.4***	Purdue pegboard	0.81	Two-point discrimination	0.56
Tactile transfer	***Roughness discrimination test***	***1.12***				
Behavior	Semi-structured interview	No data				

Significant differences in bold

Table 12.3 Performance differences as effect size—Gambia (Muntendam et al. 1996)

Functional area	Test name—effect size *d*					
Conceptual/visual perceptual	Categorization of geometrical figures	0.12[a]	Word object association	0.31[a]	Exclusion abstract figures	0.15[a]
Memory	Syllable recall	0.12[a]	Visual recall	0.002		
Speed of processing	Simple reaction time	0.01	Choice reaction time	0.04		
Motor/sensory motor	Finger tapping Ball throwing	0.04[a] 0.12	Pin board Balance	0.14 0.78	Mazes	0.02

[a]Superior performance by CM group

Table 12.4 Performance differences as effect size—Kenya (Holding et al. 1999)

Functional area	Test name—effect size *d—adjusted for schooling and unadjusted*					
Global cognitive functions	***Sequential processing***	***0.84*** (0.37)	Simultaneous processing	1.12 (0.34)		
Conceptual/visual perceptual	Construction	0.27				
Attention	***Visual search***	***0.66 (0.40)***				
Memory	Individual tests nonsignificant small effects—***sequential scale significant (see above)***					
Language	Picture vocabulary	0.87 (0.12)	***Syntax*** ***Articulation***	***0.34*** ***0.37***	Pragmatic errors	0.22
Motor/sensory motor	Pegboard	0.33				
Behavior	***BQFP***	***0.80***				
Achievement	**Arithmetic**	**0.86** (**0.**23)				

Significant differences in bold

Table 12.5 Performance differences as effect size—Senegal (Boivin 2002)

Functional area	Test name—effect size *d—adjusted for schooling and unadjusted*					
Global cognitive functions	***Sequential processing***	***1.3 (0.84)***	***Simultaneous processing***	***1.3 (1.17)***		
Conceptual/visual perceptual	***Triangles***	***2.08*** (0.27)				
Attention	***Errors***	***1.03 (0.67)***	Response time variability	1.0 (0.18)	Signal detection D prime	1.09 (0.53)
Memory	Individual tests nonsignificant small effects—***sequential scale significant (see above)***					

Significant differences in bold

Table 12.6 Performance differences as effect size—Kenya (Carter et al. 2005b)

Functional area	Test name—effect size *d or* <> calculated from odds ratios					
Conceptual/visual perceptual CM	***Construction***	***<0.33>***				
Seizures		<0.04>				
Attention CM	Visual search errors	0.21	Visual search speed	<0.04>		
Seizures		0.22		<0.08>		
Memory CM	Behavioral memory	Sig.	Means reported by no SD			
Seizures		Not sig.				
Language CM	Comprehension	<0.25>	Syntax	0.07	***Higher-level language***	***<1.63>***
Seizures		<0.87>		***<1.26>***		<0.37>
CM	***Vocabulary (content words)***	***<0.02>***	***Pragmatics***	***0.83***	Word finding	0.35
Seizures		<001>		***0.96***		0.10
CM	Vocabulary (function words)	<0.01>	**Phonology**	0.55		
Seizures		<0.001>		***0.81***		

(continued)

Table 12.6 (continued)

Functional area	Test name—effect size *d or* <> calculated from odds ratios	
Motor/sensory motor CM	Gross motor screening	0.62
Seizures		0.28
Behavior CM	***BQFP***	0.17
Seizures		***0.47***

Significant differences in bold

Table 12.7 Performance differences as effect size—Uganda (Boivin et al. 2007)

Functional area	Test name—effect size (*d*)—*adjusted for schooling and unadjusted*					
Global cognitive functions	***Sequential processing***	*2.4 (0.08)*	Simultaneous processing	3.4 (0.41)		
3 months		0.14		0.43		
6 months		0.35		0.31		
2 years						
Memory	Individual tests not reported					
3 months	***Sequential scale significant (see above)***					
6 months						
2 years						
Conceptual/visual perceptual	Triangles	0.50 (0.22)		–		
3 months						
Attention	***TOVA errors***	***1.1***	***Response time variability***	***1.27***	***Signal detection***	***2.21***
3 months		***(0.37)***				***(0.55)***
6 months		–		**–**	***D prime***	(0.56)
2 years		–		**–**		***(0.60)***
Tactile transfer	***TPT***	***2.8***	Preferred hand	0.9	Non-preferred hand	0.8
3 months	***Memory for shapes***	***(0.51)***				
6 months/2 years	Data shows no significant difference at either time period					

Significant differences in bold

Table 12.8 Performance differences as effect size—Malawi (Boivin et al. 2011)

Functional area	Test name—effect size (*d*)—*adjusted for schooling and unadjusted*					
Global cognitive function	***Malawi Developmental Assessment tool Gross motor***	***0.77 (0.07)***	*MDAT Fine motor*	0.59 (<0.01)	MDAT language	0.63
	MDAT social skills	***0.17***	*MDAT Total score*	0.69		
Behavior	***Child behavior checklist***		Internalizing	0.30 (0.20)	Externalizing	0.14 (0.10)

Significant differences in bold

Table 12.9 Performance differences from estimated mean differences—Uganda (Bangirana et al. 2011)

Functional area	Test name					
Global cognitive functions	Learning	0.27	Reasoning (planning)	0.03	Simultaneous/ sequential (see below)	
Conceptual/visual perceptual	Simultaneous processing	−0.45				
Attention	***Signal detection D prime***	***0.32***				
Memory	Sequential processing	1.39				
Behavior	***Internalizing problems***	***−0.34***	Externalizing problems	−0.15		
Achievement	Arithmetic	1.33	Reading	1.08	Spelling	0.10

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Chapter 13
Computerized Cognitive Rehabilitation Therapy (CCRT) for African Children: Evidence for Neuropsychological Benefit and Future Directions

Paul Bangirana, Michael J. Boivin, and Bruno Giordani

13.1 Introduction

Sub-Saharan Africa is one of the world's most disadvantaged regions in terms of health and socioeconomic indicators (WHO 2010; World Bank 2006, 2011). It has the highest prevalence of people living with HIV/AIDS and suffers the greatest burden of other infectious diseases like malaria worldwide (Snow et al. 2005; UNAIDS 2010; Walker et al. 2007). Children, especially those younger than 5 years of age, suffer the greatest burden of these infections due to their immature immune system, inadequate care, future educational disruption, and distress when their caregivers succumb to these diseases. In addition to the high mortality, there is evidence that children who live with HIV/AIDS or who survive severe malaria are left with severe neurological and cognitive deficits (Boivin et al. 1995; Carter et al. 2005; Drotar et al. 1999; Fernando et al. 2010; Idro et al. 2005; John et al. 2008a, b; Kihara et al. 2006; Van Rie et al. 2008).

As a whole, children with HIV infection display greater difficulties in cognitive functioning, language development, motor skills, and emotional and behavioral

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functioning (Pulsifer and Aylward 1999). Furthermore, there are executive function deficits even in neurologically and immunologically asymptomatic HIV-infected children (Bisiacchi et al. 2000). Studies among African children in the pre-antiretroviral therapy (ART) era showed that when compared with uninfected controls, HIV infection was associated with cognitive and motor deficits (Boivin et al. 1995; Drotar et al. 1999). Congolese children without HIV had significantly better working memory, visual-spatial function, and executive functioning than children with HIV (Boivin et al. 1995; Van Rie et al. 2008), with Ugandan children also demonstrating similar deficit patterns, along with difficulties in sustained attention (Ruel et al. 2012). These deficits are most likely to occur in children whose caregivers have either died or are bedridden by HIV/AIDS and hence cannot provide emotional and physical support (Boivin et al. 1995). In the ART era, these deficits are still seen in children whose immunity has not been compromised and thus do not require ART and in children who have just started using ART (Boivin et al. 2010a, b; Van Rie et al. 2008). The pattern and severity of cognitive deficits appears to be influenced in children by the HIV subtype, with subtype A leading to more cognitive deficits than subtype D (Boivin et al. 2010b).

Koekkoek and others have concluded that ART alone is not sufficient to reverse the neurodevelopmental consequences of HIV infection (Koekkoek et al. 2008; Shanbhag et al. 2005). Highly active ART (HAART) may even contribute to neuromotor decline over time (Koekkoek et al. 2006; von Giesen et al. 2003). Jeremy and colleagues studied HIV-infected children enrolled in several of the NIH-sponsored Pediatric AIDS Clinical Trials Group HAART studies and found significant improvement on only 1 of 13 neuropsychological measures. They concluded that "treatment strategies for children with HIV disease need to be re-evaluated so that they consider restoration of neuropsychological functioning in addition to lowering the viral load" (Jeremy et al. 2005). The inability of ART alone to restore HIV-infected children to "normal neuropsychological performance" is a compelling rationale for the identification of cognitive rehabilitation therapies for these children.

Though not a chronic infection like HIV/AIDS, cerebral malaria (CM) is the most common parasitic infection of the nervous system and also has been shown to affect a number of cognitive abilities (Fernando et al. 2010; Kihara et al. 2006). Both retrospective and prospective studies show that children surviving CM have impaired cognition especially sustained attention and memory that can persist up to 8 years after the malaria illness (Carter et al. 2005; John et al. 2008a). Further, the frequency of impairment appears to increase as the children get older, implying a lag in cognitive development after infection compared with their peers (John et al. 2008a). It is estimated that annually 250,000 children develop cognitive deficits after CM (John et al. 2008a). The incidence of cognitive deficits is much higher when children with HIV as well as those whose cognition has been compromised by other factors such as traumatic head injury, congenital insult, and other central nervous system (CNS) infections are included. Another estimate of the number of children whose cognitive potential has been compromised used poverty indicators and nutritional status to show that over 500 million children will not achieve their full cognitive potential (Grantham-McGregor et al. 2007). These studies are indicative of the cognitive burden children in sub-Saharan Africa face due to disease and other socioeconomic factors.

The need for interventions for children living with these cognitive deficits or at risk of developing them has been noted (Bangirana et al. 2006; Engle et al. 2007; Olness 2003). For the case of CM, possible interventions identified for those surviving the illness include computerized cognitive rehabilitation, caregiver training, physical therapy, speech therapy, and early childhood education (Bangirana et al. 2006). This chapter focuses on computerized cognitive rehabilitation interventions that have been developed recently and now have begun to be implemented in sub-Saharan Africa, highlighting the current practices, challenges encountered, and possibilities for the future.

13.2 Computerized Cognitive Rehabilitation Therapy

From a general perspective, this refers to provision of interventions specifically aimed at improving impaired cognitive ability (or abilities) and to helping a patient adapt to life after a cognitive ability is lost through injury or disease. Restitution intervention improves the impaired ability, while coping and adaptation teaches the patient to survive without the ability that has been lost. The basis for remediation of function is neuroplasticity, the potential of the nervous system to be modified in response to stimulation and activation, basically "any change in the nervous system that is not periodic and has duration of more than a few seconds" (Lundy-Ekman 1998). The permanency and extent of changes is dependent on amount of experience and success of cortical reorganization.

Restitution rehabilitative methods are preferred to coping, because they actively help the patient regain lost cognitive abilities. Computerized cognitive rehabilitation therapy (CCRT) is a restitution technique involving computer-based continuous retraining of cognitive skills that can lead to new learning through repetition and adaptive increase in challenge. The rationale behind this approach is that periodic, repeated, and increasingly challenging training of a specific cognitive skill leads to physiological changes in the brain that in turn lead to an improvement in a particular cognitive ability. In cases where the trained cognitive skill underlies other cognitive areas, improvement may be seen in several related cognitive domains.

Some physiological changes associated with cognitive function that have been identified after restitution methods include increased brain activity, increased dopamine availability, and strengthening of white matter tracts (Hoekzema et al. 2010; McNab et al. 2009; Olesen et al. 2004; Takeuchi et al. 2010). The application of restitution approaches can be traced back to early environmental enrichment studies where mice reared in cages with more play area and stimulation showed changes in the brain such as more hippocampal neurogenesis, increased length and density of dendrites, and higher numbers of glial cells and synaptic density than those reared without these amenities (Brown et al. 2003; Kempermann et al. 1997; Kolb and Whishaw 2009).

Mahncke and colleagues have proposed a CCRT neuroplasticity intervention model that explains the foundation for the CCRT restitution training process (Mahncke et al. 2006a, b). They propose that CCRT is effective because it is designed to redress four principal causes of negative brain plasticity in the face of illness and injury: reduced schedules of activity, noisy processing, weakened neuromodulatory control, and negative learning. *Reduced schedules of activity* occur when a neurological insult leads to reduction in the experiences and activities that engage the brain and normally lead to further consolidation of learning through experience. *Noisy processing* results when infection in the CNS disrupts the functioning of neural networks, which then become unreliable, of low fidelity, and have weak cortical representations of sensory experiences and the cognitive and behavioral actions they feed. Neuropsychological processing efficiency and speed deteriorate as a result of these degraded signals and cortical representations. *Weakened neuromodulatory control* compromises the action of motivational pathways that drive attention, memory, learning, and adaptation (e.g., reward, punishment systems). Response perseveration and maladaptive impairment occur when ordinary adaptive behaviors become more difficult due to illness or insult. Behavior drifts to less demanding modes and *negative learning* then takes place in the form of response perseveration, impulsivity, and maladaptive tendencies. Negative plasticity could be contrasted with positive plasticity, reflecting the benefit of interventions that improve the overall plasticity of the neural networks. Mahncke and colleagues posit that these systems can be strengthened and fortified with brain plasticity-based CCRT training programs designed to improve the sensitivity, speed, and accuracy of processing of information. They have demonstrated that this type of CCRT training can successfully improve tests measures of attention and delayed recall in healthy, older adults (Mahncke et al. 2006b; Smith et al. 2009).

13.2.1 Evidence of CCRT Effectiveness in Children with ADHD

The majority of CCRT trials to date with children have involved treatment of attention deficit-hyperactivity disorder (ADHD). Concerns over side effects of medication or other parental preferences have led to interest in alternative non-pharmacological interventions. The obvious similarity between the cognitive and behavioral deficits noted in ADHD and the often cited goals of CCRT (e.g., improvement in attention, working memory, and problem solving) have resulted in several larger trials with children diagnosed with ADHD. CCRT approaches to ADHD also are of particular interest in considering potential applications of this intervention approach to CM and HIV. The similarities of some of the basic deficit patterns seen across these disorders (e.g., emphasis on sustained attention, working memory, and executive functioning) suggest the potential appropriateness of the CCRT approach to CM and HIV.

We present some of these trials in children with ADHD to highlight CCRT's effect on cognitive functions. In the first study, 36 school-age Israeli children with ADHD received an intervention of 8 weeks of computerized attention training (1 h sessions, two times per week) (Shalev et al. 2007). The CCRT intervention (CogniFit program) was programmed so that as the children progressed through each session, the required tasks became progressively more difficult with increasing attention demands, including (a) sustained attention (the ability to maintain attention and persist on a task until completion), (b) selective attention (the ability to maintain a specific cognitive set in the face of competing distractions), (c) orienting attention (directing one's attention to critical stimuli), and (d) executive attention (allocating attention focus between competing demands and choosing those stimuli to which children must attend). Children in the active control group played computer games for the same amount of time. Parents did not know in which intervention group their child had been randomly assigned. ADHD symptoms were rated by the child's parents before and after the 8 weeks of either computer activity. Academic performance was tested pre- and post-training period using math problems, reading comprehension problems, and passage copying problems taken directly from children's school books.

Parents of children in the attention training group reported a statistically significant decline in their child's inattentive symptoms compared with parents of children in the active control group who just played computer games. Change in hyperactive-impulsive symptoms was in the same direction but was not statistically significant. After controlling for academic performance before training, children who received attention training did significantly better in reading comprehension and in speed of copying passages than controls. Math performance also improved, but did not reach statistical significance. In summary, the attention training program produced significant functional improvements as evidenced by parents' ratings of inattentive symptoms and by academic performance.

The second study was presented as a research poster at the annual meeting of the American Psychiatric Association (May 2008) by Lucas and colleagues (Lucas et al. 2008). Forty-six school-age children with ADHD participating in an intensive summer treatment program for ADHD were assigned to receive either auditory or visual-spatial working memory training using a CCRT program (RoboMemo, http://www.cogmed.com). Both the auditory and the visual-spatial training protocols automatically increased the difficulty level of the working memory tasks by increasing the number of items to be recalled as children mastered each level. Children who received visual-spatial training demonstrated significantly greater gains than the auditory training group on separate visual and auditory working memory tasks administered before and after the 6 weeks of CCRT training. These children also earned significantly more positive behavior points from the camp counsellors: doing better at consistently following camp rules and behaving appropriately. Thus, CCRT increased positive behavior above and beyond medication and behavior treatments already in place.

Rabiner and colleagues reported similar findings in a randomized control study with children undergoing CCRT training with BrainTrain's Captain's Log CCRT system, using computer tasks selected for auditory and visual sustained attention (Rabiner et al. 2010). The researchers compared 77 first graders across three groups: CCRT, computer-assisted instruction (CAI) in academic areas, and a passive control group (wait list). Children were selected for the study based on teacher rating on a DSM-IV symptom checklist for inattention. Teacher ratings following 50–60 min of computerized training twice a week for 14 weeks found that both computer interventions had significantly more children with at least a half standard deviation improvement in inattention symptoms as compared to the passive control group. It also appeared that those children rated as having the highest inattention scores prior to training benefitted the most from the computerized interventions.

Working memory is a domain that underlies a range of skills found to be at risk in children with ADHD, including reasoning and planning, control of attention, and the ability to resist distraction from irrelevant stimuli (Barkley 1997; de Fockert et al. 2001; Engle et al. 1999). Klingberg and colleagues have demonstrated that visual-spatial working memory has been shown to be a particularly sensitive measure of cognitive deficits in ADHD (Westerberg et al. 2004). They used the RoboMemo from Cogmed (Cognitive Medical Systems AB, Stockholm, Sweden) that trains for working memory skills using visual-spatial tasks (i.e., remembering the position of objects in a 4 by 4 grid and verbal stimuli remembering increasing lengths of phonemes, letters, or digits). In this multicenter, randomized, controlled, double-blind trial, children between the ages of 7 and 12 years were included if diagnosed with ADHD or either combined or predominantly inattentive subtype (Klingberg et al. 2005).

Of 53 children who started the program, 44 completed at least 25 training sessions of ~40 min each over 5–6 weeks with the Cogmed CCRT. Two study groups were used, one with the difficulty level automatically adjusted on a trial-by-trial basis (self-titrating) and the other, the active control group that consisted of a fixed, easy set of items from the Cogmed program. Assessments with a battery of neuropsychological measures, including the primary outcome, a span-board task, which was a non-practiced type of visuospatial working memory, took place after training and at a 3-month follow-up visit. The self-titrating Cogmed CCRT group improved significantly more than the comparison group on the span-board measure at initial testing and follow-up as compared to pretraining performance, demonstrating a capacity for generalization of working memory training improvements. In addition, there were treatment effects for response inhibition (Stroop task), verbal working memory (digit span), complex reasoning/general intellect (Raven’s task), and parent ratings of ADHD symptoms.

Working memory skills also have been trained in 32 healthy elementary and middle school children by means of a videogame-like working memory task utilizing an n-back working memory training procedure (i.e., a series of stimuli presented at different locations on the computer screen one at a time, with participants needing to decide whether a stimulus appeared at the same location as the one presented in n items back in the sequence compared to an active control group of 30 children whose training task involved general knowledge and vocabulary questions) (Jaeggi et al. 2011). Children were trained in 15 min sessions in both groups, five times a week for 1 month. The outcome measure for this study was performance on matrix reasoning tasks, the Test of Nonverbal Reasoning and the Ravens Standard Progressive Matrices, as general measures of functioning and reasoning. Clear differences were not seen across conditions for all participants; however, when children who significantly improved on the training tasks were compared, significantly greater improvement on the outcome measures was noted in the active CCRT group as compared to the control group. These differences continued to be evident at a 3-month follow-up. These findings by Jaeggi and colleagues demonstrate that even healthy children may be able to benefit from CCRT training, though they also highlighted potential limiting factors that should be considered in CCRT research, including individual differences in training performance.

13.2.2 Experience with CCRT in Uganda with HIV-Infected Children and Children Surviving CM

Besides approaches with children diagnosed with ADHD, CCRT has already been used in trials to treat the cognitive effects of medical illness. CCRT programs have been shown to improve attention in adults with schizophrenia, stroke or traumatic brain injury, and HIV (Bellucci et al. 2003; Rohling et al. 2009; Spina et al. 2008). With children, CCRT has been shown to be effective in improving the sustained, selective attention and problem solving with acquired brain injury and communication and reading skills in autism (Heimann et al. 1995; Hooft et al. 2005). In a recent pilot study, home-based CCRT training also was found to be reasonable to use and well accepted by children with acute lymphoblastic leukemia and brain tumors who characteristically demonstrate deficits in attention and working memory (Hardy et al. 2011).

Three studies using CCRT with African children have been published: two studies with children surviving CM and one study with children infected with HIV/AIDS. All three of these related studies were completed as pilot projects in order to evaluate the efficacy and suitability of completing CCRT training programs in both rural- and city-based populations in Uganda, an example of a resource-poor setting in sub-Saharan Africa. All three studies used 15 training tasks chosen from BrainTrain's Captain's Log program which consists of 35 games training a number of cognitive skills (Sandford 2007). The 15 training tasks chosen for these three studies following extensive pre-study pilot testing were ones that emphasized skill areas found to be impaired with CM and HIV (i.e., attention, working memory, visual-spatial processing, executive functioning), had minimal language demands, and limited mouse movements so as to ease performance for Ugandan children. Of these 15 exercises, four trained attention, four trained memory and conceptual skills, three were for visual motor skills, and four were for logic. Pretesting demonstrated that children unfamiliar with computers could effectively utilize these programs and advance through the system, though responding with a computer mouse was found to be inferior to using a response device consisting of a larger trackball with large, colorful response buttons. The use of long battery life notebooks allowed for easy presentation in field. For all children, the first session of training started at the simplest level of each training task and increased in difficulty based on the child's performance.

In the first study, 65 children who had been admitted with CM to the Acute Care Unit of Mulago Hospital in the Ugandan capital of Kampala several years earlier (mean = 3.7 years previously) were traced and enrolled into a randomized trial in which those in the intervention group would receive 16 sessions of CCRT each lasting 45 min and delivered over 8 weeks (two sessions per week) (Bangirana et al. 2009a). The control arm received no CCRT treatment (treatment as usual). Pre- and post-intervention testing was done using CogState (Westerman et al. 2001) computerized neuropsychological test battery for the neuropsychological outcomes and the Child Behavior Checklist (CBCL) validated for a Ugandan population (Bangirana et al. 2009c) for the behavioral outcomes. Immediately following the training period, significant benefits were observed for the CCRT intervention group as compared to the no-treatment group in the CogState maze chasing task reflecting psychomotor speed ($p<0.01$), maze learning task reflecting problem solving and planning ($p<0.01$), and detection, a simple reaction time measure ($p<0.04$). In addition, parents reported that the CCRT group, as compared to the no-intervention group, experienced fewer problems on the CBCL's internalizing problems scale ($p<0.02$). In addition, the CCRT intervention group showed improvements (though not significant) across all the tasks and the CBCL scores, though this was not true for the no-intervention group.

Given that benefits from CCRT could be observed at almost 4 years post illness (mean = 3.7 years), another study was planned to take advantage of the finding that the rate of impairment after CM is higher at 24 months compared with 3 or 6 months following recovery (John et al. 2008a). It was proposed that using the same Captain's Log CCRT intervention at an earlier time point post-recovery could halt the trend of increasing cognitive impairment seen with increasing time post-recovery. In this second study, 61 children admitted to hospital with malaria with neurological involvement (either CM, malaria with seizures, or malaria with impaired consciousness) were followed up at 3 months post-discharge and given assessments for neuropsychological functioning, academic skills, and behavior. The same CCRT intervention protocol as in the first study was used, namely, 16 training sessions over 8 weeks with the Captain's Log CCRT. The Kaufman Assessment Battery for Children, second edition (KABC-2), adapted for use with children in Uganda, was used to assess memory, visual-spatial skills, learning, and reasoning; the nonverbal Test of Variables of Attention was used to assess sustained attention and impulsivity; the Wide Range Achievement Test third edition was used to assess reading, writing, and arithmetic; and the CBCL was used to assess internalizing and externalizing behavioral problems. Following these assessments, children were randomly assigned to the CCRT intervention or a treatment-as-usual (passive) control groups. Immediately post-intervention testing demonstrated significant improvement in the KABC-2 learning measure for the CCRT intervention group. However, this group actually demonstrated a decline on the KABC-2 working memory score in comparison to the passive control group. No other behavior changes were evident for other test domains, academic performance, or behavior. The expectation of increased improvement in CCRT effects for children trained closer to their episode of CM was not supported. With poorer cognitive functions observed in the long term than immediately after CM, children receiving CCRT immediately may not show a bigger increase in cognition than when trained in the long term (Bangirana et al. 2011). The observed benefit at almost 4 years post-malarial episode in the earlier study could also relate to the older age of the children in that study (by ~3 years) which may have allowed more effective learning on the CCRT procedures or the possibility that additional time from the actual CM event may be necessary to enhance CCRT benefit. Better understanding of these effects will require additional, larger studies with both active and passive control groups, as now underway with both CM survivors and children with HIV/AIDS by the same investigative team in Uganda. The CCRT approach also has been used as an intervention for Ugandan children infected with HIV (Boivin et al. 2010a). Due to logistical difficulties in the rural town where this trial was completed, only 10 training sessions, rather than 16 as in the CM studies reported above, were planned. In this study, 32 children were assigned to the intervention group and 28 to a nonintervention (treatment as usual) group. The computerized CogState test battery was used pre- and post-intervention to evaluate the effect of the intervention. Significant improvements were observed post-intervention in the CCRT group on maze learning ($p<0.01$) and detection ($p=0.02$), consistent with improvements seen in the first CM study (Bangirana et al. 2009a).

These three studies provide the first evidence that CCRT can potentially be used to improve cognition in African children who survived malaria with neurological involvement or who are living with HIV. The adherence to the training sessions was high, ranging from 90 % in the first CM study to 100 % in the second CM study. The HIV study had adherence of 95 % indicating acceptability of the intervention in a rural setting. These studies all provided the same cognitive intervention training attention, memory, visual motor ability, and logic, ensuring that a variety of cognitive functions were trained.

13.2.3 Additional Evidence of Efficacy of CCRT Through Interactions with Medical Factors

In the Ugandan CCRT studies presented above, age or time since CM involvement may have influenced the ability to benefit from CCRT and therefore affected outcome, at least with the CM survivors. Jaeggi and colleagues also have suggested that ability to benefit from CCRT may predict who will experience the greatest generalization to other cognitive ability areas not specifically trained by the CCRT procedures (Jaeggi et al. 2011). Possible modulating factors related to CCRT benefit may be considered in terms of Mahncke's previously discussed neuroplasticity (Mahncke et al. 2006a, b). Specifically, it could be hypothesized that CCRT would especially benefit CM survivors who were most affected by their disease and hence had the most *negative neuroplasticity*. Children with CM and HIV with the highest degree of CNS involvement (coma, seizures, greatest level of proinflammatory immunology markers, greatest EEG disruption, high HIV viral load, low CD4 count) would be expected to show the greatest proportional cognitive and psychiatric gains from CCRT. On the other hand, if CCRT benefit is mediated by *positive neuroplasticity* model, it is possible that CCRT benefit might be greatest for those children more intact in terms of brain/behavior integrity (e.g., least severe neurological and clinical indicators of illness) and therefore better able to profit from CCRT training. The next section in this chapter outlines relationships among medical diagnostic and outcome variables with CCRT benefits among the Ugandan children with CM which have not yet been published.

13.2.3.1 Neuropsychological Benefits of CCRT Interact with ART in Ugandan Children with HIV

ART in children before the onset of neurologic symptom may have a neuroprotective benefit by delaying the onset of progressive encephalopathy (Sanchez-Ramon et al. 2003). A reevaluation of data from the preliminary CCRT study with children with HIV described above revealed that 13 of the 32 CCRT children were on ART (Triomune: Lamivudine, Stavudine, Nevirapine) and 19 of the CCRT children were not on ART. For the control group, 10 of the 28 were on ART. With respect to KABC-2 performance, a significant interaction effect ($p<0.01$) was observed in that only children on ART had significant CCRT improvements on visual-spatial processing tasks of the KABC-2. These findings would support a positive neuroplasticity model, suggesting that children with additional factors that can improve their overall outcome may benefit most from CCRT intervention.

13.2.3.2 Indicators of Malaria Illness Severity and CCRT Neuropsychological Outcomes

Uganda Cerebral Malaria Electroencephalogram (EEG) Findings. In reanalyzing the data from the first Ugandan CM study (Bangirana et al. 2009a), EEGs were available in 38 children 72 h post-admission during their acute illness. Background slow-wave abnormalities were evident in 19 of these children and were predictive of significantly lower working memory and visual-spatial processing scores at 3 and 6 months post-discharge (Table 13.1). Immunological and EEG measures of severity of malarial illness were hypothesized to be predictive of CCRT benefit because of the potential impact of severe malaria brain pathogenesis on more static measures (Sternberg and Grigorenko 2002).

When evaluating those children who had diffuse slow brain wave EEG during their CM illness, the slow-wave (abnormal) EEG group had significantly less improvement in speed on several measures from the CogState battery assessed after

Table 13.1 Cognitive mean differences for children with normal ($N=13$) and abnormal ($N=25$) EEGs

	0 months		3 months		6 months	
	Mean diff	*p*	Mean diff	*p*	Mean diff	*p*
KABC-2 simultaneous processing	−0.84	0.65	−0.91	**0.05**	−2.44	**0.01**
KABC-2 sequential processing	−1.27	0.63	−3.08	0.05	−1.97	0.02

Analysis of covariance adjusted mean differences controlling for nutritional status, home environment, and education level scores

CCRT treatment as compared to the normal EEG group (detection, $p=0.02$; identification, $p=0.01$; and Groton Maze Learning Test efficiency, $p=0.05$). These results again support the hypothesis that children with better neurological status may actually benefit more effectively from the CCRT intervention.

Cerebrospinal Fluid (CSF) Cytokine Predictors of CCRT Outcomes in Ugandan CM Children. In the first study to document that CSF tumor necrosis factor-alpha (TNF) production is associated with subsequent neurologic and cognitive morbidity (John et al. 2008b), cerebrospinal fluid (CSF) and serum levels of 12 cytokines or chemokines important in CNS infections were measured in 76 Ugandan children hospitalized with CM and 8 control children. Elevated CSF TNF levels on admission were associated with an increased risk of neurologic deficits 3 months later (odds ratio 1.55, 95 % CI: 1.10, 2.18, $p=0.01$). TNF-alpha was also negatively correlated with age-adjusted scores for attention (Spearman rho, −0.34, $p=0.04$) and working memory (Spearman rho, −0.32, $p=0.06$) 6 months later.

Endothelial cell (EC) activation appears to play a role in CM pathogenesis, but serum levels of EC activation markers and their relationships to malaria pathogenesis have not been fully characterized. Von Willebrand factor (VWF), vascular cell adhesion molecule-1 (VCAM-1), and intercellular adhesion molecule-1 (ICAM-1), all indicators of EC activation (Cardier et al. 2006; van Mourik et al. 1999) were measured in the sera of 75 Ugandan children with CM, 65 children with uncomplicated malaria (UM), and 49 healthy community control (CC) children (Park et al. 2008). VWF levels were significantly higher in children with CM than UM ($p<0.01$) and in children with UM than CC ($p<0.01$). In contrast, VCAM-1 and ICAM-1 concentrations were marginally higher in children with CM than UM (VCAM-1, $p=0.03$) but significantly higher in children with UM than CC (VCAM-1, $p<0.01$, ICAM-1, $p<0.01$).

VWF levels may therefore be a good marker of endothelial cell activation in these children and a sensitive indicator of severity of malarial illness during the acute phase. Along with CSF TNF, serum VWF may help better understand the moderating effects of these markers of illness severity on subsequent neurocognitive outcomes and responsiveness to CCRT.

Model for Severity of Malaria Illness and Neuropsychological Outcomes. EEG abnormality during illness was predictive of attention improvements for cognitive rehabilitation intervention several years after illness. The plausible association between CSF TNF and serum VWF with benefit from CCRT provide additional

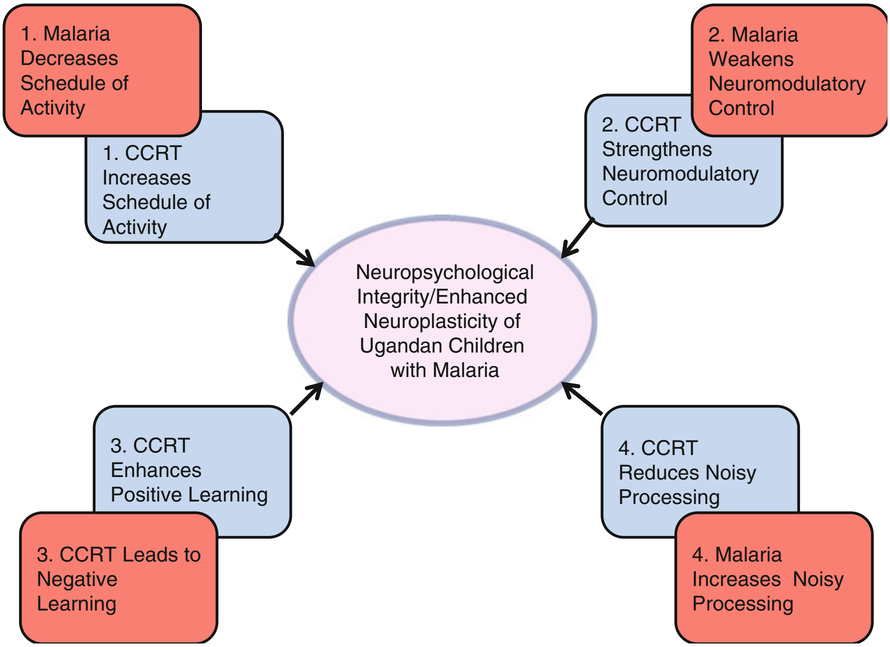

Fig. 13.1 CCRT intervention approach to Mahncke's model of negative (*outer four boxes*) and positive (*inner four boxes*) neuroplasticity as applied to cerebral malaria

support for a positive neuroplasticity model for CCRT. Figure 13.1 depicts the interaction of positive and negative neuroplasticity relationships and integrates them with the quality of the home environment (Bangirana et al. 2009b) on subsequent neurocognitive outcomes for children at risk for severe malaria. This schematic also shows the point at which CCRT interventions can have a strategic benefit on neurocognitive outcomes in the aftermath of severe malaria.

13.3 Limitations of CCRT Studies in Sub-Saharan Africa

The three studies presented using Ugandan children represent the first studies attempting to use the CCRT rehabilitative model in children in sub-Saharan Africa. Although pilot studies, their results do suggest that this approach is reasonable and applicable to both urban and rural resource-poor settings. Modifications based on language and response features can maintain the integrity of the training programs and the use of notebooks or other computers with long battery life make these portable interventions that can be used with a number of children simultaneously after minimal one-on-one experience to be sure the program requirements are understood. CCRT procedures are inherently interesting and entertaining to children in these settings and compliance was very high. Anecdotally, treatment centers have had to make computers available with related programs and games for children due to many of the training group children asking to return for more training.

The Ugandan CM interventions have generally supported the view that specific cognitive functions previously found to be vulnerable to medical illnesses such as CM and HIV can be trained with an active CCRT intervention. Cognitive skills that were seen to improve after CCRT suggested generalization of training to several of the specific aspects of cognitive functioning most at risk. However, there are a number of limitations that need to be considered while interpreting these results or deciding whether these interventions should be rolled out in their current state. Most importantly, the three Ugandan CCRT studies discussed above were lacking an active control group (e.g., nontherapeutic computer exposure). Therefore, it is possible that significant gains for the CCRT group may have related to more experience with the computer. It should also be noted that if this was the case, however, we might have expected computer-skill practice to lead to a significant advantage for all of the CogState computer-presented assessment tasks, rather than in select ones associated with attention and problem solving. Without an active control group, there is uncertainty concerning the active agent for the neuropsychological benefit from CCRT. Currently, large ongoing studies by the same study team are comparing active CCRT training with a "locked" or fixed CCRT version of the same program, which is not titrated to improve as the child works through the exercises, but rather present three task levels in a random order. This approach, still including a passive control group, will better allow for comparison of the active CCRT training in comparison to a group of children experiencing all of the computer skills and exposure basically presented to the active CCRT intervention group.

Both CM and HIV in children are associated with a number of cognitive deficits; hence the current intervention studies were designed to provide cognitive training for a number of cognitive domains. Training a number of cognitive skills while having a modest number of training sessions presents the possibility of having a less intense intervention as would have been if all the training sessions were training a single cognitive ability. Other successful CCRT studies for children with ADHD have trained working memory only and shown benefits in both the trained and nontrained tasks (Klingberg et al. 2002, 2005). It is possible that training a specific skill like working memory, which is foundational to other cognitive skills and executive functions, may produce better results than training a number of skills. Interestingly, a large study in adults of several active cognitive retraining interventions aimed at specific cognitive domains, including computerized aspects in several, however, generally did not show generalization to cognitive areas outside those specifically taught (Ball et al. 2002). These considerations in terms of approach remain for further investigation.

In line with the above limitation concerning the range of the intervention, consensus has not been reached about other practical considerations for CCRT paradigms, including the appropriate number of sessions, the ordering of sessions (e.g., every day, every other day), or the overall length of sessions. In the comparison of rural to urban settings for Ugandan children presented earlier, both a longer and shorter protocol appeared to yield similar results. Skill learning protocols often have suggested that daily training may not yield the most efficient learning paradigms due to the need for consolidation, though Mahncke's protocols involved at least five or daily CCRT presentations (Mahncke et al. 2006a, b; Smith et al. 2009). A minimum of 24 sessions over a limited period of weeks is often cited, but conclusive research results to guide this decision making remain lacking.

Regarding the results of the two CM studies presented in this chapter (Bangirana et al. 2009a, 2011), prospective studies show that the frequency of cognitive deficits after CM at 3, 6, and 24 months increases from 19 % to 21 % to 26 %, respectively. This implies that, compared with their peers who have no prior cerebral insult, children surviving CM have poorer cognitive skills which become more pronounced as they grow and have to perform more complex tasks (Boivin et al. 2007; John et al. 2008a). It was hypothesized that CCRT carried out earlier after hospitalization for CM rather than later would demonstrate greater efficacy of CM treatment and arrest this trend of increasingly poorer cognitive outcome. This hypothesis was however not supported, as clearer and stronger CCRT improvements were seen in older children trained years later after CM (Bangirana et al. 2009a) as compared to children trained closer to hospitalization for CM (Bangirana et al. 2011). Although neuropsychological deficits may be seen to increase in the years following CM, it is possible that these reflect delays in neurodevelopment due to illness and disruption of early schooling. It is possible that with time, negative neuroplasticity factors improve to a point where CCRT benefits may be more evident (positive plasticity). This finding would be consistent with the results seen in the reanalyses of the Ugandan CM and HIV studies discussed above that suggested that measures of neurological illness severity were negatively related to improvements on some cognitive measures assessed after training.

Despite the improvement in some cognitive skills in all of the pilot CM studies completed in Uganda immediately following training, the durability of these improvements is yet to be demonstrated, as has been done in Western cultures in children with ADHD, as discussed earlier. The ongoing CM and HIV trials in Uganda using active and passive control groups in comparison to CCRT training also include longitudinal follow-up. In the case of CM and CCRT, for example, the larger intervention design will allow differentiation of the moderating influence of more proximal (clinical and immunological illness severity) from more distal (impoverishment) factors in CCRT outcome benefit. Figure 13.2 depicts the current CCRT intervention (far right), outcome assessment domains (sensory/motor, cognitive, psychiatric), the principal proximal severity of illness factors serving as moderators (malaria CNS encephalopathy), and more distal risk factors (far left) affecting the outcome domains. The analyses will allow the differentiation of more proximal from more distal moderators of CCRT outcome benefit by controlling for the effects of quality of home environment on our outcome measures. Because the outcomes are comprised of neuropsychological and psychiatric gains from before to after CCRT intervention, they will be more dynamically based and thus more sensitive to the brain/behavior benefits of CCRT in terms of Mahncke's positive neuroplasticity model. This will allow a more accurate gauge of the direct impact of severity of malarial illness on CCRT brain/behavior benefit.

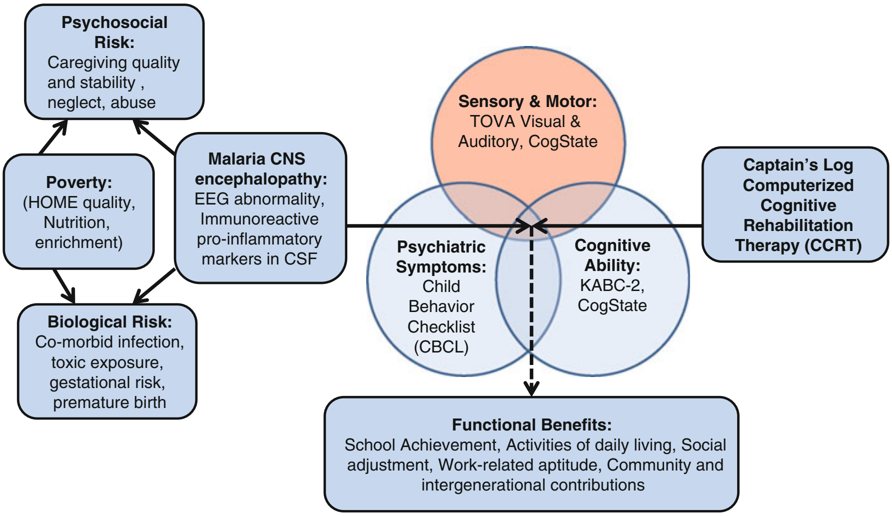

Fig. 13.2 Model of the major risk factors and assessment domains for the ongoing study of CM in Ugandan children [adapted from Walker et al. (2007) and Engle et al. (2007)]

13.4 Future Directions

The studies of children and adults presented in both Western and sub-Saharan populations suggest reasonable efficacy for CCRT approaches to rehabilitative training, though also point to significant areas in need for careful research. All three of the Ugandan CCRT studies used the same treatment protocol, training a number of cognitive skill areas. As already noted, this approach may limit the amount of time given to training a specific skill thus reducing the treatment intensity. Neuropsychological "markers" of cognitive impairment in CM and HIV need to be better identified so that future interventions can be designed to specifically target these markers. Endophenotypes are such markers and are defined as measurable hereditary traits between the disease and distal genetic genotype that indicate an individual's likelihood of developing the disease (Castellanos and Tannock 2002; Gottesman and Gould 2003). In ADHD, working memory is considered an endophenotype of the disease (Castellanos and Tannock 2002) and successful CCRT studies have trained it only (Klingberg et al. 2002, 2005; McNab et al. 2009). Further work in clearly providing endophenotypes for medical illness affecting the sub-Saharan area will be important for increased efficacy in CCRT training paradigms.

Considering CCRT studies generally, many lack adequate validation studies that demonstrate lasting benefit and tie CCRT results to other medical illness indicators. Although technical issues appear reasonably resolved for resource-poor settings, considerations remain with regard to best approaches and influence of language issues or familiarity with presented stimuli. Cost issues related to such settings also are to be considered. Most available programs are expensive to purchase and lease due to extensive programming and development work, often making these inappropriate outside of research-supported settings. Increasing humanitarian interest generated by positive results in resource-poor settings may help defray such costs or increased interest in open-source and non-copyright approaches may lead to wider use.

Additional research will be necessary in terms of comparing the efficacy of self-titrating versus fixed presentation CCRT programs. Although many researches argue that the self-titrating, increasingly challenging nature of CCRT programs is inherently important, sufficient comparisons to “locked” programs presenting repeated trials will need to be completed. The availability of feedback and the type/amount of feedback within the CCRT setting continue as other areas of interest and ones that may require careful consideration across cultural settings. Emphasis on feedback in terms of monetary representations or loud auditory feedback may not be appropriate in some cultures or settings. Ease and use of directions in local languages may be necessary, though the inherent game-like quality of most of these programs allowing for enhanced learning and understanding over time may reduce this concern.

As already discussed, the duration of use/benefit ratio of how long and in what sequence to present training sessions will require careful evaluation, as will applicability to children with possible sensory deficits (e.g., vision, hearing) related to medical illness or accident. Finally, the question remains as to whether training in very specific “foundational” cognitive domains (e.g., simple attention, working memory) will provide greater cognitive benefit and generalization to other cognitive domains as compared to attempting to train across areas.

With the recent proliferation of information communication technology in the rural areas of sub-Saharan Africa, use of the Internet to provide these interventions to remote areas is a possible scenario. Mental health interventions like cognitive behavioral therapy have been administered through the Internet in high-income countries with less costs but still highly effective in their treatment (Hedman et al. 2011; Ljotsson et al. 2011). Administration of CCRT through the Internet has also proven effective by enhancing usage of compensatory strategies resulting in respondents being satisfied with the intervention (Bergquist et al. 2009; Bergquist et al. 2010).

In summary, the current CCRT intervention example presented from work in Uganda, though effective in improving some cognitive skills, has some inherent limitations making it difficult to adopt them into policy. Future CCRT studies should include both active and passive control groups to address the issue of computer exposure for the intervention groups. Including long-term follow-up assessments will provide evidence whether these interventions are sustained over time. Identification of clinical and laboratory predictors of improvement (and treatment failure) can provide more understanding about the mechanisms of brain injury for some CNS infections like CM and also identify individuals less likely to benefit from such interventions. Much of the burden of malaria is suffered by preschool children who are not old enough for the current CCRT interventions provided. Future studies need to try other new interventions for these young children like the mediational intervention for sensitizing children (Klein and Rye 2004) who may not be able to perform the computerized training.

13.5 Summary and Conclusion

HIV and malaria are a common cause of impaired cognitive functioning in African children. Such impairment will likely compromise their school performance, impede their activities of daily living, and lessen their future economic opportunities, particularly as increasing numbers of children survive longer with increases in medical treatment success. Unfortunately, ART alone does not help remediate these cognitive deficits and no treatment intervention during acute illness to prevent CM brain-injury effects (Abubakar et al. 2007) is known. Nor are neurocognitive rehabilitative treatment programs available in low-resource settings for affected children. However, we have successfully piloted a CCRT intervention to improve cognition with school-age African children survivors (Bangirana et al. 2009a, 2011; Boivin et al. 2010a), as a model for future research. Applying key features of clinical trial approaches, including adequate controls, careful consideration of intervention comparisons, dose-titration approaches, and intention to treat design, will significantly improve the state of CCRT in sub-Saharan Africa, as well as worldwide.

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Chapter 14
Measurement of Cognitive Outcomes of At-Risk Children Using Novelty Processing in Rural Kenyan Children

Michael Kihara

14.1 Neurodevelopment in Africa

Over 200 million children under 5 years who live in developing countries will not reach their developmental potential (Grantham-McGregor et al. 2007). This includes development in domains such as language, cognition, behavior, and socio-emotional. A major challenge in measuring the neurocognitive burden of at-risk children in Africa is the general lack of culturally appropriate neuropsychological measures (Holding and Kitsao-Wekulo 2004; Kihara et al. 2010b). Recent studies have investigated the usefulness of locally developed neuropsychological tools to measure cognitive and behavioral development (Holding et al. 2004; Abubakar et al. 2008). In Western countries, neurophysiological techniques such as event-related potentials (ERPs) have been used as surrogate markers of cognition in both children and adults following brain insults. ERPs have been used to assess basic sensory abilities that have important cognitive consequences in children (Courchesne 1978; Byrne et al. 2001; Ceponiene et al. 2002a; Burden et al. 2007). ERPs can be either active, such that the child is asked to respond either by pressing a button or counting the number of stimuli, or passive, in which no overt response is required. Passive ERPs are not dependent upon language, are less likely to be influenced by culture than standard neuropsychological tests, and may be particularly useful in populations such as those in Africa. A few sensory evoked potential/ERP studies have been conducted with African populations (Elwan et al. 2003; Mwanza et al. 2003; Oluwole et al. 2003; Lombard 2005), but these have not examined long-latency ERPs that are associated with cognition.

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14.2 Event-Related Potentials

ERPs are brain voltage fluctuations that are associated in time with a physical (visual, auditory, or olfactory) or mental occurrence (attention, recognition, memory) (Picton et al. 2000). These brain potentials can provide very precise information about the timing of brain activation and some information about the spatial location of the regions activated. Thus, ERPs can potentially provide more direct insight into the earliest stages of information processing affected by cerebral disease and some ideas about the brain regions affected than general neuropsychological measures.

Brain response to novel or unexpected stimuli has been commonly studied in infants and children because it is a reliable and robust response and because orienting to novel information in the environment is considered a fundamental process in cognitive development. Studies with adults suggest that a frontotemporal brain network is involved in processing novel events. The first step in the application of ERP techniques to detect cognitive impairment in African children would be the establishment of normative ERP data in normally developing African children (Kihara et al. 2010b). This information would characterize the nature and pace of neurocognitive development in these children and would then allow the application of novelty processing in the assessment of cognitive outcomes of children exposed to brain insults such as severe malaria (Kihara et al. 2010a) or bacterial meningitis (Kihara et al. 2012).

14.3 Novelty "Oddball Paradigm"

An ERP response that has been well studied across a wide age range is the response to novelty, because the child's ability to detect and assimilate novel events is fundamental to cognitive development (Berg and Sternberg 1985). Young infants' ERP waveforms discriminate novel stimuli embedded in a train of frequent "familiar" stimuli (Courchesne et al. 1981), and their ability to do so may influence their level of general intellectual functioning later in childhood (Lewis and Brooks-Gunn 1981; Slater 1997). In the "novelty oddball" ERP task, three types of stimuli are presented (1) one that is repeated at high probability ("frequent"), (2) another that is repeated at low probability ("infrequent"), and (3) a set of trial-unique novel stimuli presented at low probability. An advantage of this task over the classic 2-stimulus oddball task, which includes only a frequent and an infrequent stimulus, is that it allows dissociation of response to low frequency versus novelty per se by comparing the two low-frequency categories. A distinct waveform for the novel events is observed in auditory and visual modalities and can be demonstrated even in passive tasks where the participant needs to look at or listen to the stimuli but does not need to actively respond (Squires et al. 1975; Courchesne 1978; Picton 1992; Polich and McIsaac 1994). This characteristic of the ERP response to novel stimuli makes it particularly useful for studying cognitive development in young children, especially in those for whom language makes use of more traditional neuropsychological assessments difficult.

14.3.1 Auditory ERP Components in Children

When using a passive ERP paradigm with an interstimulus interval of 700 ms, the P1 (a positive peak around 100 ms after stimulus onset), the N2 (negative peak around 200 ms), and the P3a (a positive peak around 250–350 ms for novel stimuli) are the typical components observed in children (Ceponiene et al. 1998, 2002b; Maatta et al. 2005). The P1 component is an obligatory cortical auditory evoked potential that reflects sensory encoding of auditory stimuli (Naatanen and Picton 1987; Sharma et al. 1997). The auditory P1 has also been interpreted as an indicator of preferential attention to sensory inputs and is thought to reflect level of arousal (Key et al. 2005). The N2 is influenced by deviation in form or context of a prevailing stimulus (Naatanen and Picton 1986) and is thought to be generated by diverse brain areas including the frontal and parietal cortical fields (Gomot et al. 2000), the superior temporal planes, and Heschl's gyrus (Takeshita et al. 2002). Studies using dipole source modeling suggest that the generators of the P1 mature slowly relative to the generators of the N2, possibly because of the slow development of superficial layers of the human auditory cortex (Ponton et al. 2000a). The P3a is interpreted as a neural correlate of the orienting response (Soltani and Knight 2000) and has been associated with involuntary orienting of attention (Knight and Scabini 1998). It may be elicited by behaviorally distracting/unexpected environmental sounds, e.g., telephone ring, dog bark, or car horn, occurring among frequently repeated tones. The P3a component is attenuated in patients with lesions of the dorsolateral prefrontal cortex (Knight 1984; Friedman and Simpson 1994; Baudena et al. 1995) and the temporal lobe (Alho et al. 1998; Kotz et al. 2007), suggesting that this component is likely to be generated by a neural network involving the temporal and frontal lobes.

14.3.2 Visual ERP Components in Children

Visual ERPs can also be useful in studying infants and children. The face-sensitive N170 ERP component is increasingly studied in children because of the important role of recognition and memory for faces in a child's cognitive and social development (Grossmann and Johnson 2007). This component is most prominent over the occipitotemporal region and in adults is maximal between 140 and 170 ms after stimuli onset (Bentin et al. 1996). It is thought to reflect the early perceptual encoding of the face, evidenced by its reduced amplitude when elicited by non-face compared with face stimuli (Bentin et al. 1996). The N170 is generated by regions including the fusiform gyrus (Shibata et al. 2002), the posterior inferior temporal gyrus (Bentin et al. 1996; Shibata et al. 2002), the lateral occipitotemporal cortex

(Bentin et al. 1996; Schweinberger et al. 2002), and the superior temporal sulcus (Henson et al. 2003; Itier and Taylor 2004). An N170-like component is detectable from infancy, though this component continues to develop well into adolescence (de Haan et al. 2007). Larger amplitudes for faces compared with non-faces are observable from a young age, but the adultlike hemispheric distribution (whereby the component is larger over the right hemisphere) is not consistently seen until 12–13 years (Taylor et al. 2004).

The visual P3a component can be obtained by presenting infrequent distracter pictures in a series of frequent and infrequent familiar stimuli (Thomas and Nelson 1996). This component, also called the novelty P3 by some authors, is maximal in the frontal/central scalp sites. It is also interpreted to reflect frontal lobe function (Knight 1984; Friedman et al. 1993; Friedman and Simpson 1994) resulting from an involuntary shift in attention (Courchesne 1978; Escera et al. 1998). However, in children, a larger P3a response to visual novelty is not reported consistently (Thomas and Nelson 1996; Van der Stelt et al. 1998). Instead, children's waveforms to novel visual stimuli typically display a frontally distributed negative component (Nc) (Courchesne et al. 1975; Thomas and Nelson 1996). The Nc component occurs between 400 and 800 ms and is the most recognizable and studied component in infant ERP research (Courchesne et al. 1981). The Nc is elicited not only by novel stimuli but also by other salient, attention-getting stimuli such as the mother's face (de Haan 2007). The Nc decreases with age over childhood and is not observed in adults (Courchesne et al. 1975). It has been suggested that the frontal P3a to visual novelty emerges as the Nc declines (Courchesne 1978). The Nc is believed to be generated in frontal brain regions, a hypothesis supported by source analyses carried out on infant ERPs (Reynolds and Richards 2005) and indirectly by parallels observed in the timing of developmental changes in Nc amplitude and the course of frontal cortical synaptogenesis (Courchesne 1990; Shibasaki and Miyazaki 1992).

Little or no information about development of commonly described ERP potentials in African children is available. Such information may be critical to the development of research into those social, environmental, and pathological influences on brain function to which children growing up in Africa are frequently exposed. Data presented in this chapter examines the development of two well-known ERP responses, those components elicited by stimulus novelty in the auditory and in the visual modality, among normally developing children in rural Kenya.

14.4 Obtaining Normative Data in an African Setting

The ERP data discussed in this chapter are recorded in both auditory and visual modalities in which children listen to sounds or look at pictures without responding overtly to them. Stimuli are presented using presentation software (Neurobehavioral Systems, http://www.neurobs.com). In the auditory experiment, 10 % of the stimuli are infrequent tones (2 kHz, 200 ms long, 5 ms rise and fall time, 70 dB sound pressure level, SPL); 10 % are composed of novel noises, e.g., dog bark, bell ring, etc.; and the remainder are frequent tones (1.5 kHz, 200 ms long, 5 ms rise and fall time, 70 dB SPL). The duration of the tones/noises is 200 ms with a stimulus onset asynchrony of 700 ms. Novel sounds are digitally adjusted in intensity so that they do not exceed 70 dB SPL as determined using a Bruel and Kjaer sound pressure meter. In the visual experiment, three types of stimuli were presented including an infrequently presented face, a frequently presented face (both were photographs of local women), and infrequently presented trial-unique, non-face paintings. The visuals were of equal size and presented at a visual angle of 16.8° × 14.3°. Two blocks of 100 trials were presented in a random order, with 60 % of the trials showing the frequent face, 20 % infrequent face, and 20 % non-face picture stimuli (trial unique). Participants were asked to look at a cross at the center of the screen. The duration of the image presentation was 500 ms with an interstimulus interval of 3 s.

The components elicited in these tasks are consistent with those described in previous studies of school-age children that used similar experimental conditions (Albrecht et al. 2000; Ceponiene et al. 1998, 2002c; Ponton et al. 2000a; Taylor et al. 1999) and are thought to represent perceptual-cognitive mechanisms. However, a comprehensive description of normal ERP development in children living in Africa has not been reported until now.

Normative data are obtained from a total of 178 children selected from a community database. These included 86 boys (mean = 6.7 years, SD = 1.8 years) and 92 girls (mean = 6.6 years, SD = 1.5 years). Sixty-eight percent of the children have attended at least nursery school. Hearing is assessed using a Kamplex screening audiometer (PC Werth, London) and vision assessed using a Sonksen-Silver chart (Salt et al. 1995). All children have normal vision and hearing.

14.4.1 Normative Results

Among Kenyan children, the latency of early components (auditory P1, N2, and visual P2) decreased with age, with the amplitudes also tending to decrease with age, while the changes occurring in longer-latency components were more modality specific (Figs. 14.1 and 14.2). In particular, the later-occurring auditory P3a showed the opposite pattern to that seen with early components: i.e., an increase in both latency and amplitude with increasing age. While Nc amplitude decreased with age, the amplitude of the visual P3 showed nonlinear changes with age, and the latency of the visual P3a did not change with age. This pattern of development change in amplitudes and latencies was common across all stimulus types within each modality, and thus likely represents changes in the general processing of auditory and visual information in the brain. A general decrease in component latency with increasing age is consistent with data obtained from non-African children of a similar age range (Ceponiene et al. 2002b; Ponton et al. 2002b). Amplitudes also had similar age effects as those reported in previous studies, with the auditory P1 decreasing with age (Ceponiene et al. 2002b; Ponton et al. 2002b; Sharma et al. 2002). These findings are likely to represent brain maturational processes (Hogan et al. 2005; Ponton et al.

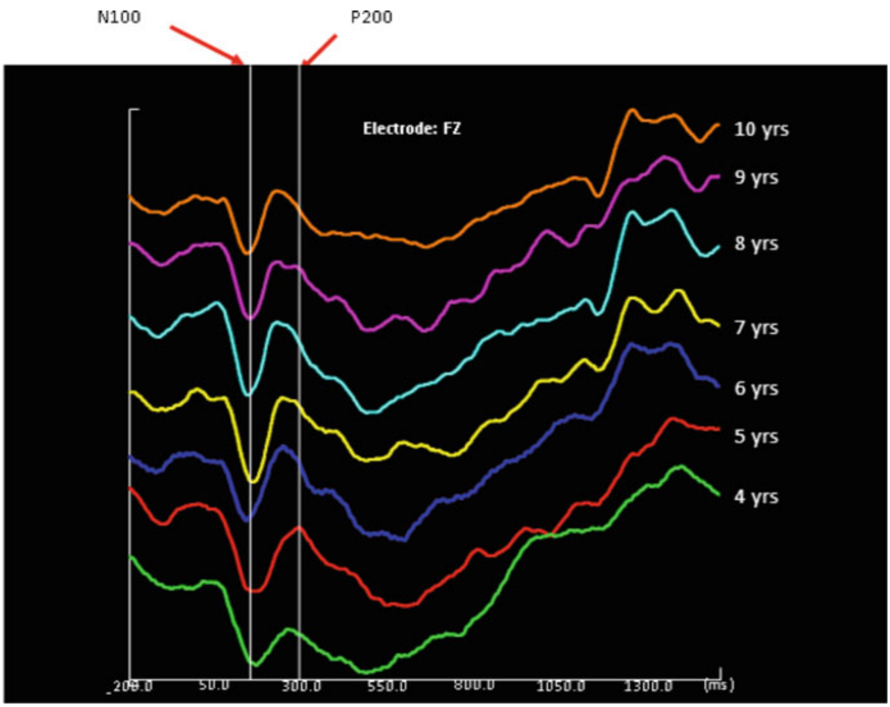

Fig. 14.1 Normal development of visual novelty processing in school-age children

2000a), particularly white matter development (Barnea-Goraly et al. 2005). Brain response was greater to novel unexpected sounds than to sounds that simply occur with less frequency (infrequent stimuli). Importantly, data from the Kenyan children also showed that the way particular stimuli were processed changed with age, as revealed by stimulus by age interactions.

14.5 Using ERPs to Study Children Exposed to Severe Malaria

Severe falciparum malaria is caused by *Plasmodium falciparum*, which is the most common parasitic infection of the central nervous system (Snow et al. 2005) and is known to cause cognitive impairment in children (Kihara et al. 2006). Seizures, prostration, and impaired consciousness are common symptoms of severe malaria and have been associated with poor cognitive outcome (Holding et al. 1999; Boivin 2002; Carter et al. 2005a). Cerebral malaria (CM) is the most severe neurological presentation of falciparum malaria and it is characterized by coma (Newton et al. 2000). Several retrospective studies in Africa have shown that between 5 % and 26 % of children with a history of severe falciparum malaria will have persistent cognitive deficits

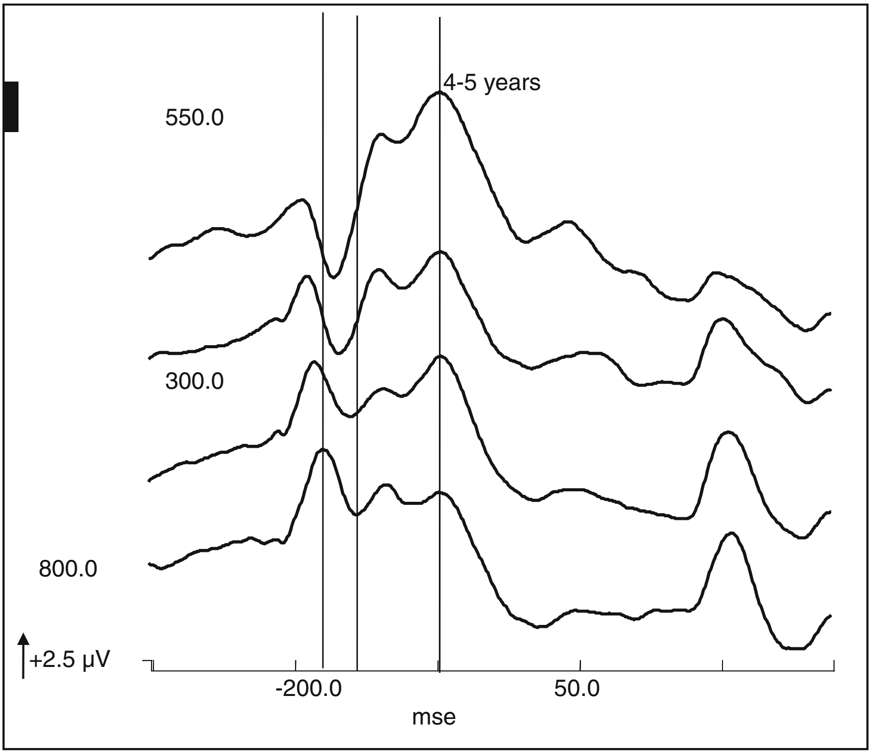

Fig. 14.2 Normal development of auditory novelty processing in school-age children

(Dugbartey and Spellacy 1997; Dugbartey et al. 1998; Holding et al. 1999, 2004; Boivin 2002; Carter et al. 2005a, b; Boivin et al. 2007; John et al. 2008). ERPs are a potentially useful approach to investigate neurocognitive outcome following pediatric severe malaria, because (a) they can provide measures of neurocognitive function that are less influenced by motor or language skills and (b) they are relatively easy-to-obtain and cost-effective measures of neural activity related to cognitive function compared with alternatives such as functional magnetic resonance imaging.

For the studies presented in this chapter, children with severe falciparum malaria were selected from the hospital database and included three diagnostic groups: those who were discharged after suffering from cerebral malaria (CM), those who had malaria with complicated seizures (MS), and those who had malaria with prostration (PM). CM was defined as Blantyre Coma Score (BCS) of ≤2 for 4 or more hours (Molyneux et al. 1989), a peripheral falciparum malaria parasitemia, and exclusion of other causes of encephalopathy (WHO 2000). MS was defined as a peripheral falciparum malaria parasitemia with >2 seizures within 24 h or focal or prolonged seizures >30 min, but without lapse into coma. PM was defined as peripheral parasitemia, a BCS of 3 or 4, and the child being unable to sit or walk without support.

Sixty-four children aged between 6 and 7 years who were admitted to Kilifi District Hospital between May 2002 and March 2004 with severe falciparum malaria were selected from the hospital database. Fourteen children were subsequently excluded due to either co-infections or misdiagnosis (six had acute bacterial meningitis, four had febrile seizures, and three had viral encephalitis excluded on the basis of a CSF cell count of more than 20 cells/mm^3) and one child was excluded due to excessive EEG artifact. The 50 children (mean = 6 years 7 months, SD = 6 months, males = 23) with severe falciparum malaria (CM = 27, MS = 14, and PM = 9) were compared with 77 community controls (males = 38) that did not have a history of being admitted with severe malaria and had no history of neurological impairment. These controls were part of a normative study on novelty detection of normally developing discussed in Sect. 14.3.

14.6 Results of Auditory and Visual "Novelty" Processing in Severe Malaria Children

Our group analysis of the visual response to novelty showed that children with MS and PM showed a reduced P3a to novelty compared to controls. The MS and PM groups also failed to show a differential P3a to novelty compared to familiar pictures displayed by the control and CM groups, suggesting difficulties in initial orienting of attention to salient events. However, later-latency processing of auditory novelty reflected in the P3a showed a different result. Children with CM and MS showed reduced amplitudes of the P3a to novelty. Children with MS and PM showed no differential P3a to novelty compared to familiar sound (Fig. 14.3).

We also examined how many children within each group showed atypical processing of visual novelty by defining atypical processing as a response greater than 2 standard deviations from the control group mean. Eleven percent of children with CM had increased P3a latencies and 7 % reduced P3a amplitudes compared to unexposed children, with none of the children in the PM or MS groups falling in this range and none of the groups doing so for Nc amplitude. A similar investigation of atypical novelty processing in the auditory experiment revealed that 14 % of children with a history of MS, 11 % of those exposed to PM, and 4 % of those exposed to CM had atypically small P3a components.

14.6.1 Discussion of Severe Malaria Results

The data in Kenyan children resulting from the studies described in Sect. 14.5 provides evidence of neurocognitive impairment in up to 14 % of children exposed to severe malaria, a figure within the range previously reported in neuropsychological studies in children of cognitive impairment following exposure to severe malaria (Holding et al. 1999; Carter et al. 2005a, b; Boivin et al. 2007; John et al. 2008). The results further suggest that children exposed to severe malaria show normal early

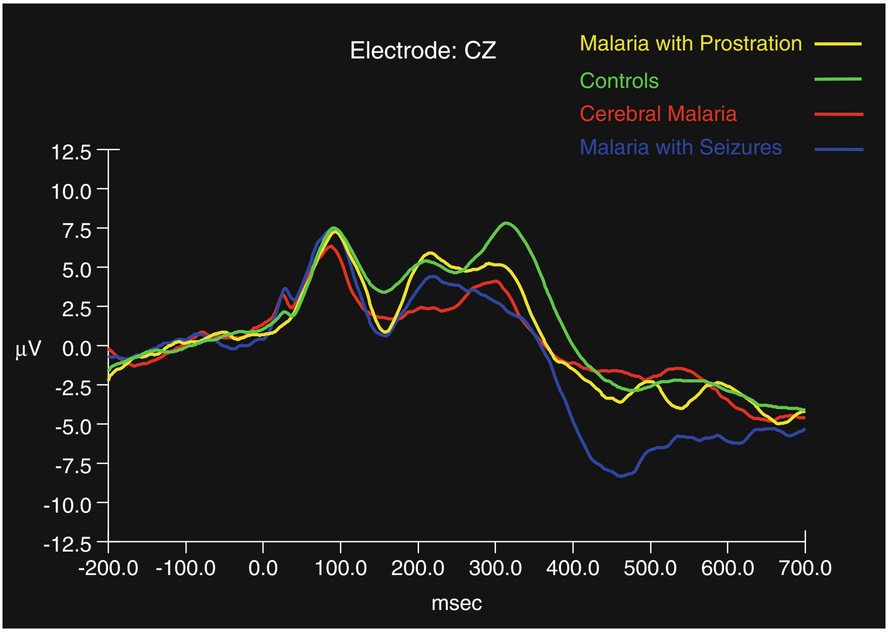

Fig. 14.3 Grand averaged waveforms for frequent, infrequent, and novel visual stimuli at Fz electrode for diagnostic groups

auditory processing and initial detection of novelty but atypical further processing of auditory novelty as reflected in the P3a (Fig. 14.3). These children also show atypical visual novelty processing, but these findings may be influenced to some extent by additional differences in early visual processing. Overall, the pattern of ERPs in Kenyan children having malaria is consistent with prior reports indicating that impairments in attention are common following exposure to severe malaria (Boivin et al. 2007; John et al. 2008) and are suggestive of atypical processing in frontotemporal brain networks involved in orienting attention to novelty.

14.6.1.1 Visual Novelty Processing

Kenyan children with MS and PM showed a reduced P3a to novelty compared with controls (Fig. 14.3). The MS and PM groups also failed to show the differential P3a to novelty compared with familiar pictures displayed by the control and CM groups, suggesting difficulties in initial orienting of attention to salient events. While children with CM did not, as a group, show impairments in P3a, 11 % of children with CM showed atypical latencies and 4 % of children with CM showed atypical amplitudes, indicating that a subgroup of children with CM also had difficulties in initial orienting of attention.

14.6.1.2 Auditory Novelty Processing

Analysis of the N2 and P3a components in Kenyan children showed both intact and atypical responses. The N2 to novelty showed no effects across the three diagnostic groups and its amplitude was smallest for novel stimuli in all groups. These results, together with the lack of effect of diagnosis on the earlier-latency P1, suggest that initial sensory processing of the sounds and detection of the novel stimulus was largely unaffected by malaria. However, later-latency processing of auditory novelty reflected in the P3a showed a different result. Children with CM and MS demonstrated reduced amplitudes of the P3a to novelty. Children with MS and PM showed no differential P3a to novelty compared with familiar sounds. The P3a component is thought to represent involuntary attention to salient or novel events (Escera et al. 1998; Friedman et al. 2001) and represents an orienting response (Courchesne et al. 1975; Knight 1996). The P3a component is attenuated in patients with lesions of the dorsolateral prefrontal cortex (Knight 1984; Friedman and Simpson 1994; Baudena et al. 1995) and the temporal lobe (Alho et al. 1998; Kotz et al. 2007), suggesting that this component is likely to be generated by a neural network involving the temporal and frontal lobes. These results suggested that children with CM and MS show a reduced activation of this network to novelty sounds while children with MS and PM fail to show differential activation of this network by novelty.

14.7 Conclusion

ERP paradigms as described in this chapter are tolerated well by Kenyan children and thus can be used to study the effects of cerebral insults and provide an alternative methodology of assessing perceptual-cognitive development in patient groups for whom more typical standardized neuropsychological assessments are not available. Also, the paradigms focus on components related to diverse brain areas, including prefrontal regions (P3a; Nc), ventral occipitotemporal pathways (N170), and superior temporal regions (N2), and thus may be useful in targeting which brain regions are most influenced by different disease processes. The feasibility of collecting ERP data from large numbers of African children and using these data to profile cognitive development was demonstrated. The usefulness of ERP procedures in characterizing neurodevelopment in children exposed to severe malaria is supported by the significant proportion of children exposed to severe malaria who had abnormal ERPs. The relationship between atypical ERPs and long-term educational and social outcomes remains to be determined. Further studies examining the relationships between neuropsychological measures, ERPs, and neuroimaging results in the African context would provide further insights into the brain damage caused by falciparum malaria and its link to atypical cognitive development.

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Chapter 15
The Neuropsychology of Sickle Cell Disease in Sub-Saharan Africa

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15.1 Introduction: Measuring Cognitive Functioning in Normal or Sickle Cell Disease Cameroonian Children

This chapter presents an evaluation of cognitive deficits in children with sickle cell disease (SCD) in Cameroon. With rates of trait carriers ranging from 8 to 34 % (Weatherall and Clegg 2001) and a homozygous prevalence of about 2 %, this genetic disease is a major public health problem in Cameroon. In Yaoundé, the capital, there are at least 40,000 people suffering from this disease, and the country has developed a national medical testing program for SCD (Cameroonian Ministry-of-Public-Health 2005).

Among other complications, SCD is the main etiological factor of stroke in children, accounting for nearly a third of stroke cases (Obama et al. 1994). Stroke prevalence was reported to be 6–7 % in a sample of Cameroonian patients with SCD, and a sickle cell stroke detection and prevention project using transcranial Doppler (TCD) has been initiated in the Yaoundé Central Hospital (Njamnshi et al. 2006).

Cerebrovascular complications constitute one of the main causes of mortality for patients with SCD. They also are responsible for persistent neurological and/or neuropsychological deficits in surviving patients. Even more frequent are the "silent" infarctions, which are difficult to detect with a standard neurological examination and are associated with neuropsychological deficits (Berkelhammer et al. 2007). The high-recurrence probability of cerebrovascular accidents calls for early detection and adapted medical intervention (e.g., blood transfusion, hydroxyurea). As CT scanner, MRI, or TCD is inaccessible to most patients in Sub-Saharan Africa, neuropsychological examination may represent a valuable means of detecting cognitive deficits indicating a possible brain effect. A quick and cost-effective cognitive

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screening could be indicative of need for urgent medical intervention and lead to specific and efficient cognitive rehabilitation (Yerys et al. 2003) or school-based interventions (King et al. 2008).

In Yaoundé, the program of neuropsychological evaluation we developed was first established in a perspective of prevention, with the aim to identify children with SCD who should benefit from cognitive remediation. At the same time, we also investigated the role of biological markers associated with this illness: anemia, fetal hemoglobin, history of cerebrovascular accidents, electroencephalography, and TCD (Ruffieux et al. 2013). The rationale for this approach was the assumption that even subtle cognitive impairments in children suffering from SCD constitute relevant clinical signs, when associated to biological ones, of actual or future cerebral sufferings. Using neuropsychological test results, personalized rehabilitation programs to improve cognitive functioning in children with SCD can be designed.

When tied to better understanding of medical, demographical, socio-educative, and psychological factors, the evaluation of cognitive functioning can play a major role in the health management of children with SCD in a developing country like Cameroon. Nonetheless, the classical issue remains in how to appropriately assess cognitive functioning in a cultural environment, such as Cameroon's, which has no tradition of testing, no established assessment tools, and no reliable means to carry out the evaluations. As a first step, for practical and economical reasons, the most effective approach was to adapt Western-based tools. A priori, none of these tools was however conceived for such a setting. As a consequence, the strategy we initially adopted consisted in selecting a set of tests targeting at cognitive domains known to be affected by SCD in Western populations, namely, executive, attentional, mnesic, and visuomotor functions (Berkelhammer et al. 2007). This selection obeyed to subjective concrete criteria such as minimizing the importance of language dimensions, which can be dramatically different even between France and French-speaking Cameroon, and minimizing the need for potentially unreliable technology in this setting, computers.

The second step to provide an effective neuropsychological assessment model for Cameroon was to establish performance norms for the chosen tests in a healthy Cameroonian population (Ruffieux et al. 2009). Because of concern over the use of Western-based tests in a resource-poor setting for which they were not designed, a decision was made that any difference between the results of the two reference populations (Western and Cameroonian norms), be it positive or negative, likely would indicate a cultural influence; reciprocally, an absence of difference would be considered as the expression of a similarity in cognitive functioning across the two cultures.

In the following section, these principles of test selection and evaluation are briefly discussed at a theoretical level. Following, data are presented on the utility and validity of these measures on the basis of a factorial approach and through comparison with the Western-based test results.

Li (2003), Park and Huang (2010), and Boivin and Giordani (2009) provided relevant and complementary theoretical frameworks in which our approach to test selection can be defended. "Plasticity" is a key concept in these considerations, in that brain-cognition relationships are considered as dependent, on the one hand, on a biological/genetic determinism and, on the other hand, on some functional and structural plasticity related to experiences. As stated by Li (2003, p. 187):

> (…) the brain offers the necessary biophysical reality for individual cognition and action; it alone, however, is not sufficient to engender the mind or behavior. On the mind-brain continuum, the individual mind is the expression emerging from the personalized brain (…). The very processes for personalizing the biological faculty of the mind take place throughout life span development in environmental and sociocultural contexts, which entail intimate dynamical exchanges between nature and nurture.

In other words, the plasticity related to various aspects of a given cultural environment allows the emergence of an original cognitive phenotype for this culture, and the plasticity related to individual experiences creates an original individual cognitive phenotype.

However, this cultural and individual plasticity is not absolute and has two sets of constraints: evident biological-genotypic constraints and physical constraints imposed by the external world. Obviously, a large percentage of the dimensions of the world children experiment in during their development are universal and permanent. This is the case for many dimensions of the physical environment (e.g., the effect of gravity on mass is permanent and invariant everywhere). It is possible to present the work that Piaget devoted to cognitive development in that light, as the chronicle of the child's progressive understanding of various physical invariants of the world (Piaget and Inhelder 1941). Several cross-cultural studies have provided empirical arguments in favor of the universality of the stages through which the child progressively masters these physical invariants (Dasen and Heron 1981). Yet, some dimensions of the physical environment, mainly the tools, and, of course, the majority of dimensions of the social environment are culturally specific. As a consequence, Li considers that cognitive development is "co-tuned" by biology and culturally situated experience. Further, she proposes that biology and culture influence each other through the behavior itself, in ontogeny as well as in phylogeny. This author refers here to a complex process she calls "*biocultural co-construction of brain, mind and behavior*" (p. 173):

> (…) culture (…) is not only the passive product of socially inherited resources of human civilizations such as tools, technology, language, knowledge, art, customs, values, and beliefs that are accumulated over the past. Rather, it is the "co-generator" of culture-gene co-evolution during human phylogeny in the long run and together with behavioral, cognitive, and neurobiological mechanisms, it is the active "coproducer" of behavioral, cognitive, and neurobiological development (…).

Park and Huang (2010) have provided substantial analyses of many works in neuroscience and in cultural psychology interested in the scenario of behavioral and/or neural plasticity related to experience (e.g., taxi drivers, postal workers, athletes, and musicians show brain structural modifications produced by their professional habits, when compared with nonspecialized people). As far as culture is concerned, these authors note that (p. 391)

> (…) sustained exposure to a set of cultural experiences and behavioral practices will affect neural structure and function. The burgeoning field of cultural psychology has provided innumerable demonstrations that there are subtle differences in the way individuals process information—differences that appear to be a product of cultural experiences. (…) According

> [for example] to Nisbett et al. (2001), Westerners, due to the individualistic, self-based focus of their culture, have a tendency to process central objects and organize information via rules and categories. In contrast, East Asians, based on their collectivist culture, tend to view themselves as part of a larger whole, resulting in a holistic information-processing bias in which object and contextual information are jointly encoded and in which relational information is priorityzed over categorical information.

This constitutes a point of high interest when assessing the cognitive functioning of people in a culture definitely different from a reference one. It means that it is extremely tricky from the outset to investigate a cognitive phenotype with evaluative tools conceived for a different cognitive phenotype. In such practices, the second key word should be "prudence."

Facing this problem, and in explicit reference to Li's biocultural co-constructivist conception, Boivin and Giordani (2009) propose the existence of an interface they call "*brain/behavior omnibus*," considered as universal across culture, ensuring the interplay between biological and cultural influences through which cognition emerges. To support the idea of a universal brain/behavior omnibus, these authors compare the patterns of results collected in the cognitive assessment of African and American children suffering from similar diseases. They consider that robust cross-cultural brain/behavior consistencies in these results are the manifestation of the omnibus. Interestingly, consistencies are found in attentional and executive functioning, as well as in working memory, possibly reflecting the existence of a universal foundation for fluid cognitive processes.

In conclusion, we believe that the neuropsychological evaluation of the African child is possible provided that the performance is assessed in reference to local norms. Secondly, since we possess African data for healthy and SCD children from Cameroon, we can compare them to data collected with the same tests in American or European comparable populations, in the perspective of Boivin and Giordani's omnibus model, as presented below.

15.2 Adaptation of Western Cognitive Tests to the African Sociocultural Context

As mentioned above, there is an evident lack of normative data for cognitive tests adapted to the African sociocultural context. African children are exposed to many diseases and acute environmental factors that can result in more or less serious cognitive sequelae. Yet, relatively few efforts have been made to create normative databases for psychological and neuropsychological tests in African countries (Boone et al. 2007; Uzzell et al. 2007).

Consequently, to complete our project we began by adapting 12 neuropsychological tests, primarily directed toward the evaluation of attentional and executive functions, to the Cameroonian sociocultural context (Ruffieux et al. 2009). These tests were already validated and of current practice in child neuropsychology in Western countries. Additionally, they were selected according to several criteria in order to improve their adaptability to Cameroonian children, emphasizing the simplicity of the material, the relative brevity (<1 h 30 min) of their administration, the limited need of language competences, and the possibility to use them across a large span of age. The selected tests cover the major executive domains according to Miyake et al. (2000), or Lehto et al. (2003), namely, selective attention (Bells Cancellation Task[1], Conners' Continuous Performance Test—CPT[2]), mental flexibility (Color Trails[3], Semantic and Phonemic Verbal Fluency), inhibition (CPT), working memory (Forward and Backward Digit Span from WISC-IV[4], Letter-Number Sequencing from WISC-IV[4], Hand Movements from K-ABC[5], Coding B from WISC-IV[4]) and planning (Hand Movements, Purdue Pegboard Dexterity Test[6]). We also considered a test of verbal learning (California Verbal Learning Test for Children—CVLT-C[7]) and the test of Block Design from WISC-IV[4] which have shown a sensibility to SCD and to silent brain infarction according to White et al. (2006). The Purdue Pegboard Dexterity Test and CPT tests have also demonstrated a sensibility to SCD (Schatz et al. 2002) and were also selected for this reason. The content of the CVLT-C, however, was modified, introducing words frequently used in Cameroon.

Test instructions were adapted to the Cameroonian children population through a pilot study and close collaboration with local psychologists. For some of the tests, the number of learning trials was increased in order to better adapt the tasks for use with native Cameroonian children and thereby reduce the possible effects of cultural bias.

The criteria used to select and adapt the tests in our battery raise some critical concerns. First, identifying tests that can be used across a wide age span, including children and adolescents, was a difficult task. It may be preferable in future to establish two different batteries, one for children from 6 to 10 years and another for the older subjects. Second, several dimensions of the cognition were not considered. The battery did not include a test assessing visuospatial working memory nor tests assessing general intelligence and basic instrumental functions, such as advocated by Schatz and Roberts (2005) or King et al. (2007). Third, we did determine that use of a computer to present a Continuous Performance Test (CPT) would be particularly appropriate for the age range and expected deficit areas in the children under study. Although the results confirmed that the test was sensitive to SCD, use of a computerized tool did lead to a number of technical problems (e.g., power failures, software problems, data loss, computer viruses). Finally, Ardila (2005) showed that a crucial factor in lowering potential cross-cultural bias is to reduce the distance

[1] Gauthier et al. (1989)

[2] Conners (1994)

[3] D'Elia et al. (1994)

[4] Wechsler (2003)

[5] Kaufman and Kaufman (1983)

[6] Tiffin and Asher (1948)

[7] Delis et al. (1994)

between the examiner and the participants, in other words by enlisting local examiners. In our original test development project, the fact that one among the five examiners who collected the data was Caucasian and of Western background was not optimal.

The battery developed by our team, as already discussed, assessed four domains of cognitive functioning (executive functions, attention, memory, and motor skills). Normative data were collected on 125 healthy Cameroonian children. Special attention was paid to the composition of this control group of healthy participants. All children were native speakers of French or secondary educated; they lived in an urban area and attended public schools in which children's families were in medium to low socioeconomic status. This was done in order to avoid a bias toward "too good" (i.e., ceiling effects) performance in this control group.

As noted earlier, to evaluate if our tests were cross-culturally adapted, our group maintained the general principle that any difference between the performances of the two reference normal populations indicated a cultural influence. This was the case for two tests that were originally included in the cognitive battery: the Block Design test and the Verbal Phonemic Fluency test. These two tests had to be excluded from the study, because of high interindividual variability of results and strong floor effects.

The Block Design test was particularly important for the general aim of the ongoing research project, as it had been shown previously to be very sensitive to cognitive deficits after silent infarcts among children with SCD (White et al. 2006). Attempts to culturally adapt this test in the past have led to difficulties (Skuy et al. 2000; Ardila and Moreno 2001; Rosselli and Ardila 2003; Holding et al. 2004), generally related to the unfamiliarity with the test stimuli and requirements in populations from the developing world. In response to these concerns, we had increased the time allowed for children to familiarize with themselves with the test stimuli and added several additional learning trials. Nevertheless, the cultural effect persisted and the test was not included in the final battery. As an alternative approach, Sternberg proposed a dynamic testing model (2004), which he held was more sensitive and consistent in characterizing cognitive ability across cultures. Dynamic testing consists of measuring active learning ability across teaching sessions on a particular cognitive test. In this approach, rather than a static assessment at a single time, the child receives feedback on his/her performances during the assessment and is taught how to improve his/her performance. The improvements of the child in the subsequent assessment sessions provide an indication of his/her capacity to adapt, learn, and progress from a feedback and learning environment (Sternberg and Grigorenko 2002). This testing approach is particularly interesting in cross-cultural settings, as it is less influenced by cultural biases.

Applying the dynamic testing approach with the Block Design test might have been a more sensitive technique in detecting cognitive deficits among Cameroonian children with SCD. Using this paradigm in Tanzania with a test presenting similar cultural potential bias (Raven's Progressive Matrices), Sternberg and Grigorenko (2002) showed that the dynamic testing was more sensitive than static assessment to the impact of brain/behavior risk factors related to poverty and health for Tanzanian children.

The performance of the Cameroonian children on the Block Design test indicated that younger children (6–9 years old) have particular difficulties with the test, with a strong floor effect and a sudden increase of performance after 9 years old. This could be explained by the fact that older children adapt more easily to the unusual material of the test than younger children who might be mentally "blocked" because of the unfamiliar material. This may be further facilitated by increased educational attainment.

Attempts to adapt the verbal phonemic fluency test also produced major difficulties, particularly for young Cameroonian children. These difficulties were not evident for the verbal semantic fluency test. The finding that phonemic fluency is more difficult than semantic is well documented in the literature (see, for example, Reis and Castro-Caldas 1997), but the mean performances for the phonemic condition were extremely low in our sample of Cameroonian children. Semantic fluency involves the activation of mental representations of concrete elements, while phonemic fluency involves the implementation of more abstract processes that are likely not trained nor favored in Cameroonian schools or culture. Interestingly, the performances of Cameroonian children in phonological fluency also are very low until the age of 12–13 years, when they enter high school. At the time of this school transition, children's performance rather abruptly increases. In American children, Gaddes and Crockett (1975) showed that such a sudden increase in phonemic fluency performance is also observed, but much earlier, between the ages of 6 and 8 years. It is thus highly probable that the teaching methods promote the development of these skills at different ages depending on the country considered.

15.3 Brain Omnibus Thesis Evidences from Factorial Analysis

Do the tests measure the same cognitive processes in different cultures? As emphasized in the introduction, this issue is fundamental. If true, separate factorial analyses on data collected in both cultures should lead to similar findings. An exploratory factor analysis conducted on all indices of the cognitive battery used in Cameroon showed a division of the tests in a four-factor model that is very consistent with the expected measures of the tests. The first factor of this analysis, labeled *executive functions*, had by far the highest Eigenvalue and regroups tests that all tap in different types of executive functioning (shifting, inhibition, updating-working memory). This factor is probably close to Spearman's general intelligence factor that underlies the performances to all cognitive tests.

The question of the structure (unity versus diversity) of executive functions remaining open in the literature, we performed an exploratory factorial analysis on the indices of the factors *executive functions* and *attention*. This analysis showed a model with three factors: *working memory-fluency*, *speed-vigilance*, and *inhibition* (Table 15.1). This structure corresponds to the "Western" dualist conception of executive functions in which inhibition and working memory constitute central components of executive functioning (Roberts and Pennington 1996). The factor *speed-vigilance* is a more basic component of cognition and is not generally included in the executive functions domain (Brocki and Bohlin 2004).

Table 15.1 Factor loadings from factor analysis on cognitive indices of attention and executive domains (only factor loadings above 0.35 are reported)

	Factors		
	Working memory-fluency	Speed-vigilance	Inhibition
BlockDesign	0.917		
Phonemic verbal fluency	0.807		
Letter-Number Sequencing	0.804		
Digit span backward	0.786		
CT2 time	–0.776		
Semantic verbal fluency	0.713		
Hand Movements	0.712		
Coding	0.707		
CT1 time	–0.657		
Digit span forward	0.544		
Bells omissions	–0.397		
CPT standard deviation		0.951	
CPT reaction time		0.905	
CPT omissions		0.706	
CPT commissions			0.783
CPT perseverations			0.580

Note: The three-factor solution accounted for 54 % of total variance: extraction method, maximum likelihood, and rotation method promax
CT color trails, *CPT* continuous performance task

Table 15.2 Factorial analysis performed on cognitive tests among 92 Swedish children

	Factors		
	Disinhibition	Speed/arousal	WM/fluency
CPT disinhibition	0.87		
CPT impulsivity	0.80		
CPT inattentive impulsivity	0.63		
Go/no-go commission	0.38		
Go/no-go RT		0.80	
CPT RT		0.73	
CPT omissions		0.39	
Go/no-go omissions		0.38	
Digit span forward			0.49
Verbal fluency (COWAT)			0.48
Digit span backward			0.40
Hand Movements			0.40
Stroop			–0.41
Time reproduction			–0.43

CPT Continuous Performance Test, *RT* reaction time, *COWAT* controlled oral word association test; Stroop = color/word version. From Brocki and Bohlin (2004)

The test measures included in this supplementary factorial analysis are similar to those used by Brocki and Bohling (2004) among Swedish children aged 6–13 years old. Interestingly, those authors found a very similar factorial structure (Table 15.2), with three factors representing the same tests as in our model. This comparison suggests that cognitive assessments used in different cultural contexts maintain the same factorial structure, indicating that these tests are assessing similar domains for children in Cameroon and in Sweden.

The results of these factorial analyses represent interesting support for the construct validity of the battery in the Cameroonian cultural context, as they suggest that the tests measure the same concepts as in Western culture. Furthermore, these analyses provide strong arguments for the brain omnibus theory.

15.4 Brain/Behavior Omnibus Evidences from Cognitive Deficits Among Children Suffering from SCD in Cameroon

Boivin and Giordani (2009) suggested that American patients with SCD and African cerebral malaria (CM) patients had similar cognitive deficits because these two diseases have similar underlying neurophysiological effects. This resulted in similar brain/behavior relationships found for two diseases in entirely different cultural contexts, even when the effect of cultural differences was controlled. The cross-cultural consistency of deficit profiles for SCD and cerebral malaria provides further evidence for a brain/behavior omnibus subtending universal cognition.

Supplementary data from our analyses offer the opportunity to compare the cognitive effects of a single disease (i.e., SCD) in two entirely different cultures. Ninety-six Cameroonian patients with SCD aged 6–24 years were assessed using the cognitive battery described previously. Results showed that Cameroonian patients with SCD presented a high frequency of cognitive deficits, with 37.5 % of the sample presenting marked cognitive impairment, a much higher prevalence than what is usually reported in resource-rich countries (Berkelhammer et al. 2007; Schatz et al. 2001). We investigated the effects of the disease on executive functions, attention, memory, and motor skills by means of a structural equation model, after controlling for age evolution (Fig. 15.1). Results showed a significant negative effect of the disease on executive functions and attention, but not on memory and motor skills. Patients with SCD had worse performances than controls on attention and executive functions, but performed as well as controls on memory and motor skills tests (after controlling for the effects of age).

These findings are very consistent with what has been reported for American patients with SCD. In their review of literature, Berkelhammer and colleagues (2007) found executive and attention deficits in 11 of the 13 studies reviewed, suggesting that attention and executive functions are particularly vulnerable in sickle cell patients. In our study, patients who did not present with cerebral vascular accident also showed specific deficits in attention and executive functions.

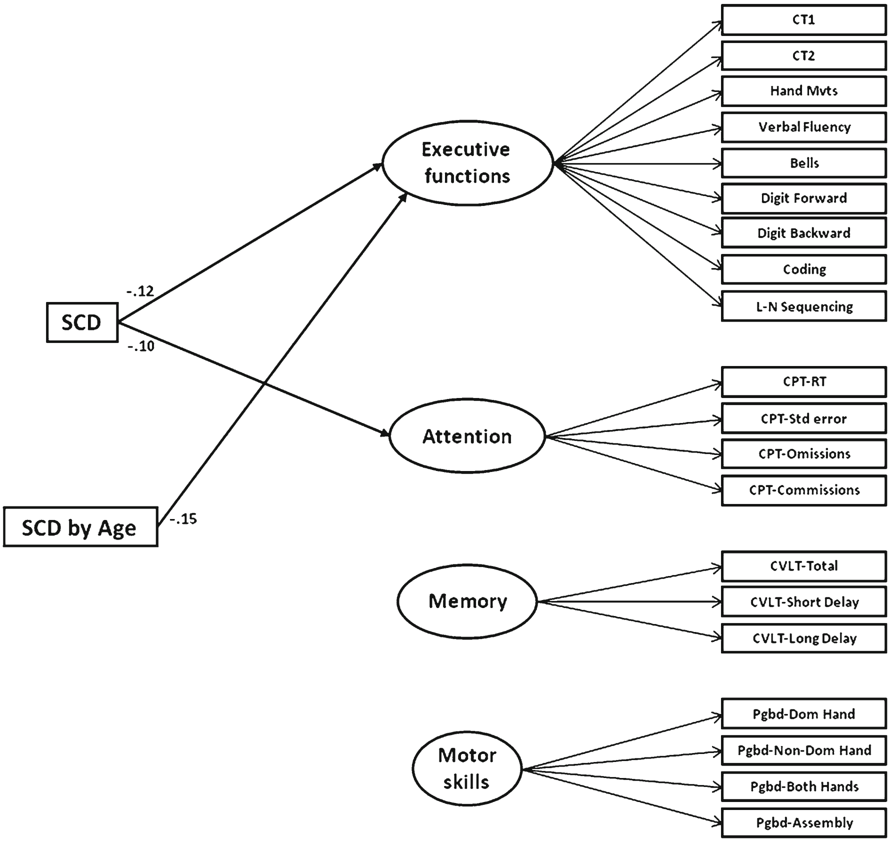

Fig. 15.1 Structural equation model testing the effects of the disease, age, age square, and the interaction between disease and age on four latent constructs. Only significant path coefficients are presented. Direct effects of age are not considered; they are all significant and positively associated with cognitive performances. Numbers represent β-scores. *CT* color trail, *CPT* Continuous Performance Test, *CVLT* California Verbal Learning test, *Pgbd* purdue pegboard, *Dom hand* dominant hand [figure extracted from Ruffieux et al. (2013)]

These findings corroborate the assumption that attention processes are very sensitive to even milder forms of brain injury (Boivin and Giordani 2009), but we propose to extend this assumption to the executive function domain.

In addition, our results indicate that cognitive deficits tend to increase with age among patients with SCD. An increase of the prevalence of cognitive deficits was observed among older Cameroonian patients, with almost half of the 17–20 years old patients presenting cognitive deficits, while the prevalence of such cognitive deficits among children aged 6–16 years old was below 20 %. The increase of cognitive deficits with age has also been reported among American children with SCD (Kral et al. 2006). We specifically observed a decline in the evolution of the executive functions, while the other functions remain relatively stable throughout the years.

The specific decline of executive functions is likely to be associated with chronic brain hypoperfusion (the hematological level significantly predicted executive functioning, but not the other cognitive domains) and the accumulation of silent/overt infarcts.

These results demonstrate that patients with SCD in Cameroon have very similar cognitive deficits profiles and developmental trends as patients with SCD in the USA. Using a more direct comparison, these findings strengthen the hypothesis of Boivin and Giordani (2009) for a common cognitive foundational platform across cultures and a universal brain/behavior relationship in developing children.

15.5 Unified Model of the Principle Mechanisms Leading to Cognitive Deficits in SCD

In light of these results, we propose a unified model describing the principal mechanisms leading to cognitive deficits in SCD (Fig. 15.2).

In this model, two major mechanisms explain the cognitive deficits in SCD: anemia and vaso-occlusive crises. Chronic anemia results in lower brain oxygenation, leading to possible chronic brain hypoxia. Chronic anemia may have two types of consequences on cognitive performances: an indirect effect related to fatigue and a direct effect related to chronic cerebral hypoxia. These two effects may cause cognitive deficits in the domains that are most vulnerable to slight lowering of cognitive resources: executive functions and attention.[8] Secondly, brain vaso-occlusion can

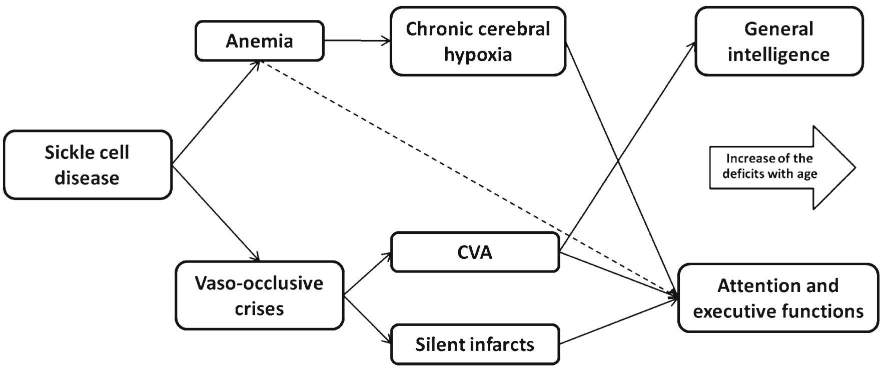

Fig. 15.2 Principal mechanisms related to cognitive deficits in SCD. *Dotted arrow* shows the indirect effect of fatigue on cognitive function; the increase of cognitive deficits with age is represented by the *full arrow*

[8]Anemia has also been associated with lower general IQ in SCD (Bernaudin et al. 2000; Steen et al. 2003), but this bowing is slight and we hypothesize that it results from the lowering of executive functions and attention.

engender CVA and/or silent infarcts. CVA generally compromises cerebral cortex and/or white matter, whereas silent infarcts are usually confined to the deep white matter of the frontal, parietal, and temporal lobes (Moser et al. 1996). Consequently, silent infarcts mostly cause subtle cognitive deficits in the areas of attention and executive functions, while CVA may alter more significantly general intelligence. Anemia and CVA/silent infarcts are likely to sum up throughout the child's development, causing an increase of cognitive deficits with age (represented by the full arrow on Fig. 15.2).

15.6 Unified Model to Deal with Cerebrovascular and Cognitive Risks Among Patients with SCD

Finally, the potential role for neuropsychological evaluation of patients with SCD needs further clarification. We propose a unified model to deal with the risk of cognitive deficits among patients with SCD (Fig. 15.3). The objective of this model is to provide guidelines to the clinician neuropsychologist regarding the content of the cognitive examination. The model is designed to be applicable to resource-rich countries, where recent brain imaging technology is available and to resource-poor countries where the access to these technologies is limited.

The patient's clinical history will first orient the neuropsychological examination. If a patient presents with a history of CVA (A), a full neuropsychological examination should be performed. A detailed investigation of the cognitive profile of the

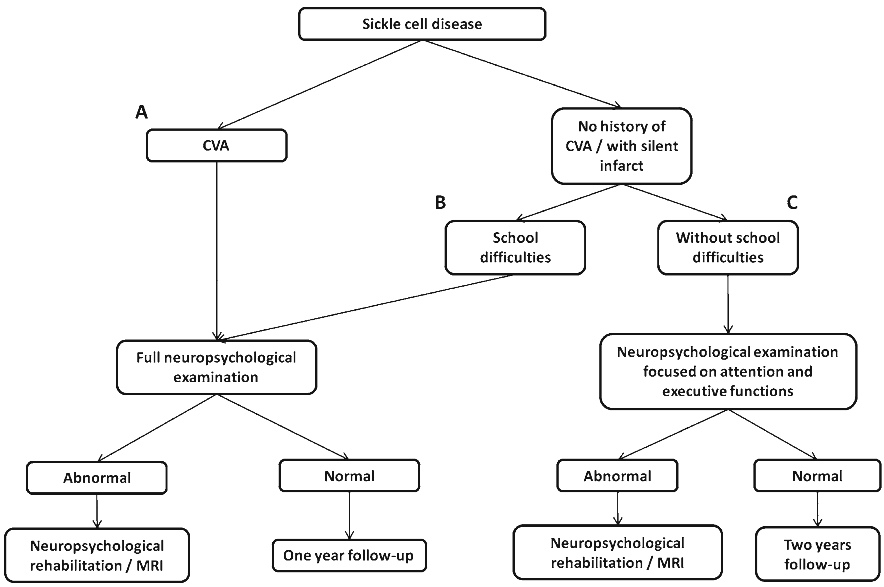

Fig. 15.3 Unified model for the neuropsychological evaluation of children with SCD

patient will then allow a determination of whether a specific neuropsychological rehabilitation (Yerys et al. 2003) and/or a school-based intervention (King et al. 2008) would be indicated. If the neuropsychological examination is normal, a 1-year follow-up exam would be recommended, as the recurrence risk of CVA is particularly high among patients with SCD.

If the patient does not present with a history of CVA/or if brain imaging shows a silent infarct, the presence of school difficulties (or specific work difficulties for adults) would indicate the need for a full cognitive examination (B). School difficulties may result from cognitive dysfunction. Indeed, MRI should be performed, as poor school performance in SCD is a potential indicator of silent infarcts (Schatz et al. 2001).

If the patient has no history of CVA and presents no school difficulties (C), the neuropsychological examination should be focused on the evaluation of attention and executive functions and looking for potential deficits that have not (yet) had school repercussions. If the patient presents attention and/or executive deficits, MRI should be performed to ensure the absence of silent lesions. If the examination is normal, a 2-year follow-up should be considered.

The importance of the neuropsychological follow-up of patients with SCD should be highlighted. Follow-up of patients with SCD over a long period of time allows monitoring of any eventual drops in cognitive performance which may result from undetected silent infarcts. In this context, repeated neuropsychological assessment should be considered at a minimum of every 2 years for patients with SCD. This is particularly true in resource-poor countries, where brain MRI and transcranial Doppler are not easily accessible. Neuropsychological evaluation is an effective tool for the identification of children with silent cerebral infarct. The study of DeBaun et al. (1998) has shown that measures from the attention and executive domains were the most useful for identifying children with silent cerebral infarct. In their study, using a battery containing measures of attention/executive, spatial, language, memory, and motor functioning, the test of variables of attention was the most robust measure and yielded a sensitivity rate of 86 % and a specificity rate of 81 % in identifying silent infarcts, and a sensitivity rate of 95 % in identifying overt stroke. Unfortunately, very few studies have addressed this question since then, and these results have not been reproduced on a large cohort of SCD patients. There is an essential need to prove the sensitivity/specificity of cognitive examination for the detection of silent infarcts, as it would be a cost-effective tool to implement in resource-poor countries.

15.7 Conclusions

SCD is a major public health issue in Africa. Patients suffering from this genetic disease are at risks of presenting cognitive deficits related to cerebrovascular complications. Surprisingly, the studies presented in this chapter are the first exploring the cognitive evaluation of patients with SCD in Sub-Saharan Africa.

Using cognitive tests adapted to the sociocultural context and local normative data, our work in Cameroon showed that patients with SCD present a high frequency of cognitive deficits, with executive functions and attention being particularly vulnerable.

Our experience with the adaptation of Western cognitive tests to a different sociocultural context calls for great prudence: the performances on each test should be carefully analyzed, and the use of different testing techniques, such as Sternberg's dynamic testing, should be considered for tests where strong cross-cultural bias can be anticipated.

Furthermore, our results provide support for the brain/behavior omnibus concept developed by Boivin and Giordani (2009). First, factorial analyses suggest that the cognitive tests measure the same concepts as in Western culture. Secondly, patients with SCD in Cameroon show very similar cognitive deficits profiles and developmental trends as patients with SCD in Western countries. Consequently, we propose in this chapter a unified model explaining the principal mechanisms to cognitive deficits in SCD and a unified model to deal with cerebrovascular and cognitive risks among patients with SCD.

These results are also important for the follow-up of these patients. If the same diseases produce similar cognitive deficits in different cultures, it suggests that cognitive rehabilitation tools developed in resource-rich countries, if properly adapted, can be used in developing countries.

In conclusion, we believe that the evaluation of cognitive functioning could play a major role in the health management of SCD in a developing country like Cameroon. Moreover, the development of neuropsychology in Sub-Saharan Africa is crucial, as African children are exposed to many diseases and environmental factors that can result in cognitive deficits.

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Chapter 16
Postscript: Towards a Universal Brain/Behavior Omnibus in the Neuropsychology of African Children

Michael J. Boivin, Karen Dobias, and Bruno Giordani

16.1 Concluding Thesis

Our principal thesis is as follows: *cross-cultural neuropsychology, brain imaging, and genomic technologies together can elucidate a brain/behavior omnibus foundational to human neuroplasticity across the life span*. The integration of these approaches can provide a powerful new paradigm in understanding the relationship between the developing brain, culture, and cognitive ability. Such a paradigm can help us better understand how, across the life span, ecological necessity sculpts culturally specific cognitive ability profiles, doing so upon a universal brain/behavior omnibus (Boivin and Giordani 2009). The neuropsychological study of risk and resilience in African children provides a rich and powerful vantage point for exploring this process.

With the sequencing of the human genome and the accessibility of brain imaging technologies through MRI and functional MRI, the paradigmatic pendulum has now swung again towards genetic and brain determinism (Moore 2002). Li (2003) has proposed a more holistic and inclusive paradigm to move child developmental

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science beyond the traditional nature/nurture debate. This approach emphasizes bidirectional reciprocal biocultural plasticity across the life span as the basis for cognitive tendencies and abilities. It has provided a useful framework for organizing our review of the neuropsychology of African children in this volume.

Co-constructivism also emphasizes the reciprocal interaction of culture and the genome in shaping brain/mind at multiple levels: neurobiological, cognitive, behavioral, and sociocultural (Li 2003). Again, we believe that the chapters in this volume provide abundant illustrations of how the neuropsychological evaluation of African children within the public health context provides a powerful and strategic vantage point from which to explore the interactions among these levels.

16.2 Co-constructivism and a Universal Brain/Behavior Omnibus

The concept of a brain/behavior omnibus is proposed as a way to conceptually interface foundational neuropsychological functions. It proposes that such functions are consistent across cultures. At the same time these neuropsychological tests must be sensitive to how brain/behavior functions are shaped by ecological necessity and cultural experience. The methodological, scientific, and theoretical work represented in the successive chapters of this book supports the power of this approach. We believe that cross-cultural neuropsychological research in the African context will continue to describe and substantiate the explanatory power of the construct of a universal brain/behavior omnibus.

Such measures can be used to evaluate the extent to which the integrity of the foundational brain/behavior domains is consistently compromised in a given manner for a given disease. These measures can also be used to see whether a favorable developmental milieu buffers brain/behavior functions from these disease processes (resilience) in a consistent manner.

The African context is fertile ground for a cross-cultural neuropsychology to reveal a universal brain/behavior omnibus. In terms of evolutionary development of such processes in a top/down manner, the brain/behavior development of African children has up to now evolved in the face of infectious diseases commonplace in the tropics (e.g., malaria, meningitis, severe intestinal parasite infections and anemia, schistosomiasis, trypanosomiasis, neurocysticercosis, dengue fever). Brain/behavior development in African children continues to take place amidst a broad array of risk and resilience factors. These can be well characterized in terms of how they modify brain/behavior development across the life span, within the evolutionary phylogeny dimension of Li's co-constructivist paradigm.

The chapters in this volume offer numerous illustrations of how cross-cultural neuropsychology can provide the methodological, conceptual, and theoretical basis for advancing brain/behavior science with a dynamic biocultural co-constructivist paradigm. What is needed is the continued development of more sensitive and innovative technologies within the cross-cultural neuropsychology of African children.

As these technologies are refined and become increasingly more powerful, the co-constructivist paradigm can better guide an understanding of how ecological necessity in differing environments can then shape the emergence of adaptive and maladaptive neurocognitive processes. Taken together, the chapters throughout this book present a wealth of information that lends interpretive power for a dynamic biocultural co-constructivist paradigm as applied to the neuropsychology of African children.

16.2.1 Cross-Cultural Neuropsychology and Evidence for a Brain–Behavior Omnibus

In several chapters, locally developed and Western-based tests together have been adapted for use in a culturally sensitive and appropriate manner, yielding valuable results. We conclude that both kinds of tests can provide a valid evaluation of neurodevelopment or neuropsychological function in the context of risk and resilience factors affecting African children.

The ability to use these tests to provide evidence in support of a consistent and sensible understanding of factors affecting brain/behavior development implies that at the foundation of these neuropsychological processes is a universal brain/behavior omnibus. With good methodology and assessment tools, this omnibus can be measured in a consistent manner across very diverse cultural contexts globally. We can also begin to better understand the processes by which risk and resilience factors shape and modify how neurocognitive function emerges out of this omnibus, ultimately being expressed within a given ecological and cultural context.

To illustrate, the valid assessment of the foundational domains of brain/behavior function with a universal brain/behavior would differentiate between a given brain disease (proximal) and environmental influences (distal) on cognitive performance in a consistent manner across cultures. Nutritional deficiencies, environmental deprivation, poor sanitation and hygiene, iron-deficiency and anemia, malaria, schistosomiasis, intestinal parasite infections, and diarrheal disease are just some of the more proximal factors afflicting brain development and function of sub-Saharan African children (see Grantham-McGregor et al. 2007 for a review).

The fact that neurodevelopmental assessments can profile the brain/behavior dysfunction from such risk factors in a consistent manner across diverse cultural contexts suggests that such risk factors undermine neuropsychological function at a foundational (omnibus) level of brain development. At the same time, the chapters in this book point to the developmental importance of factors that foster resilience in brain/behavior development. These include such interventions as good antenatal care, environmental enrichment in early childhood, positive caregiving, good nutrition, intermittent prophylactic treatment for chronic infections (e.g., malaria, schistosomiasis, intestinal parasites) (Clarke et al. 2008), and even emerging mobile-network technologies for Internet-based access to cognitive rehabilitation and training. All of these can complement traditional approaches to provide for a good education and significantly enhance cognitive performance in African school children. Together, this kind of comprehensive intervention package can foster potent modifying factors of resilience in African childhood brain/behavior development.

16.2.2 Concluding Comments on Evidence for a Universal Brain/Behavior Omnibus

Through the successive chapters of this volume on the neuropsychology of African children, we have amassed evidence for robust deficit profiles in such omnibus domains as attention, working memory, and executive reasoning. We have done so for brain injury from risk factors associated with diseases of the brain (e.g., CM, SCD, HIV), nutritional risk factors (malnutrition and anemia), across widely differing cultural contexts in Africa, representing divergent quality of developmental milieus, and in response to rehabilitative interventions (e.g., CCRT).

Li (2003) has proposed a unified and integrated cross-level dynamic, biocultural co-constructive framework. Across the successive chapters of this book, we have systematically and comprehensively reviewed research evidence from cross-cultural neuropsychology in African children. It has all been readily and sensibly interpreted within this paradigm. We have also put forth the construct of a foundational and universal brain/behavior omnibus in this conclusion and summary chapter, in order to convey how Li's co-constructive framework might be better applied *specifically* to the neuropsychology of African children.

The cross-cultural application of neuropsychology assessments has provided a means of methodologically triangulating the omnibus. It does so by using more dynamic assessments across cultural contexts, combined with neuroimaging and genomic technologies that can be applied across both African and Western contexts. The methodological triangulation of a universal brain/behavior omnibus in African children is also enhanced as it takes place embedded within the public health backdrop of risk and resilience which sculpts brain development out of ecological necessity. *Cross-cultural neuropsychology, brain imaging, and genomic technologies together can elucidate a brain/behavior omnibus foundational to human plasticity across the life span*.

The integration of these approaches and methodological tools in a co-constructivist framework are critical for understanding how, across the life span, ecological necessity sculpts culturally specific cognitive ability profiles. Furthermore, such tools and methodologies are vitally important for understanding how biocultural processes undermine (risk) and enhance (resilience) a universal brain/behavior omnibus in the face of ecological necessity. Because of this scientific power and potential, we propose that the cross-cultural neuropsychology of African children in the public health context is the basis for a major paradigmatic move forward. This will lead to evermore powerful evidence-based interventions derived from our understanding of human development across the life span. Such a paradigmatic move forward will also lead to an evermore powerful phylogenetic understanding of human adaptation across the ages.

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