Chapter 13
Metabolic, Biogenetic, Seizure, and Neuromotor Disorders of Childhood

Various metabolic, biogenetic/chromosomal, seizure and neuromotor disorders (e.g., cerebral palsy) are the focus of this chapter. These neurological disorders frequently result in accompanying neuropsychological, social/emotional, and behavioral difficulties that place stress on the child, family, and school. As with other neurological and neurodevelopmental disorders, the pediatric neuropsychologist needs to be particularly sensitive to these stressors when assessing and planning intervention programs. Study of these variables is just beginning, but clinical practice indicates that children with these various disorders require support in all environments: home, school, and social. A transactional approach to the deficits experienced by children with these disorders would be most ecologically valid while also providing information for the most appropriate interventions. A number of select metabolic, biogenetic, seizure, and neuromotor disorders will be discussed in this chapter, with attention not only to the neuropsychological assessment of deficits, but also to the contributions of the family and school for remediating these difficulties. Research on intervention outcome is sparse and is sorely needed. For each of these disorders, a review of the literature indicates that more knowledge is needed, not only concerning the neuropsychology of the disorder, but also in planning for these children throughout the life span. The demarcation of biogenetic, neurocutaneous, and metabolic disorders is one of convenience and does not imply that a biogenetic basis underlies all of these conditions. The demarcations are used only for ease of discussion.

Metabolic Disorders

Metabolic disorders have been linked to various neurological disorders including cognitive retardation; over 200 genes have been identified that produce hereditary diseases (Phelps, 1998a). Phenylketonuria (PKU) and Lesch-Nyhan syndrome (LNS) are only two metabolic disorders that will be discussed here. These disorders could easily be listed under chromosomal abnormalities, as each has a genetic basis (Cook & Leventhal, 1992). See Hynd and Willis (1988), Goldstein and Reynolds (1999), and Phelps (1998a) for an in-depth treatment of other disorders affecting metabolic processes that ultimately result in neuropsychiatric disorders in children and adolescents.

PKU

Phenylketonuria (PKU) is a rare (affecting 1:15,000 to 1:18,000) autosomal recessive disorder that affects males and females equally (Carey & Lesen, 1998; Cook & Leventhal, 1992; Hynd & Willis, 1988). PKU is a chronic disorder that affects the metabolism of phenylalanine to tyrosine (Fehrenbach & Peterson, 1989). Tyrosine is a precursor to dopamine (DA), and when phenylalanine is too low, the production of DA may be altered and may result in changes in bones, anemia, antibodies, and cognitive development. Phenylalanine is a protein and, when it is not metabolized, it begins to be stored in the body. Characteristics of the disorder, and assessment and intervention practices are briefly discussed.

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Characteristics and Associated Features of PKU

When phenylalanine levels are too high they can produce serious negative consequences, including cognitive retardation (Carey & Lesen, 1998; Hynd & Willis, 1988; Michaels, Lopus, & Matalon, 1988; Waisbren, 1999). PKU can produce neuropsychiatric disorders in children, including behavioral disruption and antisocial problems (Fehrenbach & Peterson, 1989). Cognitive retardation is usually avoided when PKU is appropriately treated (Waisbren, 1999). Lifetime ADHD was also associated with PKU even after successful dietary control (Realmuto et al., 1986). In rare instances, PKU can result in death (Hanley, Linsoa, Davidson, & Moes, 1970) or in seizure activity, abnormal EEGs, spasticity, and reflex and tremor disorders (Hynd & Willis, 1988). The development of neural tissues appears to be affected, with cellular abnormalities and incomplete myelination resulting.

Waisbren (1999) suggests that executive control functions are affected by PKU, including planning skills, integrative processing, and sustained attention. These deficits are particularly acute when information is presented rapidly or when the cognitive load is high—as tasks become more complex and processing time is fast. Deficits of this nature may also be present in early-treated children.

Implications for Assessment

Early medical screening for PKU is widespread and can be extremely effective in reducing the progressive, deleterious developmental and medical difficulties associated with the disorder (Hynd & Willis, 1988). Since universal screening in newborns was implemented in the 1960 s, the severe symptoms of PKU are rarely seen (NIH, 2008).

Neuropsychological assessment may also be important to identify cognitive, reasoning, and visuospatial deficits that have been reported in some children with PKU. Psychoeducational evaluation is effective to determine academic (e.g., learning disabilities, deficits in mathematics), and behavioral adjustment difficulties (e.g., disruptiveness, antisocial behavior, low self-esteem). Waisbren (1999) also suggests that ADHD may result in elevated blood levels of phenylalanine.

Effective interventions focus on dietary control and compliance with these restrictions. Family issues appear to affect dietary compliance, so strategies that address these related factors are discussed.

Implications for Interventions

The negative effects of PKU can be controlled through dietary changes whereby foods containing high levels of phenylalanine (e.g., meats, milk, and milk products) are reduced or eliminated (Carey & Lesen, 1998; Fehrenbach & Peterson, 1989). Thus, PKU is clearly a genetic disorder that is influenced by environmental factors (intake of foods), which directly affect the manifestation and control of the disorder. It is important to initiate dietary treatment early in life (within the first three months) to reduce the possibility of cognitive retardation (Waisbren, 1999). Although early treatment appears to reduce significant cognitive impairment, children with PKU may still have minor cognitive deficits, and the long-term consequences of early treatment are still relatively unknown. Some evidence suggests that the child's cognitive outcome is dependent on a number of factors, including maternal IQ level, the age at which treatment is initiated, and dietary compliance (Waisbren, 1999; Williamson, Koch, Azen, & Chang, 1981).

Waisbren (1999) suggests that compliance to food regimens may become problematic as children struggle with the development of their own identity. Waisbren provides an outline for developing treatment plans for PKU from infancy to adolescence. Many of the strategies shown help the children become more knowledgeable and involved with their own treatment. With age, children become more self-sufficient when taught self-management strategies for monitoring blood levels, selecting appropriate foods, and coping with peer pressure.

Family Factors Related to Dietary Compliance

Fehrenbach and Peterson (1989) investigated the affects of other family factors, including organization, cohesion, stress, and conflict, on the child's compliance with dietary restrictions. The families

of 30 children were followed, and the level of parental problem solving was related to disease control. Specifically, Fehrenbach and Peterson (1989) found that verbal problem solving abilities were related to children's compliance. Further, parents with highly compliant children were able to provide a number of solutions and parenting options available in problem situations. Family cohesion, level of conflict, and support were not related to compliance. Although family SES, age, and education of parents were unrelated to problem solving measures, these variables were related to stress levels and family functioning (Fehrenbach & Peterson, 1989). Induced stress conditions affected both groups of families (high- and low-compliant groups), and were not considered predictive of compliance. While stress did reduce the number of alternative strategies that were generated by both groups, the high-compliant parent group demonstrated higher quality solutions and reported stressful situations as less stressful. These findings are important because they point out the need to consider family members in the treatment plans for children with PKU.

Preventive Measures

Recent research suggests that maternal hyperphenylalanemia should be monitored during pregnancy (Waisbren, 1999). Dietary control (i.e., phenylalanine-restrictions) during pregnancy does have preventive effects, thereby reducing fetal complications including microcephaly. Ongoing treatment monitoring appears prudent and may increase children's compliance with dietary restrictions and other intervention strategies. Medical, psychological, and educational interventions should be coordinated, with the child and the family as the focus of treatment.

Lesch-Nyhan Syndrome

Lesch-Nyhan syndrome (LNS) is a progressive metabolic disorder that results in cognitive retardation and is often accompanied by choreoathetoid movements (Little & Rodemaker, 1998; Matthews, Solan, & Barabas, 1995). The way that LNS affects development of the nervous system remains unknown, but evidence suggests that abnormal adhesion processes occur during neuronal migration and differentiation (Stacey, Ma, & Daley, 2000). LNS causes a build up of uric acid, which produces gout, poor muscle control and cognitive retardation in the 1st or 2nd decade of life. In addition to neurological symptoms, patients with LNS often have swelling of joints and severe kidney problems. Renal failure is the major cause of early death (Little & Rodemaker, 1998). Seizure disorders are common in LNS patients (maybe as high as 50%). Other neuropsychiatric problems may include self-injury and aggression.

LNS is a sex-linked disorder that is usually inherited, although it can occur through a spontaneous genetic mutation (Davidson et al., 1991). Females rarely have LNS, but can be carriers of the disorder. LNS is associated with an abnormality or near absence of an enzyme [hypoxanthine-guanine phosphoribosynltransferase (HGPRT)] that appears prominent on the X chromosome (Cook & Leventhal, 1992). This abnormality has an effect on the individual's ability to metabolize purines, which in turn has profound neurological and behavioral consequences (Matthews et al., 1995).

Dopamine activity appears altered in various brain regions (i.e., putamen, caudate, and nucleus accumbens), with other neurochemical imbalances that may explain the movement and psychiatric problems associated with LNS (Jankovic et al., 1988). Positron emission tomography showed decreased levels of dopamine in all dopaminergic pathways of the brain (i.e., the putamen, caudate nucleus, frontal cortex, substantia nigra and ventral tegmentum) (Ernest et al., 1996). Researchers are investigating the role of dopamine in self-injurious behaviors, and the degree to which medications alter dopamine and serotonin may be useful for the treatment of LNS (Morales, 1999).

Characteristics and Associated Features of LNS

At birth, there are no abnormal characteristics, but motor delays and choreoathetoid movements appear within the first year and progressively worsen for infants with LNS (Cook & Leventhal, 1992; Morales, 1999). Children with LNS often develop normally until about eight–24 months of age, when

choreoathetosis appears and earlier motor milestones are lost (Matthews et al., 1995). Hypotonia may be present in infants, but hypertonia and hyperreflexia develop. Communication is also hampered because of poor articulation from the palsy in speech musculature (Matthews et al., 1995).

Self-mutilation is characteristic of children between the ages of three and five years, when injuries to facial areas (i.e., eyes, nose, and lips) and appendages (fingers and legs) result from chewing and biting oneself (Hynd & Willis, 1988). Almost all children with LNS show self-injurious behaviors by age eight–10 years, with spasticity, choreoathetosis, opisthotonos, and facial hypotonia also evident (Matthews et al., 1995). Malnutrition may result from severe self-injury to the mouth or from vomiting (Nyhan, 1976).

Although cognitive retardation has been reported, individuals with LNS may be brighter than measured abilities suggest (Nyhan, 1976). Using the Stanford Binet Intelligence Scale, fourth edition (SB-IV), Matthews et al. (1995) investigated intellectual levels for seven subjects. Subjects showed ability levels ranging from moderate cognitive retardation to low average ability. As a group, the sample performed equally well on verbal and nonverbal tasks, although individually they did show a strong preference for either the visual or the verbal modality. Further, attention and higher level intellectual abilities appeared most compromised in this group. Memory, word definitions, and comprehension of complex speech were impaired. Memory deficits affected mental computation, recall of digits backward, visual reasoning, and verbal reasoning. The youngest children performed the best, suggesting that there may be a ceiling for cognitive development for individuals with LNS.

Matthews et al. (1995) caution that standardized tests may not be appropriate for determining functional capacity, educational goals and occupational plans for children with LNS because significant motor difficulties interfere with their performance. Baseline information can be gathered from standardized tests to determine effects of medical, behavioral and educational interventions.

Implications for Assessment

Neuropsychologists play a role in the treatment of children with LNS by providing baseline data to substantiate initial cognitive and psychiatric features of the disorder. To date there is no prescribed assessment protocol for this group, but comprehensive, multifactorial assessment is needed to evaluate the full range and extent of deficits across motor, cognitive, academic, and psychosocial areas. Significant motor impairments may restrict the type of intellectual and neuropsychological measures that can reliably be used with this population. Therefore, the clinician needs to incorporate functional, ecologically based assessment procedures to ascertain skill levels. Efforts should be made to assess functional skills through interview and observation of the individual in a natural setting (e.g., in a classroom or home environment). Careful evaluation of family stress and coping patterns will also be helpful to aid in the planning of interventions.

Implications for Interventions

LNS can be detected during the fetal stage, and research into various medical interventions is underway. Psychopharmacotherapy may be helpful in treating individuals with LNS, but haloperidol, L-dopa, pimozide, diazepam, and clomipramine have been limited in there effectiveness (Watts et al., 1982). Serotonin reuptake inhibitors (e.g., fluoxetine) may help reduce the compulsively self-injurious behaviors (Cook, Rowlett, Jaselskis, & Leventhal, 1992), and other medications have been suggested for use (i.e., 5-hydroxytryptophan, fluphenazine, and naltreone; Cook & Leventhal, 1992). Controlled research into psychopharmacological trials is needed before these avenues can be fairly assessed.

Treatment most often occurs in acute settings where medical professionals work with families to improve the quality of life for individuals with LNS (Bernal, 2006). To date, behavioral interventions have been effective for reducing self-mutilation, although in rare cases self-restraints may be required (Little & Rodemaker, 1998). Residential care or homebound education programs may also be appropriate for some children with LNS. Family members may also require emotional support and additional therapy to deal with the stress that is placed on parents and siblings.

Chromosomal Syndromes

Selected biogenetic disorders of childhood, including Down, Fragile X, and Klinefelter syndromes, are reviewed next. See Dill, Hayden, and McGillivray (1992), Goldstein and Reynolds (1999), Whittle, Satori, Dierssen, Lubec, and Singewald (2007) and Engidawork and Lubec (2003) for a more extensive review of chromosomal abnormalities.

Down Syndrome

Down syndrome, the most common chromosomal disorder, occurs when there is a triplication of a chromosome which may result from trisomy 21 or a fragment of 21q22 during meiosis (Cook & Leventhal, 1992; Lubec, 2003). Down syndrome is the most common genetic cause of cognitive retardation, and occurs in one out of 800 births (NIH Down Syndrome, 2008). NIH has launched a major initiative to map the genome of Down syndrome, and labs across the country are investigating animal models to better understand and ultimately treat individuals with this disorder.

Although Down syndrome can be inherited, the majority of cases result from a random event in the chromosomal distribution in the development of the ovum, sperm, or zygote (NIH Down Syndrome, 2008). Risk factors increase dramatically depending on the age of the mother, from one in 800 births in mothers in their 20 s, to one in 400 for mothers at age 35 years, and one in 20 by age 46 (NIH Down Syndrome, 2008). Although the mother is typically implicated, the syndrome also increases (20%–30% greater chance of occurrence) when fathers are between the age of 50 and 55 (Erickson & Bjerkedal, 1981). Less frequently, occurrences of Down syndrome are associated with translocation of chromosomes other than 21 (Cody & Kamphaus, 1999).

Characteristics and Associated Features of Down Syndrome

Down syndrome is a disorder associated with mild to severe cognitive retardation (NIH Down Syndrome, 2008). Physical anomalies include small head, flat nose, folds at the corners of the eyes, protruding tongue, and heart, eye, and ear defects. Although infants with Down syndrome may show slower development, they follow the same sequence of development as control children.

Children with Down syndrome are also prone to spinal cord injuries due to lax ligaments between the first and second cervical vertebrate (Heller, Alberto, Forney, & Schwartzman, 1996). Dislocation of this area may weaken the child's arms and legs or, in rare instances, may result in paralysis; thus, some activities that put strain on the neck (e.g., diving and tumbling) should be avoided (Shapiro, 1992). Children with Down syndrome also have higher than normal rates of hip dislocation and dysplasia (Shaw & Beals, 1992). Alzheimer's disease may be linked to the same chromosome associated with Down syndrome. Alzheimer's is a progressive loss of memory and brain function associated with tangling/plaguing of nerve tissue. Older individuals with Down syndrome have shown physiological abnormalities similar to those seen in Alzheimer's patients, and apparently the underlying pathology in both disorders occurs from a defective gene on chromosome 21 (Goldgarber, Lerman, McBride, Saffiotti, & Gajdusek, 1987).

Other medical problems include heart disease, pulmonary hypertension, seizure disorders, hypothyroidism, gastrointestinal, orthopedic, vision disorders, and dermatological conditions (NIH Down Syndrome, 2008). Individuals with Down syndrome are at risk for shorter life spans due to medical complications particularly from congenital heart problems, respiratory illness, and gastrointestinal complications (Cody & Kamphaus, 1999). Even those without heart complications have a higher mortality rate than individuals with cognitive retardation, especially after the age of 35 (Strauss & Eyman, 1996). Data compiled by NIH Down Syndrome (2008) indicate that individuals with Down syndrome also have a 12-fold higher mortality rate from various infectious diseases. Abnormalities in the immune system may account for chronic respiratory and ear infections. Children also have recurring tonsillitis and high rates of pneumonia.

Implications for Assessment

During pregnancy there are a number of diagnostic tests for Down syndrome including amniocentesis and chorionic villus sampling (CVS; NIH Down Syndrome, 2008). In amniocentesis, amniotic fluid is drawn and fetal cells are examined for the presence of chromosomal abnormalities. CVS also involves testing of fetal cells, but these are drawn from samples of chorion which precedes the placenta (Liu, 1991). CVS can be performed early (within seven weeks after conception) and tests can be conducted on the same day. Amniocentesis requires two- to three-weeks of laboratory time to grow cultures, so results are not available until well into the second trimester of the pregnancy (NIH Down Syndrome, 2008). However, CVS may carry a higher risk for complications, resulting in a loss of the fetus in 1 percent–4 percent of cases (Gilmore & Aitken, 1989; NIH Down Syndrome, 2008). Percutaneous umbilical blood sampling (PUBS) is the most accurate diagnostic method, but this technique cannot be performed until later in the pregnancy (18th–22nd week) and has increased risk for miscarriage (NIH Down Syndrome, 2008). Newer diagnostic tests are being developed that detect a number of genetic syndromes (e.g., cystic fibrosis, Lesch-Nyhan syndrome) for mothers undergoing in vitro fertilization.

Assessment of Children with Down Syndrome

Early developmental milestones may be delayed for young children with Down syndrome, particularly with motor, language and speech delays. Ongoing developmental assessment in early childhood and later into adolescence is generally recommended to measure cognitive, emotional, behavioral and other academic growth.

Implications for Interventions

While long-term outcomes for early intervention programs are difficult to measure (NIH Down Syndrome, 2008), supportive, enriched environments are recommended for young children with Down syndrome (Cody & Kamphaus, 1999). Children with Down syndrome may experience multiple disabilities that influence their physical, communication, cognitive, and psychosocial performance (Heller et al., 1996). The design of an intervention program depends upon the unique combination of disabilities and the severity of symptoms the child displays. Cognitive retardation affects learning in general and may result in longer learning curves, necessitating repetition and increased drill and practice for academic and/or self-help, daily living skills. Antecedent or response cues appear to be effective for children with cognitive disabilities (Heller et al., 1996), although increased rates of reinforcement may also be required. Basic instruction in daily self-care skills may be necessary and reinforcement and modeling techniques have proven effective. Social interaction skills may also be enhanced through direct instruction in specific skills and reinforcement of appropriate behaviors in naturally occurring situations.

Heller et al. (1996) suggest that children with congenital heart disorders need to be monitored carefully in the classroom depending on the nature and severity of the heart defects. 504 Plans would be appropriate to outline both medical and educational goals. Physical restrictions may be necessary for those with severe forms of heart defects, while milder forms may not necessitate such restrictions. Adaptive physical education, shortened days or special rest times, and homebound education may be needed in some cases. Further, Heller et al. (1996) suggest that children with congenital heart problems should be taught about heart defects, how to identify their own symptoms, what their own limitations are, and how to be their own advocates when decisions about the level of their activities are discussed.

Although Carr (1985) found that individuals with Down syndrome are living longer lives and are in better health than in past years, the long-term outcome is still unsettling. Cody and Kamphaus (1999) suggest that career and vocational planning help older teens and young adults with Down syndrome have more opportunities than they did in the past. Transition into adulthood can be facilitated with post-secondary vocational schooling, on-the-job training, sheltered workshop or other programs that promote independent or semi-independent living.

Fragile X Syndrome

Fragile X occurs from a permutation or full mutation of the X chromosome, and is the most common form of inherited cognitive retardation (Crawford, Acuña, & Sherman, 2001). Although Fragile X occurs in females, it is more common in males and may be one reason why cognitive retardation is more frequent in males than in females (Crawford et al., 2001). Females with Fragile X syndrome appear to have higher rates of normal intelligence (70%) than males (20%) affected by the disorder (Dill, Hayden, & McGillivray, 1992). As a sex-linked genetic disorder, where the X chromosome is abnormal, the defective gene appears to have more of a profound effect on males, who have only one X chromosome, whereas females may inherit one good X chromosome to counterbalance the other defective gene (LeFrancois, 1995). The full mutation of Fragile X is found more frequently in Caucasian males and is found in other races (Crawford et al., 2001). Females appear to have a higher prevalence rate as carriers than males (1/246 to 1/468 in females versus 1/1,000 in males) (Crawford et al., 2001). Fragile X syndrome also increases in frequency for mothers over the age of 40 (Hsu, 1986).

Characteristics and Associated Features of Fragile X

Fragile X syndrome is associated with mild to severe retardation and is considered to be the most common cause of inherited cognitive retardation (Crawford et al., 2001). Although Down syndrome may account for more cases of cognitive retardation, it is not considered to be inherited from parent to child, but occurs from abnormal chromosomal divisions (LeFrancois, 1995). Unlike Down syndrome, cognitive retardation in Fragile X may not be obvious until later stages of development, where marked intellectual deterioration may occur between the ages of 10 and 15 years of age (Silverstein & Johnston, 1990). Dykens et al. (1989) suggest that the drop in IQ, which may drop from a high of 54 points (between ages five and 10) to 38 points (at older ages), may be due to a "plateau" effect rather than a loss of previously acquired intellectual skills. Nevertheless, impairments in visual and sequential processing skills appear prominent (Cook & Leventhal, 1992).

Hypersensitivity to auditory stimuli, self-injury, and interest in unusual sensory stimuli (smell) may be present. Fragile X is also one of the primary causes of autism (Hessl et al., 2007), with as many as 12 percent of children with autism displaying Fragile X (Wolf-Schein, 1992). Males appear to have more severe symptoms, including language delays, slow motor development, speech impairments, and hyperactivity. Rapid speech, echolalia, and impaired communication skills have been reported (Cook & Leventhal, 1992). Social interactions also appear compromised.

Neuropsychological Functions

Widespread structural anomalies have been found in males with Fragile X syndrome, including in the cerebellum, hippocampus, and the superior temporal gyrus (Klaiman & Phelps, 1998). These variations may account for the deficits in attention, memory, visual-spatial reasoning, language skills and mathematics that often accompany the disorder.

In an fMRI study investigating affected males, Hessl et al. (2007) found diminished activation patterns in the amygdala and other brain regions known to regulate social cognition. There was less activation of these brain regions when males were observing fearful stimuli, less startle effect, and reduced skin conduction compared to controls.

Male and female carriers are known to acquire Fragile X-associated tremor/ataxia syndrome (FXTAS) later in life (Adams et al., 2007). This is a neurodegenerative disorder with evidence of brain differences in males and females. Volumetric MRI studies show: less reduction in cerebellar volume in affected females compared to affected males, and reduced brain volume and more white matter diseases in affected females compared to controls. Further, the severity of FXTAS symptoms were associated with reductions in cerebellar volume and the form of permutation in male carriers, but not in females (Adams et al., 2007). While females appear to have milder brain changes than males, the pattern of findings is similar.

Implications for Assessment

Specific genetic tests are available to diagnose Fragile X syndrome (NIH Fragile X, 2008). There are few outward signs of Fragile X syndrome in newborns, but some physical characteristics may be observed, including large head circumference; long face; prominent ears, jaw, and forehead, and hypermobility and hypertonia (NIH Fragile X, 2008).

Implications for Interventions

While there are no effective cures for Fragile X syndrome and syndrome-specific treatments have not been found, children are eligible for early intervention services including special education (Crawford et al., 2001). The extent to which social interaction, intellectual, and communication abilities are involved may determine the long-term outcome.

Research suggests that individuals with Fragile X syndrome may need treatment for autism and/or pervasive developmental disorders (NIH Fragile X, 2008). While there is evidence that hyperactivity and attentional problems improve with stimulant medications (Hagerman, Murphy, & Wittenberger, 1988), other medications are being investigated to improve behaviors and/or cognitive functioning (NIH Fragile X, 2008). Therapeutic interventions are not well investigated to date, and Cook and Leventhal (1992) suggest that "molecular understanding of pathogenesis may contribute directly to the development of therapeutic strategies" (p. 657).

Klinefelter Syndrome

Klinefelter syndrome (KS), also known as the XXY condition, is a chromosomal variation whereby an extra X chromosome is present on most cells (NIH Klinefelter Syndrome, 2008). KS is considered the most common of the chromosomal abnormalities, and estimates suggest that it occurs in approximately one in every 500 male births (NIH Klinefelter Syndrome, 2008). KS, like other autosomal abnormalities, including Down syndrome (trisomy 2 l), Edward syndrome (trisomy 18), Patua syndrome (trisomy 13), Cri du Chat syndrome (deletion on Chromosome 5), and Turner syndrome (XO), affect CNS development and are characterized by physical variations (Hynd & Willis, 1988). During puberty, boys are more likely to exhibit above average height, breast enlargement, less body and facial hair, wider hips, and heavier and less muscular bodies (Ginther & Fullwood, 1998; NIH Klinefelter Syndrome, 2008). By adulthood XXY males look similar to non-affected males, but tend to have higher rates of autoimmune disorders, breast cancer, vein diseases, bone weakness, and dental problems (NIH Klinefelter Syndrome, 2008).

Although scientists believe that one in 500 males have an extra X chromosome, not all will have symptoms of KS (NIH Klinefelter Syndrome, 2008). Symptom presentation appears related to the number of XXY cells, the level of testosterone, and the age of diagnosis. The risks for KS increase with the age of the mother (see Ginther & Fullwood, 1998).

Characteristics and Associated Features of KS

Characteristics of KS include infertility, male breast development, underdeveloped masculine build, and social-cognitive-academic difficulties (Grumbach & Conte, 1985). Physical characteristics (e.g., long legs, tall stature, small testes and penis for body) may be distinguishing features for diagnosing KS (Ratcliffe, Butler, & Jones, 1990).

Psychosocial and Psychoeducational Correlates of KS

Males with KS often have associated behavioral difficulties (i.e., anxiety, immaturity, passivity, and low activity levels), and may present with various problems in peer relations as well as academic, and behavioral problems including impulsivity, aggressiveness, and withdrawal (NIH Klinefelter Syndrome, 2008). Because some children with KS appear shy and withdrawn, teachers may describe these boys as lazy or day dreamy. Many males with KS have difficulties with psychosocial adjustment because of passivity and withdrawal (Robinson, Bender, & Linden, 1990). Further, schizophrenia appears higher among children with KS (Friedman & McGillivray, 1992).

Language and speech delays may be present in anywhere from 25 percent to 85 percent of XXY males (NIH Klinefelter Syndrome, 2008). Children typically have average IQ (Pennington, Bender, Puck, Salbenblatt, & Robinson, 1982). Fine and gross motor delays have been found in some individuals, where dexterity, speed, coordination, and strength may be affected (Mandoki & Sumner, 1991). Children with KS often have a number of academic weaknesses, including difficulty in reading (Netley, 1987; Ratcliffe et al., 1990), spelling (Netley, 1987), and reading comprehension (Graham, Bashir, Stark, Silbert, & Walzer, 1988).

Implications for Assessment

Sandberg and Barrick (1995) indicate that most males with KS are not identified in adolescence or in adulthood, so present research may be skewed toward those individuals with more medical and/or psychological difficulties. Chromosomal analysis is necessary to identify KS, but is not routinely conducted. Careful history taking, in light of psychosocial, behavioral, and academic problems, may suggest the need for a medical consultation and genetic screening. Thorough psychological and educational assessment may shed light on other language and academic delays.

Implications for Interventions

Medical interventions may include testosterone replacement (NIH Klinefelter Syndrome, 2008), and, in cases where gynecomastia (breast development) is present, surgery may be warranted (Sandberg & Barrick, 1995). Although some individuals have been successfully treated with testosterone replacement, not all males have favorable outcomes (Nielsen, 1991). It is important to begin replacement therapy early in life for the most favorable outcomes.

Individual and family therapy may be needed to address the psychosocial needs of the individual with KS. Sandberg and Barrick (1995) suggest implementing opportunities for structured social interactions. Finally, special education interventions may address cognitive, language, and speech-related difficulties.

Neurofibromatosis, tuberous sclerosis, and Sturge Weber syndrome are among the more common neurocutaneous syndromes. These disorders are discussed separately.

Neurocutaneous Syndromes/Disorders

Tuberous sclerosis and neurofibromatosis both involve the failure of cells to differentiate and/or proliferate during early neurodevelopmental stages (Cook & Leventhal, 1992). Morphological changes in the brain occur following these early developmental abnormalities, and these morphological differences result primarily from a failure of control of cell differentiation and proliferation. Hynd and Willis (1988) suggest that these abnormalities may occur during the eighth and 24th week of gestation, when migration of embryonic cells is at its height. Most of these neurocutaneous disorders are genetically transmitted through autosomal dominant means. Thus, neurocutaneous disorders could just as easily be discussed under biogenetic diseases.

Neurofibromatosis

Neurofibromatosis (NF) is a rare disorder and has been referred to as Von Recklinghausen's disease in honor of the physician who first identified the disorder (Hynd & Willis, 1988). The disorder is "considered to be a peripheral neuropathy, brain tumors and other lesions within the brain" (Nilsson & Bradford, 1999, p. 350). There are two major forms of NF—NFl and NF2—involving either chromosome 17 (NF1) or chromosome 22 (NF2; Phelps, 1998b). NF1 is a dominant, autosomal (nonsex) inherited disorder and occurs in approximately one in 3,000–4,000 individuals in the world, while NF2 is more rare [one in 25,000 (NIH Neurofibromatosis, 2008)]. NF1 and NF2 have different features, although NF2 occurs rarely in pediatric populations.

While NF1 increases the risk for benign and malignant tumors, most NF1- type neurofibromas are non-cancerous (NIH Neurofibromatosis, 2008). Cancerous tumors do occur in some individuals

with NF1 along spinal cord nerves or other brain regions, and in the blood system (leukemia). NF2 signs and symptoms typically appear in adolescence or early adulthood, but onset can occur at any age (NIH Neurofibromatosis, 2008). Early symptoms of vestibular schwannomas are difficulty with balance, hearing loss and ringing in the ears.

The manner in which NF is expressed varies dramatically; parents may show few abnormalities, while one child may show severe symptoms and a sibling may show no signs (Hynd & Willis, 1988). When the child's father is affected by NF, the child tends to have less severe symptoms than when the mother is affected (Miller & Hall, 1978). Furthermore, children with affected mothers have higher morbidity, and show symptoms at an earlier age (38% show signs in infancy and 76% by age three years). For a more detailed discussion of neurofibromatosis, see NIH Neurofibromatosis (2008).

Characteristics and Associated Features of NF Features of NFI

NF1 is characterized by the following: spots of skin pigmentation that appear like birthmarks (cafe au lait maculas); benign tumors on or under the skin (neurofibromas); tumors in the iris that are also benign (Lisch nodules); focal lesions in various brain regions (e.g., basal ganglia, subcortical white matter, brain stem, and cerebellum), and freckles in unexposed body areas (e.g., armpit or groin area) (NIH Neurofibromatosis, 2008; Nilsson & Bradford, 1999). NF1 is also associated with learning problems, anxiety related to physical appearance, cluster tumors (plexiform neurofibromas), optic tumors, and seizure disorders. Other signs include high blood pressure, short stature, macrocephaly (large head), and curvature of the spine (NIH Neurofibromatosis, 2008).

North, Joy, Yuille, Cocks, and Hutchins (1995) found that children with NF1 displayed high rates of learning disabilities, poor adaptive social functioning, and high rates of behavioral problems. A bimodal distribution in intelligence scores was found suggesting that the group may have subtypes, specifically those with and without cognitive deficits. Individuals with lower IQs do show abnormal MRI scans (increased T, signal intensity) (North et al., 1995). These lesions are thought to arise from glial proliferation and aberrant myelination. Speech-language, attentional, organizational, and social difficulties were present, although hyperactivity and oppositional and conduct disorders were not apparent.

The physical features of NF1 vary from mild, with cafe au lait spots, to extensive pigmentation and neurofibromas all over the body (Phelps, 1998b). Neurofibromas and brain lesions may not appear until later childhood and adolescence, and with the onset of puberty they have a tendency to increase. While the cafe au lait spots may be present immediately, they too increase with age, along with increased Lisch nodules (Listernick & Charrow, 1990). Symptoms may become so severe in a large number of adolescents that by the age of 15 as many as 50 percent of individuals with NF1 may have health-related problems (Riccardi, 1992).

Cognitive and Psychosocial Correlates of NF1

Academic problems, including a variety of learning disabilities, occur in about 50 percent of children with NF1 (Nilsson & Bradford, 1999; Riccardi, 1992). Visual-spatial disorders, with accompanying reading problems, are common (Hofman et al., 1994; Riccardi, 1992). Compared to noninvolved siblings, NF1 patients have lower cognitive skills (Hofman et al., 1994), but the IQ range varies from cognitive retardation to giftedness (Nilsson & Bradford, 1999). Global and verbal intelligence appear somewhat compromised, although these skills are within the average range (Phelps, 1998b). Nilsson and Bradford (1999) suggest that both language-based and visual perceptual deficits are present, which is consistent with nonverbal learning disabilities (NVLD).

Psychosocial adjustment appears problematic in that NF1 children are often teased because of their appearance, which worsens with age. Children with NF1 often do poorly in school and have trouble establishing friendships. NF is a disfiguring disorder that produces stress and anxiety in afflicted individuals (Benjamin et al., 1993). Attempts to hide the condition often lead to isolation, and high levels of anxiety are not uncommon in adolescents (Benjamin et al., 1993).

Features of NF2

NF2 involves the eighth cranial nerve, resulting in hearing loss, imbalances, pain, headaches, and ringing in the ears (NIH Neurofibromatosis, 2008; Phelps, 1998b). These are late appearing tumors (in the 20 s or 30 s), although it is possible to diagnose NF2 in children, particularly when there are multiple skin (absent cafe au lait or Lisch nodules) or CNS tumors. Complications of tumor growth may also affect numbness and/or weakness in arms and legs, and a buildup of fluid in the brain (NIH Neurofibromatosis, 2008).

Implications for Assessment

The presence of cafe au lait spots is often used as a clinical marker for the presence of NF1. However, the number of spots needed to make a diagnosis is controversial, ranging from five to six distinct spots at least 1.5 cm in diameter (Hynd & Willis, 1988). Diagnosis of NF2 is often made following MRI scans, genetic testing, and a review of family history of the disorder, particularly when the physical appearances described above are present (Mautner, Tatagiba, Guthoff, Samii, & Pulst, 1993). MRI, CT scans, X-rays and blood tests may also be used to identify defects in the NF1 gene (NIH Neurofibromatosis, 2008). Doctors also look for hearing loss, conduct audiometry and brainstem evoked potential response tests to determine damage to the 8th cranial nerve, and investigate family history when making a diagnosis of NF2. Prenatal genetic testing may be used for both NF1 and NF2 when there is a history of NF in the family.

Neuropsychologists may assess the child to establish a base rate of cognitive and academic deficits, and to ascertain subsequent neurodevelopmental deterioration that may occur. Thus, the use of a broad-based assessment protocol is advised, including measures of intellectual, language, motor, academic, and psychosocial functioning (Nilsson & Bradford, 1999; North et al., 1995). Executive functions and reasoning skills should also be assessed.

Implications for Interventions

Although specific treatment plans have not been investigated, techniques for addressing learning, behavioral, and academic difficulties may prove helpful. Access to special education services may be appropriate under the category of "Other Health Impaired" (Nilsson & Bradford, 1999; Phelps, 1998b). Children with NF require academic as well as psychological support. Educational staff may need to be informed about the nature, course and features of NF in order to design appropriate interventions. Nilsson and Bradford suggest that interventions for NVLD may be helpful for some children. Compensatory, adaptive strategies may be helpful to increase skills and avoid frustrations.

Surgical removal of tumors may be necessary (Hynd & Willis, 1988). Long-term follow-up is needed because children with NF may show deficits at a later age as demands increase (Montgomery, 1992). Parents may also benefit from counseling and realistic planning for the child's future. Family education and support is also recommended, as families often are not well informed about the disorder (Benjamin et al., 1993; Nilsson & Bradford, 1999). Further research is needed to more clearly establish how these factors affect interventions with this population of children and adolescents.

Tuberous Sclerosis

Tuberous sclerosis (TS) is a genetic condition characterized by numerous nonmalignant tumors on various body parts (i.e., skin, brain, kidneys, lungs, retina, and other organs), and affects about one in 6,000 infants (NIH Tuberous Sclerous, 2008). CNS symptoms are common (i.e., seizures, cognitive retardation), and a majority of individuals develop significant medical problems involving the heart, lungs, bones, and kidneys. Symptom presentation varies depending on the tumor location. Distinct facial lesions—adenoma sebaceum—that appear like acne are present in approximately 53 percent of five-year-olds and 100 percent of 35-year-olds with the disorder (Bundey & Evans, 1969). Other white spots—amelanotic naevus—may be present on the face, trunk, or limbs in half of patients with TS (Chalhub, 1976). A rough discolored patch also may be observed in the lumbar region in a smaller number of individuals (20–50%).

CNS lesions result from an abnormal proliferation of brain cells and glia during embryonic development (Chalhub, 1976). Cortical tubers often occur in the convulsions of brain tissue and ultimately interfere with the lamination of the cortex. Tumor-like protrusions also may enter the ventricular regions from an outgrowth of astrocytes. These calcium-enriched tubers are visible on CT scans. White matter heterotopias also may be one of the CNS lesions found in patients with TS. When tumors are present near the lateral ventricular region, hydrocephalus may appear.

Characteristics and Associated Features of TS

Children with TS often have cognitive retardation, epilepsy, and hemiplegia (Hynd & Willis, 1988). Seizure activity is common in individuals with TS, and may be as high as 85 percent to 95 percent of those affected. Infantile spasms are common and may worsen with age (NIH Tuberous Sclerous, 2008). However, there appears to be little connection between physical signs (lesions), seizure activity, and intracranial lesions. Psychological and behavioral characteristics have been noted in children with TS, including hyperactivity, aggression, destructive tantrums, and other behavioral control problems (NIH Tuberous Sclerous, 2008; Riccio & Harrison, 1998). Autism has been associated with TS and schizophrenia also appears in some individuals (Cook & Leventhal, 1992; NIH Tuberous Sclerous, 2008).

Implications for Assessment

Surgical removal of CNS tumors (near the ventricular region) may be necessary, but does not always produce good results and may have a high morbidity rate (Hynd & Willis, 1988). Children may require medical evaluations including ultrasound to identify tumors in visceral regions, and EEGs for seizure activity or spasms. Children with TS and severe seizure disorders are also likely to have significant cognitive retardation (Riccio & Harrison, 1998).

Neuropsychological assessment, including academic and psychological evaluation to identify associated features such as hyperactivity, aggression, autism, and other behavioral/psychiatric disorders, is recommended. It is important to identify the full range of associated difficulties prior to designing effective interventions.

Implications for Interventions

Similar to other neurocutaneous disorders, little is known about a specific course of action to take for interventions, other than medical treatment and seizure control. Although psychoeducational interventions for school-related difficulties seem reasonable, efficacy and outcome research has not been conducted. Thus, careful follow-up and monitoring of specific interventions should be conducted on an individual basis to determine which strategies and approaches are most effective for addressing educational and psychological problems. Medical follow-up is essential, and may help determine the long-term outcome of children with TS.

Sturge-Weber Syndrome

Sturge-Weber syndrome (SWS) is characterized by a number of significant neurodevelopmental anomalies, including seizure disorders, cognitive retardation, behavioral difficulties, and infantile hemiplegia. These anomalies appear to result from various neuropathologies involving (1) intracranial calcification in the occipital and parietal regions, and sometimes in the temporal region, and (2) abnormal production of endothelial cells, which leads to leptomeningeal angioma and, in some cases, to subarachnoid or subdural hemorrhage (Cody & Hynd, 1998; NINDS Sturge-Weber, 2008). Calcification usually is not observable during infancy, but can be seen with neuroimaging at a later age. Vascular lesions and abnormal blood flow have also been found using carotid angiography. Facial naevus (port wine staining) is characteristic of SWS (Cody & Hynd, 1998).

Seizures usually occur in the hemisphere opposite the birthmark (NINDS Sturge-Weber, 2008). Children with SWS are also at risk for glaucoma—this increased pressure causes the eye to enlarge, often resulting in a bulging outside the eye socket.

Characteristics and Associated Features of SWS

SWS is associated with seizure activity usually occurring within the first two years of life, and progressively worsening with age (NINDS Sturge-Weber, 2008). The extent to which seizures can be controlled often predicts later outcome of the disorder. Cognitive and behavioral problems are common, and the risk for cognitive impairment especially when seizures occur before the age of two years (NINDS Sturge-Weber, 2008).

Implications for Assessment and Intervention

Medical follow-up is required to identify the nature of neuropathology and to treat seizure activity. In rare cases, hemispherectomy may be necessary to control intractable seizures. While the outcome of neurosurgery has been variable, seizure control has been effective, although severe cognitive retardation was an outcome when the left hemisphere was removed early in life (Falconer & Rushworth, 1960). Severe behavioral disturbances were also reduced following surgery. Neurosurgical intervention is used with caution because of the serious complications associated with hemidecortication, including hemorrhaging into the open cavity, hydrocephalus, and brainstem shifts (Falconer & Wilson, 1969). Furthermore, improved medications for seizure control have reduced the need for invasive surgical techniques (Hynd & Willis, 1988).

Educational services are appropriate to address cognitive and behavioral problems. Disruptive, acting out problems may be reduced with behavior management strategies (Cody & Hynd, 1998). Physical therapy may be needed for some children with muscle weakness (NINDS Sturge-Weber, 2008). Research is currently underway with NINDS support to better understand, diagnose, treat, and prevent this disorder.

Seizure disorders are reviewed next, with attention paid to the transactional nature of the associated features and the need for a transactional, multifaceted intervention plan including medical, academic, and psychosocial approaches.

Seizure Disorders

Seizure disorders can occur in children with developmental disorders and may be caused by metabolic disorders, hypoxia, or other congenital problems (Teeter & Semrud-Clikeman, 1998). *Epilepsy* refers to chronic disturbances in brain functions affecting perceptions, movements, consciousness, and other behaviors, while *seizures* refer to individual episodes (NIH Seizures, 2008). Neppe (1985) describes seizures as paroxysmal firing of neurons, which may cause perceptual, motor disturbances or loss of consciousness. Although epilepsy occurs in only 1 percent–2 percent of the population (Hynd & Willis, 1988), it is considered to be the most prevalent of childhood neurological disorders (Black & Hynd, 1995). National data suggest that approximately 2 million individuals have epilepsy and one-half of those are children (NICHY, 2004).

Seizures, or single episodes, caused by high fevers (above 102°F) are the common cause of convulsions. Febrile seizures are most common in children between three months and five years of age (Hynd & Willis, 1988). Most children (70%) experience only one seizure episode; when a second seizure does occur, it is usually within a year of the first episode (Hynd & Willis, 1988).

There are several classification systems based on changes in EEG activity during (ictal) and between (interictal) seizures (Neppe & Tucker, 1992). Most recent systems ignore neuroanatomical sites of seizure activity, age, gender, and pathological explanations of epileptic seizures, and emphasize major descriptions, including partial (i.e., simple, complex, generalized tonic-clonic), generalized (i.e., absence, myoclonic, clonic, tonic, etc.), or unclassified generalized seizures (Neppe & Tucker, 1992). McDonald and Saykin (2007) indicate that temporal lobe seizures are the most common form of complex partial seizures. Older classification systems for seizure disorders (grand mal, petit mal, psychomotor), have been replaced (Hartlage & Hartlage, 1989). Seizures that appear for unknown reasons (idiopathic) typically are differentiated from those occurring for known reasons such as brain trauma or tumor activity (Hynd & Willis, 1988).

Stages of Seizure Activity

The seizure itself may be divided into stages: the prodome, aura, automatism, and postictal changes (Besag, 1995). According to Besag (1995), the *prodome* is the time before a seizure or cluster of seizures occurs. The child may show irritability, lethargy, or apathy during this period, with these symptoms ending when the seizure begins. The *aura* occurs just prior to the seizure and has been described as a seizure itself. The aura is a simple partial seizure type that can lead to a complex partial seizure. The aura, which occurs while the child is fully conscious, has been described as more distressing to the child than the actual tonic-clonic seizure (Besag, 1995). The aura is actually a seizure with a focal charge, lasts a few seconds, and can occur many times a day. Besag (1995) reports that auras can result in mood (mainly anxiety) and behavioral change; thus, the aura may herald not only the beginning of a seizure, but also significant behavioral change in the child.

Automatisms have been defined as a "clouding of consciousness, which occurs during or immediately after a seizure and during which the individual retains control of posture and muscle tone but performs simple or complex movements and actions without being aware of what is happening" (Fenton, 1972, p. 59). Automatisms may include lip smacking, hand flapping, eye blinking, twirling, and other similar behaviors.

Postictal changes are behaviors that occur after the seizure and vary depending on the parts of the brain involved, the duration of the seizure, and whether the seizures come in clusters. Behaviors during the postictal stage can range from drowsiness to significant behavioral and cognitive changes such as paranoid ideation. Usual symptoms include irritability and confusion. Besag (1995) strongly recommends that parents and teachers realize that these postictal changes *are* related to the seizure and require understanding and empathy for the child.

Partial Seizures

Partial seizures are associated with diagnosable structural lesions. These seizures do not involve a loss of consciousness, but can evolve into generalized clonic-tonic seizures (Dreifuss, 1994).

Simple Partial Seizures

This type of seizure results from a specific focus in the gray matter of the brain, which causes an abnormal electrical discharge. The most commonly seen seizure of this type involves the jerking of one part of the body without loss of consciousness. The simple partial seizure foci is in the motor strip area. Other types of simple partial seizures include sensory (simple hallucinations), autonomic (sweating, pallor, hair standing on end on limbs), and psychic (affective problems, speaking, distortion of time sense) seizures with no impairment of consciousness (Hartlage & Telzrow, 1984).

Complex Partial Seizures

Complex partial seizures generally involve a loss or impairment of consciousness. This alteration of consciousness occurs before the attack or shortly after its beginning. These seizures involve behavioral automatisms such as lip smacking, hair twirling, and hand patting. Problems in orientation in time and space also occur. The focus of this type of seizure is in the temporal lobe as well as the frontal lobes. Some believe the complex partial seizures arising from the frontal lobes are associated with automatisms, while those with a temporal focus relate to a cessation of activity (Delgado-Escueta, Bascal, & Treiman, 1982).

Generalized Seizures

There are three main types of generalized seizures. Of the three, febrile seizures are not considered a seizure disorder. This type of seizure is associated with a fever experienced by a previously neurologically intact child. Although these seizures may reoccur, medication is not used due to the benign nature of the seizure (Hartlage & Telzrow, 1984). The other two types of generalized seizures are absence and tonic-clonic.

Absence Seizures

This type of seizure was previously labeled petit mal. Seizures of this kind involve an abrupt loss of consciousness. The child's eyes may flicker, roll back, or blink rapidly. When the seizure ceases, the child resumes his or her activity as if nothing unusual has occurred. These seizures may occur very frequently; some children have been known to have over 100 in a day (Hartlage & Telzrow, 1984). Age of onset is 4–8 years. School performance is often seen to fall off, and the child may be described as dreamy or unmotivated. The diagnosis of absence seizures is confirmed by EEG. The EEG will show spikes that are synchronized bilaterally and frontally (normal brain activity is *not* synchronized), with alternating spike and slow wave patterns (Lockman, 1993). To induce a seizure during an EEG, hyperventilation is used whereby the child is asked to take 60 deep breaths for three or four minutes (Lockman, 1993). Although the etiology of absence seizures is suspected to be genetic in origin, the genetic mechanism has not yet been identified. The risk of siblings also showing absence seizures is approximately three times greater than for the general population (Ottman et al., 1989). Absence seizures are generally treated with one medication. Zarontin is the medication with the fewest side effects (Dooley et al., 1990), followed by valproate (Sato et al., 1982) and clonazepam (Hartlage & Telzrow, 1984). Absence seizures have been known to worsen with the use of carbamazepine (Horn, Ater, & Hurst, 1986). The prognosis for absence seizures is favorable, with approximately half of affected children becoming seizure-free. The other 50 percent may develop tonic-clonic seizures or may continue to experience absence seizures (Lockman, 1993). Sato et al. (1983) found that 90 percent of children of normal intelligence and neurological function with no history of tonic-clonic seizures were seizure-free in adolescence. Conversely, those children with automatisms and motor responses during the absence seizures had a poorer prognosis. Lockman (1994) concluded that typical absence seizures are not necessarily benign and that medical management of these seizures does not necessarily influence the eventual outcome.

Tonic-Clonic Seizures

Further, increased seizure activity correlated with this type of seizure was formerly called grand ma1 seizure. Epidemiological studies have shown this type of seizure to be the most commonly found in children (Ellenberg, Hirtz, & Nelson, 1984). Tonic-clonic seizures begin with a loss of consciousness and a fall accompanied by a cry. The limbs extend, the back arches, and breathing may cease for short periods of time. This phase can last from several seconds to minutes. The limb extension is then followed by jerking of the head, arms, and legs. This is the clonic phase, which can last for minutes or may stop with intervention (Dreifuss, 1994). Most commonly, the jerking decreases and the child regains consciousness. Headaches and confusion usually ensue. Generally, the child falls into a deep sleep lasting from 30 minutes to several hours. Tonic-clonic seizures can occur after focal discharges and then are labeled as secondary generalization (Dreifuss, 1994). Tonic-clonic seizures are related to metabolic imbalances, liver failure, and head injury. On rare occasions, tonic-clonic seizures may persist for extremely long periods of time or may be repeated so close together that no recovery occurs between attacks. This type of seizure is called *status epilepticus* (Lockman, 1994). Underlying conditions such as subarachnoid hemorrhage, metabolic disturbances, and fevers (e.g., bacterial meningitis) can trigger status epilepticus in children (Phillips & Shanahan, 1989). Treatment for status epilepticus includes very high dosages of medication and, in some cases, inducing a coma (Young, Segalowitz, Misek, Alp, & Boulet, 1983).

Associated Features

While seizures can occur in children with normal cognitive abilities (Hartlage & Hartlage, 1989), seizure disorders occur more frequently in individuals with depressed intelligence (Cook & Leventhal, 1992). Low IQ (less than 80) with intractable epilepsy usually has a poor outcome for remission (Huttenlocher & Hapke, 1990). Further, increased seizure activity is correlated with more severe cognitive deficits (Farwell, Dodrill, & Batzel, 1985). It is

also important to note that children with early seizure onset are likely to have lower IQ (Aldenkamp, Gutter, & Beun, 1992).

Curatolo, Arpino, Stazi, and Medda (1995) investigated risk factors associated with the comorbidity of partial seizures, cerebral palsy (CP), and cognitive retardation in a group of children from Italy. Cerebral malformations (e.g., agenesis of the corpus callosum, NF, cortical dysplasia, lissencephaly) were found in half of the group. Children with an early onset of seizures were likely also to have CP and cognitive retardation. Children with a family history of epilepsy may have a "genetic predisposition to neurological disorders in general which range from epilepsy to CP" to cognitive retardation (Curatolo et al., 1995, p. 779). Cardiopulmonary resuscitation was also found to be a risk factor only in the group of children who did not have cerebral malformations. These authors suggest that resuscitation may be the first neurological abnormality that appears in this group, rather than a cause of the cerebral palsy.

Academic problems may also occur in children with seizure disorders (Pazzaglia & Frank-Pazzaglia, 1976), and LD may occur in approximately 15 percent–30 percent of children with epilepsy (Matthews, Barabas, & Ferrai, 1983). Epidemiologic studies of children with epilepsy have found that approximately 50 percent have school difficulty ranging from mild to severe (Pazzaglia & Frank Pazzaglia, 1976; Sillanpaa, 1992). In a study of Finnish children with epilepsy compared to non-epileptic controls, Sillanpaa (1992) found that the most frequent associated problems were mental (cognitive) retardation (31.4%), speech disorders (27.5%), and specific learning disorders (23.1%).

Children with seizure disorders have shown impaired performance on tests of reading, written language, and spelling (Seidenberg et al., 1986), as well as on teacher reports of attention, concentration, and information processing (Bennett-Levy & Stores, 1984). Reading comprehension appears to be more compromised than word recognition skills. However, social and cultural factors may also influence academic outcome and IQ for children with epilepsy-related disorders, as family factors (e.g., family setting and parental attitudes) were significantly correlated with underachievement. Finally, psychomotor and visual-motor coordination problems have also been found to be poorer in children with seizure disorders than in typically developing children (Cull, 1988).

Psychosocial Correlates

Although children with epilepsy differ from normal peers on a number of social-emotional variables, they do not appear to have higher rates of psychopathology than children with other chronic medical or neurological conditions (Hartlage & Hartlage, 1989). Psychosocial features often include external locus of control, poor self-esteem (Matthews, Barabas, & Ferrai, 1982), and increased dependency (Hartlage & Hartlage, 1989). Neppe (1985) indicates that individuals with epilepsy do experience psychosocial stress due to the effects of having a chronic illness, anxieties over social interactions, and restrictions in everyday activities (e.g., driving). Seizure disorders in childhood are related to other psychiatric conditions. The majority of children (85%) with temporal lobe epilepsy have cognitive retardation (25%) and disruptive behavior disorders, including hyperactivity and "catastrophic rage" (Cook & Leventhal, 1992). Psychopathology, including psychoses, has been described in individuals with epilepsy (Neppe & Tucker, 1992), and psychiatric disorders (i.e., cognitive retardation, hyperkinesis, and rage disorders) have been reported in 85 percent of children with temporal lobe epilepsy (Lindsay, Ounstead, & Richards, 1979). Cook and Leventhal (1992) suggest that the loss of control children may experience as a result of epilepsy may be a special challenge during development, and children may react either passively or aggressively. However, these reactions may be related to how seizure activity affects cognition and impulse control.

Implications for Assessment

Children with seizure disorders require medical diagnosis and follow-up by a child neurologist. Ongoing assessment of neuropsychological, cognitive, and psychosocial functioning is useful for measuring the long-term effects of chronic seizure disorders. Because many children with epilepsy are not

easily categorized, each child would benefit from a team that includes a physician, psychologist, teacher, and counselor (Black & Hynd, 1995).

Moderator Variables

There are a number of moderator variables which need to be recognized when evaluating the performance of a child with a seizure disorder. These variables are etiology of the seizure disorder, age of onset, seizure type, seizure frequency, medication, and family environment. Each of these moderator variables will be discussed in the following sections.

Etiology

The main classes of etiology for seizure disorders are idiopathic, where the cause is unknown, and symptomatic, where the cause is associated with organic and/or identified neurological problems (Cull, 1988). Children with symptomatic epilepsy generally have lower IQ scores, with many showing cognitive retardation (Sillanpaa, 1992), whereas those with idiopathic epilepsy show normal distribution of intellectual ability. Symptomatic epilepsy is also associated with poorer academic and intellectual outcome. Recently, neural developmental abnormalities have been implicated in the development of seizure-related disorders. Specifically, abnormal cell migration has been associated with both mental retardation and epilepsy (Falconer et al., 1990). As cells migrate and move into their final destinations during embryonic development, genetic and/or environmental factors may disrupt this process and ultimately result in epilepsy.

Age of Onset

The majority of studies evaluating the significance of age of onset in relation to cognitive development have found a direct relationship between the two, with children with early onset generally showing poorer cognitive attainment (Seidenberg, 1988). Ellenberg and Nelson (1984) reported that children with normal neurological development prior to the first seizure have a better prognosis for intellectual development at age seven than those who had earlier seizures *and* poorer neurological attainment. O'Leary, Seidenberg, Berent, and Boll (1981) compared the performance of children with tonic-clonic seizures on the Halstead-Reitan Test Battery for Children. Those children with seizure onset before the age of five years were more impaired on measures of motor speed, attention and concentration, memory, and complex problem solving than those with a later onset. These researchers then evaluated the relationship between age of onset and partial seizure type. O'Leary et al. (1981) found that children with partial seizures and early onset performed more poorly than those with later onset, regardless of whether their seizures were partial or generalized. Similarly, Hermann, Whitman, and Dell (1988) found that children with early onset performed more poorly on eight of 11 scales of the LNNB-C. Evaluating age of onset with seizure type found that children with complex-partial seizures *and* early onset performed more poorly on Memory, Expressive Speech, and Reading, whereas generalized seizures *and* early onset were associated with poorer performance on Receptive Speech, Writing, Mathematics, and Intelligence Scales.

Duration of seizure has been found to co-occur with age of onset as a crucial variable and is frequently difficult to evaluate apart from age of onset. Generally it has been found that the earlier the onset of seizures, the longer the duration (Black & Hynd, 1995). Early onset and long duration appear to be associated with a poorer prognosis for learning. The number of seizures over the life span is a contributing factor to poor outcome as well. Seidenberg (1988) makes the point that further study is needed in this area to determine whether the neuropsychological impairment is broad-based and general, or whether there are specific areas of functioning that are more vulnerable during specific periods of development. This may be a likely case given what we know about neurodevelopment and increased cognitive, language, memory, and reasoning abilities in children. Thus, age of onset and seizure duration are important variables to consider when evaluating children with seizure disorders, particularly when planning for their educational and vocational needs.

Seizure Type

The relationship between seizure type and intellectual and educational attainment is currently unclear. Some investigators have found memory deficits to be associated with partial-complex seizures with a temporal lobe focus, whereas others have found that children with mixed seizures perform more poorly on measures of ability and achievement (Seidenberg et al., 1986). However, O'Leary et al. (1981) found few differences between seizure types, and those significant differences that did appear occurred more frequently in children with generalized seizures. Seidenberg (1988) concluded from his review of this literature that further study is needed using subtypes of seizure disorders. Most research has not identified subtypes of the seizure disorders when evaluating neuropsychological functioning.

Seizure Frequency

The relationship between seizure frequency and cognitive development is presently unclear. Methodological considerations may account for this difficulty, as many studies have not investigated subtypes of seizures, thereby possibly obscuring important findings.

Studies that have looked at seizure subtypes have generally found an inverse relationship between seizure duration and cognitive performance (longer duration = poorer test performance). Seidenberg (1988) found that with increasing frequency of seizure activity, performance on the full, verbal, and performance intelligence scales (FSIQ, VIQ, and PIQ) of the Wechsler, and the Trailmaking and Tactual Performance of the Reitan Battery declined significantly. When seizure type was also factored into the analysis, significant correlations for seizure duration, seizure frequency, and seizure type were found only for the tonic-clonic subtype.

Seizure control is also related to seizure frequency. Hermann et al. (1988) found that poor seizure control was related to poorer neuropsychological performance *only*for generalized epilepsies. Such a finding was not present for those children with partial seizures.

Seidenberg (1988) suggests that not only is subtyping of seizures important, but that researchers need to pay attention to seizure frequency, age of onset and duration, seizure type, and seizure control when evaluating neuropsychological functioning. He also suggests that seizure severity may be an overlooked variable in all investigations. Thus, etiology, age of onset of a seizure disorder, duration and frequency, type of seizure disorder, and possibly severity of the seizure all appear to contribute to the neuropsychological impairments that children may experience. In addition to these intraindividual variables, two major extra individual variables interact with the seizure disorder—namely, medication effects and family environmental influences. Each of these will be developed in the following sections.

Medication

Antiepileptic drugs such as Phenobarbital and clonazepam have been associated with cognitive difficulties (Besag, 1995). Others, including ethosuximide, sodium valporate, and carbamazepine generally have been found to be beneficial (Cull, 1988). Carbamazepine has been found to impair memory (Forsythe, Butler, Berg, & McGuire, 1991). Some researchers have found that decreases in dosage are associated with better performance, while increases show no such effects (Cull, 1988). Moreover, children with more than one antiepileptic medication show more cognitive impairment. Whether polydrug treatment is related to a more severe seizure disorder and, therefore, to more cognitive impairment, this is currently unclear.

Family Influences

Family and environmental influences on children with seizure disorders are just beginning to be explored. Given our transactional model, it is important to gather information concerning family and school environment influences.

Preliminary data indicate that negative reactions to the child's behaviors from peers and teachers can have a significant deleterious effect on the child's school attainment (Dreifuss, 1994). As discussed earlier, behavioral changes during aura and

postictal stages are frequently seen. When peers and teachers interpret these behaviors as willful and deviant, significant adjustment problems can arise. Research evaluating interventions such as educating the child's peers about seizure disorders and any resulting changes in attitudes has not been conducted. Such investigations are sorely needed. These influences on the child with a seizure disorder are probably more easily solved than variables such as age of onset, frequency of seizures, and severity of seizures.

Socioeconomic status (SES) is significantly related to intelligence. In a study with Indian children, Singhi, Bansal, Singhi, and Pershad (1992), found that SES was the second most powerful indicator of cognitive impairment, second only to status epilepticus. This finding is similar to that of Caucasian and African-American children (Dodson, 1993).

Family variables such as stress, divorce, parental control and dependency, financial difficulty, and fewer family social supports have been shown to have a negative impact on cognitive development in children with seizure disorders (Teeter & Semrud-Clikeman, 1998). Austin, Risinger, and Beckett (1992) sought to evaluate the relative importance of demographics, seizure, and family variables on the behaviors of children with seizure disorders. In this study, no differences were found between boys and girls, children with mono- versus polydrug therapy, one-parent versus two-parent homes, or seizure type in behavioral problems. Significant findings were present for age, seizure frequency, family stress, and extended family social support. When stepwise multiple regression techniques were employed, intrafamily strain and marital strain emerged as the most significant predictors of behavioral problems. This finding is similar to those linking family discord to psychopathology in children without seizures (Breslau, 1985; Austin, 1988).

Hoare and Russell (1995) describe an assessment measure for identifying quality-of-life issues for children with chronic epilepsy and their families. This scale measures the impact of the illness on the child, the parents, and the family, and the cumulative impact. Further research is needed to determine the efficacy of this scale for intervention planning, but initial reports suggest that parents do have significant concerns, and these appear related to age of onset and seizure frequency.

Summary

Seizure variables interact with family variables to influence the child's intellectual and educational attainment as well as his or her emotional adjustment. Investigators are just beginning to evaluate these transactional relationships and their contributions to appropriate interventions. It is not clear, at present, whether interventions that target environmental (school and family) influences can improve the child's eventual cognitive attainment. However, it is important to consider these variables when designing treatment plans for these children, as they have been found to be potent predictors. The following section discusses intervention strategies for children with seizure disorders.

Implications for Intervention

Interventions addressing pharmacological, environmental, and educational strategies are briefly reviewed. In many cases, a dynamic plan may include one or more of the following strategies.

Pharmacological and Surgical Treatments

While anticonvulsant medications are commonly prescribed for children with nonfebrile seizure disorders, these medications (e.g., Phenobarbital) produce adverse side effects (e.g., sedation) that interfere with academic performance (Cook & Leventhal, 1992), and may increase hyperactivity (Vining et al., 1987) or depression (Brent, Crumrine, Varma, Allan, & Allman, 1987). Newer medications (lamotrigine and felbamate) may be used when side effects are not well tolerated or when traditional medications (i.e., valporate and carbamazepine) do not control seizure activity (Williams & Sharp, 2000).

In a review of pediatric pharmacology, DuPaul, McGoey, and Mautone (2003) list common anticonvulsant mediations for treating various seizure types: (1) Phenobarbitol, phenytoin, carbamazepine, and valporate for clonic-tonic seizures; (2) ethosuximide or valporate for absence seizures; (3)

carbamazepine, phenytoin, and valporate for partial seizures, with (4) gabapentine or felbamate as second line medications.

In rare cases of intractable seizures, surgical transactions may be an option when the seizures are localized to one region in the brain. In a meta-analysis of studies, it was concluded that surgery produces long-term seizure-free outcomes, especially for temporal lobe resective surgery (Tellez-Zenteno, Dhar, & Wiebe, 2005); however, it is clear that not all children who undergo brain surgery are seizure-free. Studies appear to document resiliency in the developing brain, where intact brain regions compensate for regions that have been removed. For example, Meyer, Marsh, Laws, and Sharbrough (1986) found that children who had undergone surgical removal of the dominant temporal lobes, including the hippocampus and amygdala, showed no significant decline in verbal, performance, or full-scale IQ scores. Smith, Walker, and Myers (1988) also found that a six-year-old made remarkable postoperative recovery following surgical removal of the right hemisphere. The child had perinatal epileptogenic seizures that worsened and spread from the right to the left hemisphere. Post-surgical test scores showed average verbal intelligence (96), low average performance abilities (87), and average full-scale (90) potential. The extent to which cognitive abilities improve or develop following surgical interventions depends on a number of factors, including the age of the child and the location of the lesion, once intact brain regions are freed from the abnormal influences of the lesioned regions.

Alternative Interventions

Recent studies have investigated the kerogenic diet (KD) to determine safety and efficacy for treating intractable epilepsy (Kang & Kim, 2006). The diet has a ratio of 1:4 fat to nonfat foods, is high in protein and restricts carbohydrate intake, and has both anticonvulsant properties and also reduces the development of recurring seizures and epilepsy (Freeman, Kossoff, & Hartman, 2007). In a review of patients treated with the kerogenic diet at St. John's Hospital, Groesbeck, Bluml, and Kossoff (2006) found that after six years, seizure activity was significantly reduced in children on the diet. Side effects included kidney stones, slowed growth, and bone fractures. Other studies document early onset (i.e., gastrointestinal disturbances, dehydration, biochemical disturbances) as well as late onset (i.e., heptic failure, mineral and vitamin deficiencies) symptoms which require scheduled medical assessments to evaluate adverse effects of the diet (Freeman et al., 2000). Henderson et al. (2006) found children with generalized seizures and those who showed more than a 50 percent reduction in seizure activity were more likely to remain on the diet.

Despite their efficacy, neurologists are not likely to prescribe kerogenic diets for patients, even though they adhere to other evidence-based practices (i.e., antiepileptic medications) when treating children with epilepsy (Mastriani, Williams, Hulsey, Wheless, & Maria, 2008). See Freeman et al. (2007) for a more extensive review of the KD treatment for seizure disorders.

Environmental Interventions

Given previous research, it appears imperative to assess variables such as family strain, behavioral concerns, and discipline, and to plan interventions taking these factors into consideration. Parenting, stress management, and epilepsy education are likely avenues for intervention. It is important in the course of epilepsy education to discuss the potential for parents to overcompensate for their child's illness and the possible guilt that may accompany a diagnosis. Parents who expect to provide lifetime care for their child do not facilitate the development of independent behaviors. Moreover, parents may lower expectations for their child's academic performance. Therefore, it is crucial to discuss these possibilities with parents and to help them set realistic goals for their child and encourage coping skills for the child with epilepsy and seizure disorders (Freeman, Vining, & Pillas, 2003). When a transactional approach is not taken, the child's program will be incomplete and most likely will be at least partially unsuccessful.

Educational Interventions

Students with seizure disorders or epilepsy may access educational services under "other-health impaired" as defined by the Individuals with Disabilities Act (IDEA; NICHY, 2004). The school should not only be aware of the diagnosis of epilepsy, but educational staff should develop and institute a plan for working effectively with the child who has a seizure disorder. 504 plans may also be helpful to address medication issues (i.e., efficacy and side effects), and to establish home-school-physician communication.

The pediatric neuropsychologist can be helpful in the initial planning and implementation phase of the educational program. At the very least, medication monitoring is important. Sachs and Barrett (1995) list behavioral side effects of medication, such as drowsiness, lethargy, overactivity, confusion, and motor signs (e.g., clumsiness), and suggest that teachers should be on the look-out for these signs. Moreover, information on what action should be taken in the event of a seizure in school is very important for teachers and staff. Generally, little action is needed except when the child needs to be protected from injury. It is not appropriate to place items in the child's mouth, to restrain the child, or to perform cardiopulmonary resuscitation (NICHY, 2004).

Communication between the school and the physician is important for monitoring the child's seizure frequency and medication response (Lechtenberg, 2002; NICHY, 2004). The pediatric neuropsychologist may serve a much needed service in interpreting medical information for school personnel and parents. Linking these services is desirable to understand the child's needs and to develop a comprehensive intervention program for the child. Formulating the program can assist in planning for psychosocial stressors that may occur at home or in school, monitoring medication compliance and effectiveness, and enhancing the child's school performance in either special or regular education (Teeter & Semrud-Clikeman, 1998). Helping peers to understand the child's needs and his or her occasional unusual behaviors (during seizure activity) may smooth the way for children with seizure disorders to develop healthy peer relationships.

In summary, a transactional approach is an important vehicle for understanding and planning for the needs of children with seizures disorders. Similarly, children with head injuries would benefit from this type of integrated approach. See Chapter 14 for a discussion of interventions for children sustaining traumatic brain injury. Cerebral palsy is reviewed next.

Cerebral Palsy

Cerebral palsy (CP) is a neurological disorder that first appears in infancy or early childhood (NINDS Cerebral Palsy, 2008). Body movements and muscle coordination are permanently damaged and typically do not worsen with age. CP is caused by an insult to the developing brain usually between prenatal development and age three. Birth complications are a major cause of CP in newborns, although encephalitis, meningitis, and traumatic brain injury (from car accidents, falls, or abuse) may also cause CP in early childhood. Maternal and infant infections are also associated with increased risk for CP.

Muscle coordination is particularly compromised during voluntary movements (ataxia). Other motor signs include tight muscles and exaggerated reflexes (spasticity); walking on toes, on one foot or leg dragging; crouched or "scissor" gait, and floppy or stiff muscle tone (NINDS Cerebral Palsy, 2008). Other health problems have been found in children with CP including the need for feeding tubes, respiratory problems, and lower global health scores (Liptak et al., 2007). Liptak et al. found that children with the most severe disability who also have feeding tubes are particularly fragile children with other health problems.

Etiology of Cerebral Palsy

Prevalence rates for CP range from 2.12 to 4.45 per 1,000 births, in six countries (Odding, Roebroeck, & Stam, 2006). Incidence rates appear higher in less affluent communities where pre-pregnancy and pregnancy risk factors may be higher, including poor maternal health and access to quality health

care. A minority of identified cases can be traced to documented brain injury from infection or trauma after four months of life.

A two-fold increase in the rate of CP across the spectrum has also been reported in England (Colver et al., 2000). Colver et al. found that low weight newborns (< 2,500 g) now represent one-half of the cases, where past data showed they accounted for one-third of cases. They suggest that modern neonatal care for babies < 2,500 g are now surviving at higher rates than previously reported, and these infants are surviving with CP. Males also appear to have an increased risk for CP compared to females, most likely because of other biological vulnerabilities including preterm births and mortality due to stillbirth and neonatal strokes (Johnston & Hagberg, 2007; Odding et al., 2006).

Low Birth Weight Factors

Low birth weight babies are at high risk for developing CP. As a result of increased rates of survival, CP in low birth weight babies is increasing (Colver et al., 2000). Survival rates for CP appear to depend on the severity of the disorder and the level of intelligence. Children with severe motor involvement and extremely low IQ have a shorter life expectancy.

Premature infants who are significantly smaller than expected appear to be at high risk for CP (Colver et al., 2000). Frequent medical difficulties found in these infants may contribute to the development of CP. These complications include intraventricular hemorrhage, white matter necrosis, and variation in cerebral blood flow (Leviton & Paneth, 1990). Evidence for the involvement of these complications in CP has been found by ultrasonography in infants and neuroimaging for older children and adults (Krageloh-Mann et al., 1992).

Twins who are low birth weight appear to be at special risk for CP as well (Nelson Swaiman, & Russman, 1994). If one of the twins dies at or before birth, the remaining twin appears to be at high risk for CP (Szymonowicz, Preston, & Yu, 1986). In fact, the incidence of twins in the general population is 2 percent, with a 10 percent incidence rate of CP within this sample (Grether et al., 1992).

Pregnancy and Birth Complications

Babies who sustain brain damage during delivery are at high risk for CP. Occlusion of a cerebral artery or prenatal strokes that restrict blood flow to the brain are the most common causes of hemiparetic CP (Lee et al., 2005). Strokes were most common in first born children and other birth complications (i.e., emergency C-section, ruptured membranes, prolonged second stage labor, and vacuum extraction). Infants sustaining strokes appear to have heart anomalies, inflammation of the placenta, and umbilical cord abnormalities. More than half of infants with one of these risk factors did not suffer a perinatal stroke.

Infants born with brain damage frequently show low tone, breathing problems, low APGAR scores, delayed reflexes, and seizures (Nelson & Leviton, 1991). When all these symptoms are present, the child is at greater risk for CP, with the risk decreasing as the number of presenting symptoms decreases (Ellenberg & Nelson, 1984; Seidman et al., 1991).

While subtypes of CP appear related to different causes, most children and adults with CP did not experience oxygen deprivation during birth. Asphyxia has been most closely related to quadriplegia (Nelson & Leviton, 1991). In most cases, however, it is not possible to determine the cause of CP.

Pre- and Postnatal Medical Complications

There are a number of pre- and postnatal complications that increase the risk for CP. In a review of research investigating pregnancy and pre-pregnancy infections, Dammann and Leviton (2006) reported that maternal infections place fetal brains at risk for neonatal white matter damage, including CP. New research investigating how to prevent infections to the mother prior to and during pregnancy is needed as well as an investigation of effective methods to protect the developing fetus. Wu and Colford (2000) also found that inflammation of the fetal membrane (chorioamnionitis) is associated with an increased risk for cystic periventricular leukomalacia and CP in pre-term and full-term babies. Other studies have shown that intra-amniotic inflammation following amniocentesis

and subsequent inflammatory responses in the fetus (funisitis) place newborns at higher risk for CP by the age of three years (Hun et al., 2000).

Pre-term infants (before 12 hours of age) who received a three-day course of dexamethsone to prevent chronic lung diseases were at a risk for a range of medical problems including hypertension, gastrointestinal hemorrhage, and hyperglycemia (Shinwell et al., 2000). Stoll et al. (2004) also found that pre-term infants are at risk for infections (e.g., sepsis, meningitis), which increases the risk for CP. It has been hypothesized that cytokines, chemicals that fight the infections, may cause damage to the brain. These young infants were also at greater risk for CP, with the most common form being spastic diplegia, and developmental delays were also higher (Shinwell et al., 2000). Maternal infections (i.e., bladder or kidney) appear to be risk factors of infants with normal birth weight (Grether & Nelson, 1997).

Brain Malformations

Children with CP appear to have structural brain disorders which may be related to abnormal neuronal migration (Volpe, 1992). In these cases cells have migrated to the wrong place and, thus, brain layers are disordered, cells are out of place, and/or there are too many or not enough cells in certain critical brain regions. Volpe (1992) estimates that approximately 33 percent of CP in full-term infants involves some disordered cells and layers due to cortical malformation deficits.

Cerebral palsy is not a unitary disorder; rather, it consists of many subtypes, which share the common symptoms of movement disorder, early onset, and no progression of the disorder (Nelson et al., 1994). Cerebral palsy is generally subtyped by the area of the body involved, level of difficulty experienced, and concomitant disorders.

Subtypes of Cerebral Palsy

Six subtypes of CP are currently identified, although some controversy exists in the field as to their delineation. The subtypes presented in this book have been adopted by many pediatric neurologists (Nelson et al., 1994; Thorogood & Alexander, 2007). They are spastic hemiplegia, spastic quadriplegia, spastic diplegia, extrapyramidal, atonic, ataxic, and mixed. These subtypes are based on the motor systems, the body regions, and the amount of impairment involved.

Spastic Hemiplegia

Children with this subtype show difficulties on one side of their body, with more arm than leg involvement. The right side of the body (left hemisphere) appears to be at the highest risk for involvement and is found in two-thirds of patients (Crothers & Paine, 1959). The child's walk is characterized by toe walking and swinging the affected leg in a semicircular movement when taking steps. Moreover, the affected arm does not follow the reciprocal movement usually seen in walking. The foot faces in toward the middle of the body, with hypotonia present throughout the limbs. The affected side often appears smaller and during development becomes noticeably smaller than the unaffected side. This condition frequently causes lower spinal and walking difficulties as the child develops (Nelson et al., 1994). Children with this type of CP may show cognitive retardation (28%) and seizure disorders (33%) (Aicardi, 1990). In addition, brain studies using MRI and CT scans have frequently found atrophy of the affected hemisphere with areas of cortical thinning, loss of white matter, and expansion of the same-side lateral ventricle (Uvebrandt, 1988).

*Spastic Quadriplegia*In contrast to spastic hemiplegia, spastic quadriplegia is characterized by increased muscle tone, with the legs the most involved (Nelson et al., 1994). Some difficulty with articulation and swallowing may be present when the corticospinal tract is involved. Almost half of children with this subtype are cognitively retarded or learning disabled (Robinson, 1973), and a large percentage have tonic-clonic seizure disorders (Ingram, 1964). These children also frequently have visual impairments. Children with this type of CP often have morphological abnormalities, generally in the white matter, including death of white matter, edema, and cysts (Chutorian, Michener,

Defendini, Hilal, & Gamboa, 1979). In addition to missing white matter in specific areas, the cortex underlying the white matter exhibits a thickening of the meninges and gliosis in the white matter (Nelson et al., 1994). Nelson et al. (1994) further report that these lesions can vary from one full hemisphere to one lobe, to a specified portion of a lobe. Some structural deviations are also found in the brainstem (Wilson, Mirra, & Schwartz, 1982).

Spastic Diplegia

Spastic diplegia generally involves both legs, with some arm involvement. This type of CP is commonly found in premature infants, with approximately 80 percent of infants with motor abnormalities showing this type of CP (Hagberg, Hagberg, & Zetterstrom, 1989). These children may later develop ataxia and frequently toe walk (Nelson et al., 1994). The clinical picture of children with spastic diplegia includes hypertonia with rigidity. Many children show generalized tonic-clonic seizures (27%) (Ingram, 1955), strabismus (43%) (Ingram, 1955), and cognitive retardation (30%, with increasingly higher rates as more extremely low birth weight babies survive) (Hagberg et al., 1989).

The brains of these children often evidence porencephalic cysts and microgyria (many small gyri) with abnormalities in tracts which serve the legs as they transverse the internal capsule (Christensen & Melchior, 1967). Atrophy, abnormal cortical formation, and periventricular lesions have been found to strongly correlate with severe impairment (Hagberg et al., 1989).

Extrapyramidal Cerebral Palsy

This type of CP involves problems with posture, involuntary movements, hypertonia, and rigidity (Nelson et al., 1994). Extrapyramidal CP can be further divided into choreoathetotic and dystonic CP.

Choreoathetotic Cerebral Palsy

This type of CP is characterized by involuntary movements that are very large and marked by slow, irregular, twisting movements seen mostly in the upper extremities. This type of CP has been most clearly associated with birth asphyxia and oxygen deprivation (Nelson et al., 1994). Use of ventilation and brain lesions due to asphyxia are frequently seen immediately after birth. Changes in the caudate nucleus are generally found, with cysts present where arteries and veins have swelled and neighboring cells are negatively affected (Volpe, 1987). Demyelinization is often present, with deviations in critical columns and neuronal loss in corticospinal tracts. An MRI study by Yokochi, Aiba, Kodama, and Fujimoto (1991) reported that a majority of children have basal ganglia, thalamic, and white matter lesions. In this subtype of CP, muscle tone will fluctuate between hypertonic, normal, and hypertonic. Choreiform movements are present in the face and limbs, and are asymmetric, involuntary, and uncoordinated (Nelson et al., 1994). Children with choreoathetotic CP frequently have speech production problems, with unexpected changes in rate and volume. The upper motor neuron unit appears to be affected, and this is frequently accompanied by seizures and cognitive retardation (Nelson et al., 1994).

Dystonic Cerebral Palsy

This form of CP is believed to be uncommon, with the trunk muscles being mostly affected. The trunk may be twisted and contorted, which affects the head's movement (Nelson et al., 1994).

Atonic Cerebral Palsy

Children with atonic CP have hypertonic and muscle weakness in the limbs. This type of CP is less common than the other subtypes and is associated with delayed developmental motor milestones. Its cause is unknown, and it is not known which brain region is affected in this subtype of CP (Nelson et al., 1994).

Ataxic Cerebral Palsy

Ataxic CP is associated with dysfunction of the cerebellum leading to difficulty with skilled

movements (Hagberg, Hagberg, Olow, 1975). Hypotonia, poor fine motor skills, and clumsiness are seen and identified late in the first year of life. Walking develops very late (three or four years of age), and frequent falling is observed in children with ataxic CP (Nelson et al., 1994). Findings of brain pathology in ataxic CP are inconsistent. Some researchers have found abnormality in the cerebellar vermis (Bordarier & Aicardi, 1990), while others have found differences in the cerebral hemispheres (Miller & Cala, 1989).

Neuropsychological Aspects of Cerebral Palsy

Neurocognitive deficits seem to progress as high risk children mature (Majnemer, Rosenblatt, & Riley, 1994). In a study by Majnemer et al. (1994), 23 healthy and 51 high risk neonates were tested at birth, one year, and three years. Findings included 13 (7%) delayed at age one year, increasing to 39 percent at age three. Those subjects who were high risk *and* normal at the neonatal stage had the most favorable outcome. Additional studies have found a decline in abilities in life (ages 18–25 years) that is attributed to ongoing psychological stress rather than to medical reasons (Pirnm, 1992).

The finding that many children with CP have concomitant learning disabilities, cognitive retardation, and attention-deficit disorders has implications for educational planning (Blondis, Roizen, Snow, & Accardo, 1993). This result, coupled with the finding by Majnemer et al. (1994), indicates not only that the needs of these children are multiple, but that they become more evident as the child matures.

In addition, localization of brain damage also has an impact on the type of learning difficulties experienced by children with CP. Children with motor difficulties appear to be at higher risk for deficits in arithmetic and visual-spatial skills than those who do not have such difficulties (Roussounis, Hubley, & Dear, 1993). In a further study of motor effects on visuospatial abilities, Howard and Henderson (1989) found that compared to athetoid CP and normal children, children with spastic CP showed more difficulty in visual-spatial judgment. These researchers also found that experience and training can improve skills dramatically.

Right-sided hemiplegia (left-hemisphere involvement) has been found to result in language impairment in girls, but not in boys (Carlsson et al., 1994). Similarly, in a study by Feldman, Janosky, Scher, and Wareham (1994) preschool boys with CP did not show language impairment. In children with right and left hemiplegia, both boys and girls showed significant impairment on nonverbal tasks. It was not clear why boys showed less language impairment. The extent to which these findings are related to other research showing gender differences between normal males and females for language lateralization is unknown. For example, Witelson (1990) indicates that women have more focused representation of language and speech functions in the anterior left frontal regions than men. Further research may add to our understanding of these gender differences in language deficits in children with CP.

Working memory, a skill associated with attention, has not been found to be an area of impairment for children with CP (White, Craft, Hale, & Park, 1994). White et al. (1994) taught children with spastic CP to utilize memory strategies such as covert and overt rehearsal in order to improve articulation skills. Impairment was found in phonemic discrimination in children with CP and speech impairment. Bishop, Brown, and Robson (1990) also reported that children with impaired speech and CP have difficulty discriminating same-different nonwords. There were no difficulties found in receptive language skills or in their ability to discriminate altered sounds in real words. Therefore, it appears that CP children with speech impairment do *not* show concomitant language problems, but do show phonological processing difficulty. Speech production ability has been found to correlate significantly with sound blending skills. Reading difficulties have not been found in this population to the same degree as arithmetic-based learning disabilities and visual-perceptual deficits (Rowan & Monaghan, 1989). This is somewhat surprising given the relationship between phonemic awareness deficits and reading disabilities in learning disabled samples. Reading deficits have also been shown in children who have both phonological and visuospatial deficits; so the absence of high rates of reading problems in CP groups is interesting.

Attentional skills in children with CP have been found to be deficient (Blondis et al., 1993). White et al. (1994) found that children with bilateral anterior lesions showed significant problems in focusing attention, while those with bilateral posterior lesions showed slower reaction times. These researchers interpreted their findings to indicate problems in visual attention when anterior lesions, particularly in the left hemisphere, occur. Using a dichotic listening paradigm, Hugdahl and Carlsson (1994) found significant auditory attentional difficulties in children with both left and right hemiplegia.

The most striking finding in the neuropsychology of CP children is the heterogeneity of problems experienced by this varied population. Early identification of CP, development of appropriate intervention program, and the use of a multidisciplinary team approach have been found to relate strongly to later success in school and life (Rowan & Monaghan, 1989). Kohn (1990) found a strong link between psychoeducational, family, and vocational support and positive outcome. She strongly recommends that pediatricians acquaint themselves with community resources and utilize early referrals to appropriate early childhood programs for young children with CP.

Psychosocial Correlates of Cerebral Palsy

Although parents of children with motor disabilities have been found to report more sadness, these symptoms have not been found to be strongly related to the child's rate of development or to parent-child interactions (Smith, Innocenti, Boyce, & Smith, 1993). Further studies of mothers with CP children have found that professionals who interact with these families disregard information provided by mothers (Case-Smith & Nastro, 1993). These difficulties are compounded by the frequent change in professionals who work with families. Perrin, Ayoub, and Willett (1993) found that mothers' feelings of control over their child's program were a potent predictor of the child's adjustment. This finding is important to consider when designing intervention programs for children with CP, and provides further evidence of the need for an integrated, transactional model.

Family interactions have been linked to the psychological adjustment of children, regardless of age and socioeconomic status (Perrin et al., 1993). Dallas, Stevenson, and McGurk (1993a) found that children with CP often are more passive and less assertive than their siblings and generally were treated as if they were younger than their chronological age. Maternal intervention between children with CP and siblings was found to be more common than with non-disabled siblings. Similarly, Dallas, Stevenson, and McGurk (1993b) found that the tendency toward sibling and maternal control of interactions resulted in lower self-efficacy and poorer development of social skills in children with CP.

The findings of Dallas et al. (1993a, 1993b) were supported by results of a study by King et al. (1993), who found lower self-efficacy and self-control on self-report measures in a group of male and female children with CP. Level of social self-efficacy was found to be a good predictor of the adolescent's later independence and persistence. A follow-up study of adults with motor disabilities found that they were more frequently unemployed, left the parental home at a later age than normal peers, and completed less schooling (Kokkonen et al., 1991). Recommendations were for earlier vocational training and support and additional family assistance for individuals with CP. Moreover, for adults who received such support in adolescence, self-esteem and self-efficacy measures have not found them to differ from typical adults (Magill-Evans & Restall, 1991). A cognitive-behavioral approach to social skills and assertiveness training appears to meet the needs of adolescents with CP.

Implications for Treatment

Many children with CP receive comprehensive services in educational settings, including physical and occupational therapy, language and communication therapy, and academic instruction (Thorogood & Alexander, 2007). Assistive technologies, including augmented communication devices, have revolutionized treatment options and the functional abilities of children with CP. Synthesized and augmented speech devices, specially designed computers and other electronic devices are commonly used.

Physical and occupational therapy often centers on movement therapy as well as adaptive equipment to improve motor development and mobility. Stretching, range of motion, progressive resistance and strengthening, postural and motor control are typical physical therapy activities (Thorogood & Alexander, 2007). Orthotic devices may also be helpful. Occupational therapy generally focuses on increasing daily living skills and may also incorporate adaptive equipment.

In a study to determine the effects of constraint-induced movement therapy, Sutcliffe, Gaetz, Logan, Cheyne, and Fehlings (2007) found increased motor function in a child with hemiplegia CP. Three weeks of therapy also produced changes in brain activity and cortical reorganization six months following therapy. This is the first study to document cortical reorganization and shows great promise for other children with hemiplegia CP.

Other researchers have established motor development curves for children with CP. Five distinct patterns of motor development were created after careful assessment of a full spectrum of CP in children from one to 13 years of age (Rosenbaum et al., 2002). These curves can be helpful for parents, therapists, and educators for planning short- and long-term treatment plans for children with CP, and to measure therapeutic progress.

Finally there are several medical treatments that may be necessary for some children with CP, including surgery to reduce spasticity, skeletal muscle relaxants and neuromuscular blocker agents (e.g., baclofen, dantrolene, diazepam, botulinum).

Conclusions

Children with CP are more different from one another than the same on neuropsychological measures. What they seem to have in common is the need for early intervention that is tailored to their specific needs and provides vocational and family support. A transactional approach is particularly relevant for this population given the findings that when psychoeducational objectives, vocational training, and parental support are interwoven, the child's later outcome is most optimal. For these children, the neuropsychologist needs to move beyond the diagnostic role into the role of advocate and counselor. The Americans with Disabilities Act of 1990 empowers disabled adults, children, and adolescents to gain the vocational and educational training needed for life success. The extent to which we can foster this kind of ecologically valid intervention may mean the difference between developing individuals who are self-reliant, self-sufficient, and independent or semi-independent.

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