

Chapter 15

Childhood Cancer

Childhood cancers, though relatively rare, are found in children at all ages. The two most common forms of childhood cancer are childhood leukemia and brain tumors. Although the etiologies for these disorders differ, treatment frequently involves chemotherapy and cranial irradiation. The chemotherapy regimen has not been found to have the same effects on later outcome that irradiation produces. It is these “late effects” that most concern the child neuropsychologist. Many more children are surviving given the improvement in treatment over the past few decades. Survival for brain tumors is approximately 70 percent (Brenner, 2003) and above 70 percent for acute lymphoblastic leukemia (ALL) (Gatta, Capocaccia, Coleman, Ries, & Berrino, 2002).

Childhood cancer includes leukemia, brain tumors, and tumors outside the CNS (i.e., kidney). These diseases are, by definition, life threatening and pose challenges in all areas of the child’s life as well as in family functioning. Initially the emphasis is on securing appropriate treatment and undergoing procedures which are unpleasant and frequently painful. These treatments can extend for years in the child’s life and are fraught with anxiety and stress. For example, treatment for acute lymphoblastic leukemia (ALL) can last for 3–4 years prior to remission. During this time there are numerous doctor visits, hospitalizations, and procedures.

Treatment of childhood cancer in the central nervous system (CNS) varies depending on the type of tumor, the level of malignancy, the location of the tumor, the age of the child, and how much tissue is involved. Treatments include surgery and irradiation as well as chemotherapy. Damage from

surgery depends on the extent of the tumor and the involvement in the CNS. Surgery has proven to be less damaging, generally, than radiation and/or chemotherapy (Beebe et al., 2005; Moore, 2005). Surgery is utilized for brain tumors while ALL is treated via radiation and/or chemotherapy. Each of these types of childhood cancers will be discussed in the following sections. Emphasis will be on the neuropsychological aspects of brain tumors and ALL, as well as the family and psychosocial variables in the treatment and recovery for these children.

Neuroimaging in Childhood Cancer

Studies of brain imaging with children with ALL and brain tumors have found that the treatment has significant effects on the brain. Demyelination and lesions in the white matter are found following chemotherapy and irradiation (Burger & Boyko, 1991). Difficulties have also been found in the white matter with intrathecal chemotherapy (ITC), and particularly with the chemotherapy agent, methotrexate (Hudson, 1999).

In the past 10 years, methotrexate treatment was associated with a stroke-like syndrome that included hemiparesis and aphasia and occurs in 3–10 percent of the ALL population (Creutzig et al., 2005; Pui & Evans, 2006). It has been suggested that these difficulties are due to problems with blood perfusion (Laningham et al., 2007). These difficulties are generally monitored and treatment is stopped temporarily for approximately a week until the symptoms subside.

Another issue is the significantly increased risk of CNS neoplasms in children who have undergone cranial irradiation for brain tumors or leukemia (Neglia et al., 2006; Paako, Talvensaaari, Pyhtinen, & Lanning, 1999). Leukemia survivors had more gliomas than meningiomas (tumors in the meninges) while children with previous brain tumors developed more meningiomas. These tumors occurred within the first nine years following diagnosis for gliomas, and 17 years for meningiomas (Laningham et al., 2007). Approximately 20 percent of survivors were found to develop neoplasms (Pui et al., 2003).

White matter involvement appears to be present in children with ALL or brain tumors following treatment, particularly with methotrexate. Findings of a smaller volume in the cerebral white matter suggest white matter injury following the major treatments (Reddick et al., 2005). A relation between this white matter injury and cognitive ability has been found, particularly for patients with medulloblastomas (Mulhern, Reddick, & Palmer, 1999). When the white matter is compromised in the cerebral hemispheres, particularly in the frontal lobes and the anterior cingulate gyrus, attention and executive functioning abilities are affected (Mulhern, White, & Glass, 2004; Reddick et al., 2005).

This change in white matter may well interfere with normal development once treatment has ended. The disruption to the brain in its ability to transfer neuronal impulses likely interferes with learning as well as with speed of information processing. As is evident from the following sections on brain tumors and ALL, difficulties are frequently present in attention and problem solving skills that are associated with frontal white matter development (Semrud-Clikeman, Pliszka, Lancaster, & Liotti, 2006).

Brain Tumors

Brain tumors are estimated to constitute 20 percent of malignancies of childhood, and are most frequently diagnosed in children between the ages of three and nine years (Sklar, 2002). Treatment protocols often include whole-brain radiation, chemotherapy, and/or surgical interventions, and 50 percent to 60 percent of children are cancer-free after five years (Butler & Haser, 2006).

Survival from brain tumors varies depending on the type of tumor present. Medulloblastoma is the most common type of malignant tumor in children and the survival rate is approximately 65 percent. In contrast, children with brain stem gliomas show a less than 10 percent survival rate. For the majority of children with brain tumors of all types, the survival rate is approximately 65 percent.

Associated Features

Risk factors associated with the development of brain tumors include: (1) genetic syndromes, including neurofibromatosis and tuberous sclerosis; (2) presence of epilepsy and stroke in families of children with brain tumors; (3) immunosuppression prior to organ transplant, and (4) infections (Connelly & Malkin, 2007; Shaw & Infante-Rivard, 2006). Some environmental toxins (e.g., aromatic hydrocarbons) have been implicated, as have maternal use of barbiturates, heat, and prenatal exposure to X-rays (Bunin, Robison, Biegel, Pollack, & Rorke-Adams, 2006; Umansky, Shoshan, Rosenthal, Fraifield, & Spektor, 2008).

Types of Tumors

The most frequently diagnosed type of tumor is the astrocytoma. In an epidemiological study of malignant brain tumors in children under the age of 15, astrocytomas accounted for 57 percent of the tumors, while 23 percent were medulloblastomas and 8 percent were ependymomas (Briere, Scott, McNall-Knapp, & Adams, 2008; Burzynski, 2006; Lum, Halliday, Watson, Smith, & Law, 2006). Although brain tumors can occur at any age, the five- to nine-year-old interval shows the largest occurrence, followed closely by ages 0–4 years and 10–14 years of age (Scott, Elkin, & Thompson, 2001). Poorer outcome, particularly in cognitive development, has been found for children diagnosed at an early age (Mulhern et al., 1998).

In children under age two, the most common types of tumors are medulloblastomas (in the medulla portion of the brainstem), low-grade

astrocytomas, and ependymomas (arising from the lining of the ventricles and spinal cord or ependyma). At ages 5–9, the most commonly diagnosed tumors are low-grade astrocytomas, medulloblastomas, high-grade astrocytomas, and cerebellar astrocytomas (Zhou et al., 2008). Children with astrocytomas in the cerebellum have had the highest survival rates, while those with brainstem gliomas have the poorest survival rate. Astrocytomas are graded from 1 to 4, depending on the degree of malignancy. The lower grade of a tumor indicates less malignancy.

Implications for Assessment

Accurate and timely diagnosis of brain tumors is especially important. Clinical manifestations may include changes in personality and cognition, and neuropsychological changes, depending on the type, size, and location of the tumor, and on the presence of cerebral edema (e.g., hydrocephalus and/or increased intracranial pressure). Tumors may be preceded by nausea, headaches, visual deficits (e.g., blurred or double vision, visual field blindness), lateralized sensory or motor impairments, vomiting, or seizures. Presence of these symptoms warrants immediate referral to a child neurologist and may necessitate CT scans or other neuroradiological scans (e.g., MRI). Low-grade tumors often have a gradual rather than acute onset, with neural tissues becoming compressed or displaced at a slow rate (Nortz, Hemme-Phillips, & Ris, 2007). Consequently, neurological signs may not always appear early. Brain tumors have been shown to produce behavioral, personality, academic, intellectual, and neuropsychological deficits in children (Butler & Haser, 2006).

Implications for Assessment

Cognition

Intellectual and academic declines have consistently been found for children who had cranial radiation therapy (CRT) (Reimers et al., 2003). The age at

which treatment commences appears to have a significant effect on resulting intelligence test scores. Some have found that the late effects that occur after radiation begin approximately one year after treatment and can steadily worsen with development (Ris, Packer, Goldwein, Jones-Wallace, & Boyett, 2001).

A review of 12 studies of children treated for medulloblastoma or ependymoma found that those treated with CRT showed IQ declines over time, with the youngest patients showing the greatest decline in ability (Mulhern, Merchant, Gajjar, Reddick, & Kun, 2004). Those who had surgery or irradiation confined to the back of the brain (posterior fossa) showed less decline in IQ. The declines that have been found after treatment appear to be in the first few years after treatment (Spiegler, Bouffet, Greenberg, Rutka, & Mabbott, 2004). These declines are not due to regression, but rather to an inability to learn new skills and information (Palmer et al., 2003). In addition, children with higher ability levels have been found to show the most decrement in ability (Ris et al., 2001).

Academically children with brain tumors have significant deficits in learning, particularly in mathematics (Buono, Morris, & Morris, 1998). Those who have an accompanying diagnosis of hydrocephalus show the most difficulty in academics and often require special education (Mabbott et al., 2005). For all of the children with cancer, younger children were found to be at highest risk for later reading difficulties, spelling, and mathematics, while behavioral functioning was found to be within normal limits by parent and teacher report.

Attention

Additional difficulties have been found in memory, attention, and processing speed. Children treated at the youngest ages had the most severe deficits in these areas (Maddrey et al., 2005). Focused and sustained attention appear to be most directly affected in these children (Reddick et al., 2005). In addition, problems have been found in selective attention, cognitive flexibility, and processing speed (Briere et al., 2008; Reeves et al., 2005).

Visual-Spatial Perception

Difficulties have also been found in visual-motor integration, visuo-spatial organization, and poorer performance IQ abilities (Beebe et al., 2005; Carpentieri et al., 2003), particularly when these problems were present comorbidly. This profile is similar to that of children diagnosed with nonverbal learning disabilities and is found most frequently in children treated with radiation therapy and chemotherapy (Anderson, Godber, Smibert, Weiskop, & Ekert, 2000). Girls may be at higher neuropsychological risk following treatment for brain tumors compared to boys (Ris et al., 2001).

Memory

Memory skills have been problematic for children following brain tumor treatment. Children treated with radiotherapy have exhibited poorer memory skills on all aspects. Radiotherapy treatment, location of the tumor, and shunt for hydrocephalus were strong risk factors for memory difficulties (Reimers, Mortensen, & Schmiegelow, 2007). When FSIQ was used as a covariate, the presence of a shunt or tumor location within the hemispheres became more predictive of memory difficulties than did radiotherapy.

Pathways involved in memory are located in the temporal lobe extending into the third ventricle region. Children who had a tumor in this region showed poorer verbal memory skills than those with cerebellar tumors (King et al., 2004; Mickelwright, King, Morris, & Morris, 2007). In addition, those children with tumors in the cerebellum were found to experience significant problems with repetition and attention span (Steinlin et al., 2003).

Social-Emotional

Findings have indicated that there are social, emotional, and behavioral difficulties following treatment for brain tumors. Among children who had surgical treatment, 56 percent of the participants

showed sufficient psychological distress that qualified for diagnoses of depression or externalizing behavioral difficulties (i.e., oppositional defiant disorder)(Meyer & Kieran, 2002). Another study found that children with a brain tumor history were evaluated for social skills difficulties. Findings indicated significant problems with socialization as well as a decrement in nonverbal reasoning abilities (Carey, Barakat, Foley, Gyato, & Phillips, 2001).

Most have not found lasting social-emotional dysfunction in children following cancer (Nortz et al., 2007). Some difficulties have been found in social withdrawal and in social skills for some children with brain tumors (Poggi et al., 2005). Family dysfunction following a child's brain tumor treatment has been found, with post-traumatic stress disorder being reported in families of cancer survivors (Kazak, Alderfer, Rourke et al., 2004; Streisand, Kazak, & Tercyzak, 2003). Poorer adjustment was found for children with lower IQs and poorer adaptive functioning, single-parent families, a chaotic family environment, and low socioeconomic status (Carlson-Green, Morris, & Krawiecki, 1995).

Summary

Thus, late effects of brain tumor treatment generally have an impact on academic, intellectual and neuropsychological functioning. Mediating factors such as the amount of radiation, pre- and post-operative status, complications (e.g., shunts, infections), and the extent of the tumor, as well as the age of onset, all affect the child's outcome. Additional study is needed on the quality of life children with brain tumors enjoy and on the level of their psychosocial functioning.

Childhood Leukemia

Leukemia means white blood. There are two types of blood forming cells, myeloid and lymphoid. Myeloid cells mature into red blood cells while lymphoid cells mature into white blood cells, including

B cells and T cells. This maturation is altered in leukemia and the ability of these cells to mature is impaired. There are two types of leukemia based on the cells that are affected: acute lymphocytic leukemia (ALL) which is 75–80 percent of all childhood leukemias, and acute myelogenous leukemia (AML) which is 20–25 percent of all cases (Colby-Graham & Chordas, 2003). Chronic forms of leukemia are uncommon in childhood and will not be discussed in this chapter. AML is less common and less is known about the neuropsychology of this disorder. The emphasis in this chapter will be on ALL.

Children with acute lymphocytic leukemia (ALL) experience significant learning difficulties similar to those of children with brain tumors. ALL accounts for approximately 75 percent of leukemia in children and is the most common type of cancer in childhood (Butler & Haser, 2006). ALL generally presents with initial symptoms of bleeding, fever, irritability, fatigue, and bone pain. Ninety-five percent of children with ALL survive, and 55 percent of those continue in remission five years after treatment (Spix, Eletr, Blettner, & Kaatsch, 2008; Yamamoto & Goodman, 2008). The peak age of onset is between the ages of three and five. ALL is more common in Hispanics and whites than in African-Americans, and in boys more than in girls. Genetics, environmental factors, and viruses have been implicated in the etiology of ALL. There is a one in five chance that an identical twin of a child with ALL will also have the disease (Zipf et al., 2000).

Belson, Kingsley, and Holmes (2007) report that many heritable syndromes as well as immunodeficiency disorders may be related to an increased risk of developing leukemia. Exposure to X-rays either pre- or postnatally is also associated with a higher risk for leukemia. Finally, several viral infections seem to co-occur with childhood leukemia (e.g., Epstein-Barr, human T lymphonea-leukemia virus). Environmental risk factors include radiation, hydrocarbons, and pesticides. Additional risk factors that have been identified are present for mothers who are 35 years or older at conception, large birth weight, neonatal jaundice and women who had two previous pregnancies which ended in early fetal death (Podvin, Kuehn, Mueller, & Williams, 2006).

Important Variables

Important prognostic indicators are initial white blood cell count, sex, age at diagnosis, CNS therapy, degree of lymph node enlargement, hemoglobin level, and platelet count at diagnosis. Initial white blood cell count (WBC) and age at diagnosis are strong predictors for length of remission and survival (Brenner et al., 2001). Patients who are younger than two or older than 10 and who have high WBC have the poorest prognosis.

Symptoms usually occur 1–6 weeks prior to diagnosis and can vary from child to child. During this time the bone marrow has been replaced by the leukemic cells which decrease red blood cells, white blood cells and platelets. Anemia is frequently present, which decreases the oxygen carrying ability of the red blood cells. Symptoms accompanying anemia include fatigue, lethargy, and headache as well as pale skin, nail beds, and the inner lining of the mouth. Cranial nerves can also be involved, particularly in the third (eye movement), sixth (tongue and pharynx), and seventh (face) nerves (Margolin, Steuber, & Poplack, 2002).

Treatment

Treatment differs depending on the risk factors, and patients with more risk factors are generally more aggressively treated. In contrast, those children who are at lower risk are treated by less toxic and less intensive means. There are three stages of treatment: remission induction, consolidation, and maintenance. The first stage, based on National Cancer Institute guidelines, uses age and white blood cell count as indicators to determine the degree of treatment. Children aged 1–9 years of age and with a white blood cell count less than 50,000 mm³ show the best prognosis and are treated with less chemotherapy during induction than those outside of these guidelines (National Cancer Institute, 2002). Generally, post induction begins 29 days after induction has started. It is determined by how the child responds to treatment, the child's age, and the white blood cell count at diagnosis (Colby-Graham & Chordas, 2003).

The goal of treatment is to induce a remission, and approximately 95 percent of children with ALL are in remission 3–4 weeks after treatment begins (Chessells, 2000). During consolidation treatment the remission is strengthened through intensification of treatment. Methotrexate is the most common medication used during this time and has been found to be highly effective (Pui, 2000). During maintenance therapy a long-term, low dose treatment regimen is used often with daily doses of a cancer medication (often 6-mercaptopurine) and weekly doses of methotrexate with additional steroids as needed. Treatment occurs over a period of 2–3 years and has resulted in fewer relapse rates than those with shorter treatment periods (Chessells, 2000). Children who have had chemotherapy for ALL are at a higher risk for the development of brain tumors.

Intrathecal chemotherapy is used to reduce the possible spread of leukemia to the CNS (Westlake & Bertolone, 2002). For those children at highest risk additional cranial spinal radiation is used. Such treatment is used cautiously since it can cause lowered cognitive functioning, poorer psychomotor skills, and disruptions in neuroendocrine functioning (Margolin et al., 2002).

Neuropsychological Effects of Treatment

Neuropsychological impairment has been found in children treated with low doses of cranial radiation (1,800 rads). Declines in intelligence have been found in children who have undergone cranial radiation, with the most profound effects in younger and brighter patients. Studies in the 1980s and 1990s found that cranial radiation therapy was very detrimental to the child's cognitive and neuropsychological deficits (Butler & Haser, 2006). CRT is not used as often, except for children who do not respond well to the traditional methods. Chemotherapy has been evaluated with regard to late effects and, generally, has not been found to be as detrimental to the child's cognitive and neuropsychological development as CRT, although some difficulties are present even with chemotherapy (Espy et al., 2001).

Attentional deficits that affect the encoding of new materials have been found to be the most significantly affected in children following treatment for ALL (Lockwood, Bell, & Colegrove, 1999). Particular problems were found for those children who received CRT prior to five years of age. Difficulties were found in focusing and shifting of attention, cognitive flexibility and problem solving skills. Those children who had CRT at age five years or older had milder problems with attention, sustained attention and cognitive flexibility (Schatz, Kramer, & Albin, 2004).

When children are treated with intrathecal chemotherapy (ITC) alone, findings are of average academic attainment and normal cognitive development. Declines are found in visual-motor integration, verbal fluency, and arithmetic skills (Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veeman, 2005; Espy et al., 2001). Girls are more significantly affected on nonverbal skills while boys with ALL have not shown such difficulties (Brown, Madan-Swain, & Walco, 1998).

A meta-analysis of the studies evaluating neurocognitive outcome following treatment of ALL evaluated 28 empirical studies (Campbell et al., 2007). The effects were uniformly negative with significant deficits present for survivors of ALL in cognitive ability and academic achievement in the areas of reading, arithmetic, and spelling. In addition, significant deficits were found in attention, speed of information processing, visuo-spatial ability, verbal memory, visual memory, and fine motor skills. Therefore, these results suggest that these domains that should be particularly evaluated during a neuropsychological assessment. Difficulties with mathematics for children with ALL were found to be related to attentional problems (Buizer, de Sonnevile, Van den Heuvel-Eibrink, & Veerman, 2006). Difficulties have also been found in speed of information processing (Reeves et al., 2007). Sluggish cognitive tempo was found in survivors of ALL which, in turn, creates problems following lectures and completing homework; all difficulties that impact the child's functioning in the classroom. Some difficulties have also been found in visuomotor control, particularly when it requires the child to quickly trace a figure that is moving around a screen (Buizer, de Sonnevile, Van den Heuvel-Eibrink, Njikiktjen, & Veerman, 2005).

Analysis of the behavioral functioning of children with childhood cancer has found symptoms that are consistent with a diagnosis of ADHD (Mulhern et al., 2004a). Further study has found that childhood cancer survivors frequently have problems with attention, oppositional behavior, and in cognition (Helton, Corwyn, Bonner, Brown, & Mulhern, 2006). Children with childhood cancer are also more likely to be compared to their siblings to reveal problems with mood, antisocial behaviors, and attention-deficit (Schultz et al., 2008). In this study survivors from brain tumors and ALL were not differentiated.

Based on the current state of the research, many unknowns remain. While it is fairly clear that there are some neuropsychological problems associated with treatment, the range of the difficulty, relation to dose and type of treatment has not been established. Further study is needed to more completely understand the areas of difficulty that continue to be present for the child and his/her family.

Family Issues

The ability of parents to cope with the child's disease appears strongly related to the child's coping level (Kazak et al., 2001). Some of the difficulties found in these families include increased marital discord, financial difficulty brought on by medical costs, anxiety, sibling adjustment problems, and discordant family life. Mothers appear to be at highest risk for developing depression following treatment, possibly due to being most responsible for the daily care of the child and the demands required by the medical care for the cancer (Sahler et al., 2005). Financial issues are also present, as well as the fear of the child's death. These issues affect the entire family including the siblings. Despite all of these stressors, nearly 70 percent of these parents report stable and close marriages (Manne et al., 2001). For families with limited English fluency, lower socioeconomic status, lower educational levels, and lack of insurance, the difficulties are compounded when a child is very ill, particularly with cancer (Kodish et al., 2004; Kouyoumdjian, Zamboanga, & Hansen, 2003). Certainly further study is needed in these areas in order to provide support for the child as well as his/her family.

Interventions for Childhood Cancer

One of the main psychological treatments for childhood cancer survivors is the use of cognitive remediation. Reviews of the literature have found that brain injury rehabilitation shows mild to moderate improvement of functioning (Cicerone et al., 2000; Cicerone et al., 2005). A major program that has been developed is the Cognitive Remediation Program (CRP) (Butler, 2007) which has adapted practices from brain injury rehabilitation, special education, and clinical psychology sources. This program consists of 25 two-hour sessions and significant improvement has been found on attention and response inhibition following the program (Butler & Copeland, 2002; Butler & Mulhern, 2005). It includes practicing specific skills, teaching of problem solving strategies, and cognitive-behavioral interventions. In addition, it includes the Attention Process Training cognitive remediation program developed by Sohlberg and colleagues (Sohlberg & Mateer, 1999). A multicenter clinical trial of this program found improved attention and academic achievement skills in children with childhood cancer (Butler et al., 2008). The findings were of modest effects and the authors caution researchers and clinicians against the belief that the child's functioning will return to pre-disease states.

Another approach to cognitive rehabilitation involves teaching problem solving skills directly to mothers of children newly diagnosed with cancer (Sahler et al., 2002). The eight-week group experience utilizes a cognitive behavioral approach and includes homework assignments that are tailored to the individual mother's difficulty. Empirical validation of the program has found moderate effect sizes for improvement. In addition, the improvement continued on reevaluation three months later, particularly in the areas of problem orientation as well as in ability to take responsibility and control of areas of difficulty (Sahler et al., 2005).

Another program that has been used to reduce the distress felt by families and survivors after treatment ends is the Surviving Cancer Competently Intervention Program (SCCIP) (Kazak et al., 1999). This intervention involves four sessions conducted over one day. Sessions 1 and 2 teach the use of cognitive-behavioral principles to help relieve sadness and emotional distress and generally

involve separate groups of survivors, parents, and siblings. Sessions 3 and 4 utilize family therapy with the entire family unit. For session 1 the discussion is conducted for each group on “how cancer has affected me and my family.” In session 2, in the separate groups, specific cognitive-behavioral techniques are taught, including self-talk issues, adversity-beliefs-consequences model, and reframing of issues. For session 3 the families are reconstituted and meet all together. Information about cancer and recovery is provided, and families have an opportunity to role-play different situations. For example, some would be selected to play the ‘mother’ role, and as they talk about how cancer has affected them (as mothers), the rest of the group listens. This exercise is repeated for survivors, fathers, and siblings. In session 4 the individual families work together on a task that involves the family members’ different perceptions about what has happened and how others are coping with the problem. These questions are formulated by the family and put into writing; at the end of this session all families come back together and share their answers. Empirical validation of this approach has found that emotional adjustment and post-traumatic stress improved directly after the intervention, and again when retested 3–5 months later (Kazak, Alderfer, Streisand et al., 2004).

Social skills training has also been emphasized as a supportive intervention during school reintegration. The training program that has been designed includes social-cognitive problem solving, assertiveness training, and how to manage teasing and bullying (Barakat et al., 2003). This program was found to improve functioning for children with brain tumors in social competence and in emotional distress.

Educational Interventions

In addition to the emotional and adjustment issues, educational interventions have also been utilized. One of the major difficulties is reintegration into school following treatment. Many cancer centers have a protocol for such re-entry. These programs raise awareness for parents and teachers about the child’s needs, both educational and medical,

provide information for the child’s peers, and develop an appropriate IEP (Mitby et al., 2003). A comprehensive program involves school personnel for further information and offers consultation for issues that can arise. Studies have found that children who receive appropriate interventions upon school re-entry exhibit improved reading and written language skills during the first two years of re-entry (Anderson et al., 2000). Others have found that close monitoring of the child’s progress and direct teaching of skills does not increase the child’s ability to progress in mathematics and reading (Goldman, Briery, Ward, Delgado, & Armstrong, in press; Nortz et al., 2007).

Pharmacological Interventions

Methylphenidate (Ritalin) has been utilized to treat the attentional problems frequently seen in children recovering from childhood cancer and has been fairly successful in alleviating these difficulties. In one study of 32 children with a history of brain tumors or ALL who were administered methylphenidate, improvement was found for every child on sustained attention tasks, compared to placebo (Thompson et al., 2001). These findings were further replicated in a study utilized a three-week, randomized and placebo double-blind procedure (Mulhern et al., 2004b).

Case Illustration

Brian was 14-years- and eight-months-old when seen for a neuropsychological evaluation. He was diagnosed with a cancerous brain tumor at age eight which was removed from the posterior right area of his brain. Chemotherapy was utilized for treatment and the cancer was not evident in the past three MRI scans. His initial neuropsychological examination conducted at age 10 indicated some difficulty with language, processing speed, and with sadness. He was being reevaluated at his mother’s request due to concerns about increased feelings of anxiety, withdrawal, and possible depression. Brian had completed eighth grade the past year and was

entering high school in the fall. His mother reported that he was in speech and language services as well as in occupational therapy in middle school. Brian's current IEP called for support in all academic classes in high school through a study hall, as well as continued language therapy. He was dismissed from occupational therapy classes. He was not prescribed any medications and has not entered into therapy.

Behavioral Observations

Brian came to the testing session willingly and was cooperative and forthcoming on all measures. He was attentive to the work at hand and was diligent in completing the tasks presented to him. Brian's mood was somber and quiet. While he answered all questions, he did not readily volunteer any additional information. Brian's language was to the point and he did not elaborate on any ideas or thoughts. He became somewhat frustrated on the language portion of the WISC IV and at times would answer "I don't know" very quickly. However, when pressed to answer, Brian would provide a reasonable answer.

Tests Administered

WISC IV, WJ III, Children's Memory Scale, Sensory Perceptual Examination, CELF-3, Purdue Pegboard, DKEFS Trails, Sorting, and Color-Word Interference test, BASC—parent, adolescent, teacher forms.

Test Interpretations

Brian achieved a Full Scale IQ of 81 on the WISC III which places him at the 10th percentile and in the below average range of intellectual functioning. His verbal comprehension score of 77 is in the below average range while his perceptual reasoning score of 92 is in the average range. There is a difference of 15 points between these abilities which is significant,

but not unusual. His working memory scores are in the average range at a standard score of 97 while his processing speed abilities are in the below average range at 78. There is a significant difference between his perceptual reasoning skills and all of the indices indicating that Brian's nonverbal abilities are relatively better developed than his language skills.

Brian's achievement skills indicate that his overall achievement is in the low average range with a standard score of 87 and a percentile of 20. His skills in reading are in the low average range overall and commensurate with his ability. This finding is true in his broad mathematics skills as well as in his writing ability. His poorest score is in the area of reading fluency and in story recall. In order to further evaluate Brian's language and memory skills, the Children's Memory Scale and the CELF-3 were administered.

On the Children's Memory Scale Brian scored in the average range on all tasks. His verbal memory was in the average range for both immediate and delayed conditions. His visual memory was also in the average range for all conditions. Brian showed some difficulty with attention and concentration on the CMS, particularly when asked to complete work in a distracting environment.

On the CELF 3 Brian achieved scores in the below average range for expressive language and in the low average range on measures of receptive language. He showed particular difficulty on tasks that required him to understand relationships between words, and categorize words into appropriate semantic relationships. He had great difficulty in constructing sentences using selected words as well as in using correct nouns and verbs. These scores are consistent with the difficulty Brian experienced on the WISC III in the areas of vocabulary and comprehension.

The TOVA was also administered to determine whether Brian was experiencing significant problems with attention. His scores were in the at risk range, but not significantly indicative of an attentional difficulty. An interview with his mother indicated that Brian met five of the nine inattention criteria, and two of the impulsivity/hyperactivity criteria. Although he does not meet criteria for a diagnosis of ADHD, his attention difficulty is present and particularly evident in situations that require complex processing or processing of material quickly.

Parts of the Delis-Kaplan Test of Executive Functioning (DKEFS) were also administered to evaluate Brian's cognitive flexibility, working memory, and ability to inhibit. On the Trails portion of the DKEFS Brian showed good ability in all areas. On the measure of verbal fluency Brian found it difficult to generate as many words as possible to a selected letter. Brian's response inhibition on the Color-Word Interference subtest was well within the average range. These findings are consistent with the results of the WISC IV working memory subtests which were within the average range for Brian's age.

The Purdue Pegboard was administered in order to determine whether Brian showed any difficulty in the area of fine motor dexterity. Brian showed significant problems with his dominant (right) hand on this measure, but not with his nondominant hand. These findings are consistent with right-sided difficulty on the measure of fingertip writing. Brian experienced 13 errors with his right hand, but none with his left. On the tactile, auditory, and visual tests Brian scored well within the average range.

Psychosocial evaluation indicated concerns by his mother as to Brian's feelings of anxiety and depression. He scored in the significant range on these scales on the BASC-Parent form. The teacher forms indicated significant concerns about anxiety, depression, and withdrawal. Brian achieved no scores in the clinically significant or at risk range on the self-report.

An interview with his mother indicated the likely presence of a mood disorder for Brian as well as significant problems with language. Although Brian scored within the average to low average range on achievement tests, his mother and teacher reported significant problems in the classroom with processing instruction, following directions, and completing homework appropriately. These findings are consistent with the difficulties identified by the neuropsychological evaluation of left-hemispheric dysfunction. Brian's problems with language, right-handed fine motor tasks, and processing of information quickly are all consistent with this area of concern. Given that the tumor was located in the left temporal region, it is likely that these difficulties are related to the treatment of the tumor as well as to residual difficulties. It was recommended that Brian have a follow-up MRI to

evaluate the integrity of his brain at the current time. At follow-up it was found that Brian's tumor had recurred and surgery was again needed to resect it. Radiation was utilized at that time to further treat the tumor and Brian was scheduled for a re-evaluation of his abilities in three months following the end of treatment. It was also strongly recommended that Brian begin treatment for his mood disorder. In addition, consultation with his school and teacher was strongly recommended. Following treatment for his brain tumor and the subsequent radiation treatment, Brian re-entered his ninth grade year and was provided additional support on his IEP. Although he continued to struggle with his language skills and his right-sided coordination, he responded very well to therapy and was placed on an antidepressant which lightened his mood. He also reported that he was experiencing improvement in his ability to complete his work and participate in class. He went on his first date to the homecoming dance and had re-established friendships with his peers.

Psychometric Summary

WISC IV

Scale/Subtest	Standard/Scaled score	Percentile
Full Scale IQ	81	10
Verbal Comprehension	77	6
• Similarities	7	16
• Vocabulary	6	9
• Comprehension	5	5
• Information	7	16
• Word Reasoning	9	37
Perceptual Reasoning	92	30
• Block Design	7	16
• Picture Completion	13	84
Working Memory	97	42
• Digit Span	11	63
• Letter-Number Sequencing	8	25
• Arithmetic	6	9
Processing Speed	78	7
• Coding	4	2
• Symbol Search	8	25
• Cancellation	9	37

WJ III Achievement

Cluster/Test	Standard score	Percentile
Total Achievement	87	20
Broad Reading	91	14
• Letter-Word ID	88	21
• Passage Comp	93	31
• Reading Fluency	80	9
Oral Language	86	18
• Story Recall	82	11
• Understanding Directions	91	27
Broad Math	93	33
• Calculation	99	47
• Math Fluency	90	25
• Applied Problems	92	30
Broad Written Language	101	53
• Spelling	98	45
• Writing Samples	112	79
• Writing Fluency	100	50
Supplemental Test		
• Word Attack	94	35

Children's Memory Scale

	Standard score	Percentile
General Memory	93	32
Verbal Memory Immediate	103	58
Verbal Memory Delayed	88	21
Visual Memory Immediate	94	34
Visual Memory Delayed	94	34
Learning	88	16
Attention/Concentration	82	12
Delayed Recall	94	34

CELF-3

Scale	Standard score	Percentile
Total Language Score	81	10
Receptive Language Score	86	18
• Concepts and Directions	10	50
• Word Classes	7	16
• Semantic Relationships	6	9
Expressive Language Score	78	7
• Formulated Sentences	6	9
• Recalling Sentences	8	25
• Sentence Assembly	5	5

Delis-Kaplan Test of Executive Functioning

Scale	Scaled score
Trailmaking	
• Visual Scanning	12
• Number Sequencing	14
• Letter Sequencing	14
• Number-Letter Sequencing	12
• Motor Speed	12
Verbal Fluency	
• Letter Fluency	7
• Category Fluency	12
• Category Switching	9
• Category Switching Accuracy	10
Color-Word Interference	
• Color Naming	11
• Word Reading	11
• Inhibition	12
• Inhibition/Switching	12

Purdue Pegboard

Dominant	Z score	-1.7
Nondominant	Z score	.2
Both Hands	Z score	-1.22

Behavior Assessment System for Children (BASC)-Parent

Scale	T Score	Percentile
Internalizing Problems	76	98
Anxiety	76	99
Depression	71	96
Somatization	66	92
Atypicality	65	90
Attention Problems	60	83
Teacher Scales		
Internalizing Problems	75	98
Behavioral Symptoms Index	62	89
Anxiety	80	99
Depression	70	94
Somatization	63	91
Atypicality	68	93
Withdrawal	63	90

Chapter Summary

Childhood cancer and its treatment pose a myriad of challenges for the child and the family. Initial concern about the child's survival, financial pressures, and medical challenges contribute to

difficulty with adjustment for the entire family. In addition, there are indications of neuropsychological difficulty following treatment, particularly in the areas of attention, memory, mathematics, social skills, and speed of information processing. These domains contribute to difficulties with adjustment and school re-entry for many children who are survivors. White matter changes following treatment have been linked to difficulties in attention and speed of information processing. The neurological differences do not change over time and likely impact the child's development at older ages. In addition, females appear to be more affected than males in development of necessary skills. Research has indicated that the problems that arise following treatment continue throughout the life span and many childhood survivors of cancer have difficulty with vocational and educational attainment.

For the neuropsychologist, the challenge is providing appropriate evaluation and remediation support as well as assisting the child and his/her family in adjusting to the aftermath of treatment. A transactional approach would be most appropriate for working with survivors of childhood cancer. Such an approach would assist in understanding the 'whole' child. Evaluating a child without input from the school or understanding the social relations with peers prevents a full understanding of the challenges faced by the child. Similarly, evaluating a child without understanding the family dynamics will not assist in developing appropriate interventions.

Emerging research indicates that working with parents, siblings, and survivors of childhood cancer can help the family utilize the available remediation supports in the school and community more effectively. Such time-limited interventions have been shown to be very helpful. Major cancer centers are adept at providing support for the child upon re-entry to school. However, many families do not live near major cancer centers and need information and support that may not be accessible in more rural areas. Such support can be provided by the neuropsychologist who has an understanding of the various systems that are needed to assist the child.

Particular interventions that are helpful for re-entry include educating school professionals and developing an appropriate IEP. The IEP needs to be tailored to the individual child's needs and the

neuropsychologist can be instrumental in its development. In many cases school personnel are not trained to work with children with a history of cancer. Thus, it is important to not only provide this information, but to approach key school personnel and suggest a teacher in-service on these issues. Many of these children would not have survived in the past. Training of regular education teachers (and most special education teachers) does not routinely include information about medically involved children.

Finally, it is important to provide serial evaluations of the child's progress in order to monitor any possible problems that may occur as the child ages. Difficulties in executive functioning, inferential reasoning, and higher order cognitive skills may not appear until several years after treatment ends. These difficulties are associated with the decrease in white matter volume that has been found in cancer survivors. Flexible programming and support to develop compensatory strategies in adolescence to support these difficulties is important, and the serial evaluation can assist in the development of these programs.

Research is needed to continue understanding the challenges these children and their families face, as well as to validate appropriate treatments. Neuroimaging can also provide support for our understanding. Current research is generally restricted to volumetric imaging and DTI. Functional imaging may assist in understanding how the brain is processing information and, eventually, what interventions are most appropriate.

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