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Arithmetic Processing in Adolescents Treated for Leukemia

by

Karen Ghelani

A thesis submitted in conformity with the requirements for the degree of Master of Arts
Department of Human Development and Applied Psychology
Ontario Institute for Studies in Education of the
University of Toronto

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Arithmetic Processing in Adolescents Treated for Leukemia

Master of Arts June, 1999

Karen Ghelani

Department of Human Development and Applied Psychology

Ontario Institute for Studies in Education of the

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Abstract

The present study investigated arithmetic processing in adolescents, aged 14-16 years, treated for acute lymphocytic leukemia with (CRT) and without cranial irradiation (non-CRT). Although the CRT group achieved lower scores on most cognitive, memory and academic measures compared to the non-CRT group, differences were not significant. Relative to test norms, the two groups performed significantly lower on Freedom from Distractibility factor, immediate visual-spatial and multitrial learning tasks and arithmetic achievement. Arithmetic performance was associated with both verbal and visual-spatial abilities. Younger age at diagnosis was associated with difficulties in neurocognitive and academic functioning for the CRT group only.
Acknowledgments

Completing a Master's thesis is analogous to traveling an uncharted journey. There are many delightful discoveries that can enhance clinical and research skills. There are also unexpected chasms that cause detours and frustrating obstacles. I am grateful for the skillful navigators who ensured that my thesis journey was filled with experiences that have been invaluable in developing my professional skills.

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encouragement throughout this process and in so doing discovered his own inner talents and strengths.

I would like to dedicate this thesis to my son, Jason, who inspired me to return to school and to follow my professional goals. Throughout his short life, he not only encouraged me, but others as well, to enjoy the precious moments in life and not to take life for granted but to seize all opportunities that arise.
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Introduction

Children and youth who have been treated for cancer, particularly those treated with cranial irradiation, have been identified as being at risk for difficulties in academic achievement (Copeland et al., 1985; Mulhern, Fairclough & Ochs 1991, 1992; Peckham, Meadows, Bartel, & Marrero, 1988; Pfferbaum-Levine et al., 1984; Ochs et al., 1991; Taylor, Albo, Phebus, Sachs, & Bierl, 1987). Cranial irradiation has been reported to produce structural changes in the brain such as white matter abnormalities and calcifications (Copeland et al., 1988) which have been occasionally correlated with neuropsychological performance (Brouwers & Poplack, 1990; Poplack & Brouwers, 1985). Difficulties in information processing caused by neurological changes are reflected in specific areas of academic functioning. The research investigating the academic profiles of children treated for cancer has confirmed the existence of a core deficit in arithmetic processing (Copeland et al., 1985; Mulhern et al., 1991; Ochs et al., 1991; Pfferbaum-Levine et al., 1984). However, the research has not described the nature of the arithmetic difficulties nor the correlation between such difficulties and neuropsychological and cognitive processes in the same patients. It is important to investigate these correlations so that relevant remedial and compensatory interventions can be provided. This is crucial for the older student, whose impairments in neurocognitive processes may become more problematic with increased academic demands.

The investigation of neurocognitive processes and their relation to specific arithmetic difficulties requires a synthesis of knowledge from several areas of investigation: treatment
for childhood cancer, the iatrogenic effects of such treatment, and applicable findings from the research into arithmetic processing. A review of the relevant literature follows.

Childhood cancer survivors are a very heterogeneous group and this research will focus on the most common childhood cancer: acute lymphoblastic leukemia (ALL), the form of childhood leukemia with the most favorable prognosis. Treatment parameters depend on the stage of the disease and the age of the child. The conventional treatment for leukemia involves combination chemotherapy (IV and oral) and intrathecal methotrexate (IT-MTX), chemotherapy injected directly into the spinal column to kill leukemia cells that may be growing in the central nervous system (CNS). For children considered at high risk for CNS relapse or where leukemia cells have already spread to the brain, cranial irradiation (CRT) in addition to IT-MTX is required. At the Hospital for Sick Children in Toronto, the present protocol for children considered at high-risk for CNS relapse includes CRT of 1800 cGy. For children who are considered to be at low to moderate risk, IT-MTX without CRT is found to be equally effective. Systemic combination chemotherapy is required for all children.

**Effects of ALL Treatment on Cognition**

Studies investigating the effects of treatment for leukemia on children's cognitive development have produced variable findings. A seminal study was done by Meadows (Meadows et al., 1981) in which children diagnosed with ALL and treated with or without CRT were assessed over a period of time. Declines in intelligence scores (IQ) were noted in the group that had received CRT. These findings have been supported by similar studies
comparing ALL groups treated with and without CRT (Copeland et al., 1985; Pfferbaum-Levine et al. 1984) and comparing ALL groups treated with CRT to children treated for solid tumors (Copeland et al., 1988) and to siblings (Lansky et al., 1984; Moss, Nannis, & Poplack, 1981; Said, Waters, Cousens, & Stevens, 1989; Taylor et al., 1987). Other studies have identified a greater decline in IQ scores in younger children who had received CRT (Brown & Madan-Swain, 1993; Copeland et al., 1985; Cousens, Waters, Said, and Stevens, 1988; Lansky et al., 1984), and a decline over time from diagnosis and treatment (Lansky et al., 1984; Meadows et al., 1981). Some investigators, however, found no statistically significant declines in overall intelligence scores when comparing a non-CRT ALL group with ALL groups that were treated with either 18 cGy or 24 cGy CRT (Mulhern et al., 1991; Ochs et al., 1991). However, statistically significant decreases were found for all three groups when within-group comparisons were made. In these two studies, the non-CRT group received high-dose IV methotrexate (MTX) as CNS-directed therapy.

Although many earlier studies indicated a general "downward shift" in intelligence in children treated with CRT, it is important to describe the specific cognitive areas in which these children are showing difficulties. Specific areas identified have been different types of memory including nonverbal memory (Copeland et al., 1985; Pfferbaum-Levine et al., 1984), verbal memory (Brouwers & Poplack, 1990), and visual memory (Peckham et al., 1988). Other identified processes include attention and concentration (Fletcher & Copeland, 1988; Meadows et al., 1981; Peckham et al., 1988), visual perception (Eiser, 1978; Gamis & Nesbitt, 1991; Moss et al., 1981), visuomotor integration (Copeland et al., 1988; Meadows et al., 1981) and visual processing speed (Cousens et al., 1988; Fletcher & Copeland, 1988). These specific deficits will have an impact on the child’s ability to attend to and remember
factual information, perform sequential tasks efficiently, and meet other academic expectations that become increasingly demanding as the student moves into the higher grades. As several authors point out, the child is able to learn but is slower to process new information compared with his or her peers (Jannoun and Chessells, 1997; Peckham, 1989).

A few studies have outlined the effects of treatment for ALL on objective measures of academic success. Peckham and her colleagues (1988) found that children treated for leukemia who had received CRT, had academic difficulties, particularly in the area of arithmetic. Taylor et al. (1987) compared children with CRT and their normal siblings on measures of academic skills using the Wide Range Achievement Test-Revised (WRAT-R; Jastak & Wilkinson, 1984). Mean scores for the ALL group fell below the 50th percentile (but still within the average range) on the subtests of Arithmetic and Spelling (34th and 46th percentile, respectively), but not Reading (53rd percentile). Mean percentiles for the sibling group fell above the 50th percentile for all measures. Several authors have compared children treated with CRT and IT-MTX to those treated with IT-MTX alone. The CRT group performed more poorly on the Arithmetic subtest (Pfferbaum-Levine et al., 1984) or on both Arithmetic and Spelling subtests (Copeland et al., 1985; Deasy-Spinetta, Spinetta, & Oxman, 1988).

In the longitudinal study completed by Mulhern et al. (1991) in which the WRAT-R was administered to three groups of children treated for leukemia (IT-MTX and 1800 cGy, IT-MTX 2400 cGy, and IT-MTX with moderate dose IV-MTX), analyses of Reading, Spelling, and Arithmetic scores on the WRAT-R over the study period, found no significant differences between the three groups at any time interval for any of the achievement measures.
Although the studies show rather conflicting findings as a result of different group composition, control groups and time since treatment, there does seem to be evidence of a CRT treatment effect on cognitive and academic function. For example, in the Mulhern et al. (1991) study described above, although no significant differences were obtained between the three treatment groups at any time interval for any of the achievement measures, the three treatment groups did display significant declines in Reading and particularly Arithmetic over time. Comparisons made in this area of research have often tended to be cross-sectional rather than longitudinal, resulting in unspecified within-group differences. However, when within-group differences have been specifically measured, arithmetic is frequently an area in which there is an identifiable decline (Copeland et al., 1988; Ochs et al., 1991). This observation is consistent with the finding that the type of deficits characteristic of children treated with intracranial irradiation, such as different types of memory processing, visual motor integration, attention allocation, and processing speed, are critical components in arithmetic processing (Geary, 1993; Morris & Walter, 1991).

Arithmetic Processing

The study of arithmetic processing comes from both the neurocognitive and the cognitive developmental literatures. From a neurocognitive stance, the study of adults with acquired brain injury has contributed greatly to the understanding of the neurological processes underlying arithmetic. From an extensive survey of medical case reports of adults who displayed computational disorders following cerebral trauma, Henschen (1919) described specific disturbances in calculation, acalculia, associated with cerebral lesions in adults. From his study, Henschen concluded that: a) the integrity of several cortical areas is
necessary for calculation and b) a distinct cortical network for arithmetic functioning probably exists (Fleischner & Garnett, 1983).

Hecaen and his colleagues (1962) produced seminal work derived from error analysis in adults with brain damage. They described three broad categories of acalculia and attempted to relate the three types to particular cortical regions:

1. *Number alexia* or *agraphia* refers to errors related to reading numbers, writing numbers, or handling numbers as words. This type of acalculia has been correlated mainly with left cerebral lesions (Hecaen, 1962).

2. *Visual-spatial* acalculia refers to errors related to an inability to align problems or to sustain place holding values, horizontal and vertical spatial confusion, disorganization in aligning the rows of figures in long multiplication (Badian, 1983), the inability to maintain the decimal point, inversion and reversal errors, and visual neglect (Benson & Weir, 1972; Hecaen, 1962; Levin, 1979). This type of acalculia is thought to be produced by posterior right-hemisphere damage or dysfunction.

3. *Anarithmetria* was defined by Hecaen as a problem in carrying out arithmetical operations (Hecaen, 1962). In the most severe cases, the patient is incapable of even the simplest written calculations. In less severe cases, the operations of calculations are simplified, or one operation is confused with another. Retention or memory is a problem. Mental calculations are, in general, severely disturbed. Of the cases studied by Hecaen, 50% of the patients with anarithmetria also exhibited general intellectual deterioration. This category is associated with widespread pathology (Badian, 1983), but primarily posterior left or bilateral lesions.
Rourke and Conway (1997) caution against generalizing the results of research with adults with acalculia to children, stating that whereas adults bring a history of established functioning, learned skills, and accomplishments to the clinical situation, children have experienced a loss or disruption of developing those specific skills. Furthermore, the various neurodevelopmental impairments have an impact on the order, rate, and level of future development and learning capacity.

Several researchers (Badian, 1983; Cohn, 1968; Kosc, 1974) have used the term developmental dyscalculia to designate disorders that some children exhibit in acquiring arithmetic competence (Fleischner & Garnett, 1983). Rourke and his colleagues (Rourke, 1988, 1989; Rourke & Conway, 1997) have studied children who presented with difficulties in mechanical arithmetic relative to their performance in reading and spelling. They have suggested that children who have this profile, exhibit a nonverbal learning disability (NLD). Rourke has developed much of his research on the Goldberg and Costa model (1981) which points out that the ratio of grey matter (neuronal mass and short nonmyelinated fibres) to white matter (long myelinated fibers) is higher in the left hemisphere than in the right hemisphere. That is, there is relatively more white matter than grey matter in the right hemisphere than in the left hemisphere. Rourke has postulated that children who have received significant destruction and/or disturbance of white matter (which includes children who have received cranial irradiation) will show characteristics of the NLD syndrome. Although the left hemisphere is generally believed to mediate the numerical symbol system, retrieval of number facts from semantic memory, and simple linear equations with a 2+4=6 form (Geary, 1993; Spiers, 1987), the right hemisphere plays an important role in mathematical performance that
requires adaptive reasoning and/or visual-spatial organization of the elements of the problem (Rourke, 1993).

**Cognitive Perspective**

Within a broad framework of cognitive science, efforts have been aimed at constructing models of cognitive processes or strategies used during the performance of arithmetic tasks and at describing developmental changes in those processes (Fleischner & Garnett, 1983). A model of arithmetic skill acquisition has been developed through research into arithmetic skills of normally-achieving and arithmetic-disabled children (AD). However, fewer research studies have been completed on children with arithmetic disabilities compared to research on children with reading disabilities. Moreover, much of the research into arithmetic processing has been on lower-order cognitive processes of elementary school-aged children rather than adolescents.

**Arithmetic Skill Acquisition**

In the early elementary years, children have been observed to acquire arithmetic competency through identifiable developmental stages (Geary & Brown, 1991). Children in elementary grades have been described as using a number of strategies in solving addition problems from counting fingers to retrieving facts from long-term memory (Ashcraft, 1982; Geary, 1990; Groen & Resnick, 1977; Siegler, 1986). According to Siegler (1986), skilled performance is represented by the error-free retrieval of basic information from long-term memory.
As children move through the elementary grades, the demands of arithmetic tasks become more complex and require more mature problem solving techniques. Several models have been used to describe this progression. Ashcraft and his colleagues (Ashcraft, 1982; Ashcraft & Fierman, 1982; Hamann & Ashcraft, 1985) proposed a development from counting-based procedures used in the early grades to fact retrieval used by older children and adults. For example, when given the problem 7 + 3, children in upper grades and adults will simply retrieve the answer from long-term memory. Garnett and Fleischner (1983) reported that with age, children solve problems more quickly. Furthermore, they indicated that fluency with basic number facts implies sufficient automaticity of subskills such that attentional resources need to be diverted towards them only minimally for smooth coordination within complex operations.

Based on Ashcraft's model, the development of arithmetic competence can be described as involving an increase in the efficiency of both procedural knowledge and most importantly, information retrieval. Older children know more facts, can retrieve those facts more easily, and when necessary, can use arithmetic procedures more efficiently than younger children. As Ashcraft observed (Ashcraft, 1982), the use of increasingly mature problem solving strategies cannot simply be characterized by the substitution of one strategy, such as memory retrieval, for another less mature strategy. Rather, as Siegler and Jenkins (1989) pointed out, development involves changes in the mix of existing strategies as well as construction of new ones and abandonment of old ones.
Children with Learning Disabilities in Arithmetic

A number of researchers (Rourke & Finlayson, 1978; Rourke & Strang, 1978; Siegel & Feldman, 1983; Siegel & Ryan, 1988, 1989) have identified a subgroup of children and adolescents with learning disabilities who have a specific disability in arithmetic relative to average to above-average scores in reading and spelling. The studies have shown that these children suffer from several processing deficits which distinguish them from children identified as reading disabled. Children who have specific arithmetic disabilities have been found to have: well developed auditory-perceptual and verbal related skills but deficient visual-perceptual-organizational skills (Rourke & Finlayson, 1978); difficulties in certain types of verbal memory, particularly when novel (Brandys & Rourke, 1991); and deficits in short-term and working memory tasks particularly as they relate to nonverbal stimuli (Fletcher, 1985; Siegel & Linder, 1984; Siegel & Ryan, 1988, 1989). From their research with children with learning disabilities, Siegel & Feldman (1983) found that the Beery Visual Motor Integration Test and short-term memory tasks (particularly visual, nonverbal, and numerical tasks) clearly differentiated the arithmetic disabled group from their normally-achieving peers.

Studies from the cognitive area indicate that when solving arithmetic problems in relation to their normal peers, AD children tend to use immature problem solving strategies, have rather long solution times, and frequently commit computational and memory-retrieval errors (Fleischner et al., 1982; Garnett & Fleischner, 1983; Geary, 1990; Geary, Widaman, 1987). The computational and memory-retrieval errors might be related to the availability of working-memory resources, which in addition to being influenced by counting speed, is influenced by several components such as attentional allocation and rate of decay (Woltz,
1988). The processing deficits identified in children with arithmetic learning disabilities will be reflected in their basic number fact skills and more complex operations.

From both a neurological and cognitive perspective, the findings have supported a modular approach to arithmetic processing. McCloskey, Caramazza, and Basili (1985) have proposed that specific deficits in number processing can be considered from the perspective of whether they implicate disorders at the level of comprehension, retrieval of written or spoken numbers, or a deficit in the basic operations of calculations themselves. Theories and models of mental arithmetic from a cognitive framework have long speculated that fact retrieval, procedures such as carrying and borrowing, and special rules, reflect separate components in simple arithmetic processing. Fact retrieval takes place within an organized network or associative structure in long-term memory, variously termed Declarative Knowledge (Ashcraft, 1982) or simply Arithmetic Facts (Sokol, McCloskey, Cohen, & Aliminosa, 1991). Individual facts differ with respect to how strongly they are stored in memory, and differences in strength influence retrieval time and accuracy (Ashcraft, Yamashita, and Aram, 1992). Procedural Knowledge (Ashcraft, 1982) or Calculation Procedures (Sokol et al., 1991) is the second component and is thought to contain algorithmic as well as a variety of strategies and rules on which performance is based (Ashcraft et al., 1992).

Error Analysis

How adolescents treated for cancer process arithmetic can only be inferred from the research described thus far in the area of acalculia/dyscalculia and arithmetic disabilities. There are no substantial studies at this time that describe how these adolescents perform on
arithmetic tasks. One of the methods of investigating how children process arithmetic is to examine their error patterns (Englehardt, 1977; McCloskey, Harley, & Sokol, 1991; Strang & Rourke, 1985). Morrison and Siegel (1991) stated that children's errors in arithmetic are not random but systematic. Therefore, by examining the quantity and quality of errors made, information can be obtained about how the child is processing arithmetic information. Furthermore, by understanding the relationships between the quantity and quality of errors made and the neurocognitive processes involved (memory, visual motor-integration, attention and concentration, and speed of processing), teachers' knowledge of how to provide instruction to these children will be greatly enhanced.

Researchers from the neuropsychological, cognitive and educational perspectives have developed their own paradigms for investigating errors. For example, Badian (1983) analyzed the arithmetic errors made by 50 dyscalculic children in grades 2 through 9, following Hecaen's division of acquired acalculia and adding a fourth and fifth category (attentional-sequential and mixed disorder). Badian found that among the children whose arithmetic errors were analyzed, 24% made predominantly spatial errors, 14% exhibited anarithmetria, 42% were attentional-sequential cases, and 20% showed a mixed disorder. The most severe cases of dyscalculia tended to occur among those with a mixed disorder.

Strang & Rourke (1983) found that children who exhibited normal reading and spelling skills but markedly poor arithmetic performance tended to 1) make a larger number of errors; 2) make a wider variety of errors and exhibit some difficulty with the appreciation of mathematical concepts. Rourke (1993) classified the errors made by children with arithmetic disabilities into seven types:

1) **Spatial organization**: Errors include misaligning numbers in columns and
directionality (e.g., subtracting the minuend from the subtrahend in a subtraction question).

2) **Visual detail:** Errors involve misreading the operational sign or omitting decimal point or dollar sign.

3) **Procedural errors:** Children may miss or add a step to a procedure or they may mix operations (e.g., use addition and multiplication on a 2-digit multiplication problem).

4) **Failure to shift psychological set:** When two or more operations of one kind (e.g., addition) are followed by an operation of another kind (e.g., subtraction), these children will sometimes continue to apply addition procedures.

5) **Graphomotor:** Children may crowd their work or write numbers so poorly that they cannot read them afterwards resulting in errors.

6) **Memory:** Errors appear to be the result of failure to remember a particular number fact. The child may have the procedure available in memory but is unable to retrieve it.

7) **Judgment and reasoning:** Children may attempt questions that are clearly beyond their expertise and make errors.

Cognitive theorists Russell and Ginsburg (1984), found that among younger children who exhibited difficulties in mathematics, errors in subtraction were the most frequent type in a task involving addition and subtraction questions with two or three digits. Errors in writing numbers, carrying and borrowing, and misalignment were also frequent errors.

From an educational approach, Roberts (1968) identified four error types:

1) **Wrong operation:** An operation is performed other than the one required (e.g., the child performs addition for a subtraction question).
2) **Obvious computational error**: The correct operation is applied but the response is based on retrieval error of number facts.

3) **Defective algorithm**: The child attempts to apply the correct operation but makes errors other than number fact errors in carrying through the necessary steps (e.g., inversion of order, grouping error, or mixed operation).

4) **Random response**: The response shows no discernible relationship to the given problem.

In analyzing errors on the computation section of the Stanford Achievement Test in 3rd graders, Roberts (1968) found the following trends: the actual number of errors due to careless numerical errors and/or lack of familiarity with the addition and multiplication tables, is fairly constant throughout the competency levels; errors primarily due to performing a different operation than the one required occurred more frequently in the lower achievement group; weakness in the use of the appropriate algorithm accounted for the largest number of errors in all levels except in the lowest, where random responses predominated instead.

Engelhardt (1977) extended Roberts' efforts at classifying computational errors. He described eight types of errors:

1) **Basic fact error**: Errors involving incorrect retrieval of number facts. An error was classified as a basic retrieval error if the child employed a simple number sentence that was untrue (e.g., 2+3=6; 6x3=15). Such errors were observed most often within the context of multi-digit computations: For example,
26
\* 8
216 Error: 8x6 = 56

2) **Defective algorithm:** The pupil responds with a systematic but incorrect procedure. Errors of this type are not random responses but explainable and predictable. For example,

\[
\begin{array}{c c c c c c c}
123 & \times 42 & 33 \\
& & 32 & 996 \\
186 & - & 9 \\
& & - & 96 \\
& & - & 9 \\
& & - & 6 \\
& & & 0 \\
\end{array}
\]

3) **Grouping error:** The child's computation is characterized by a lack of attention to place value. These errors are particularly obvious in tasks requiring regrouping. For example,

\[
\begin{array}{c c c c c c c}
57 & + 93 & 13 \\
& \times 14 & \times 14 \\
1410 & 52 & 13 \\
& & 65 \\
\end{array}
\]

4) **Inappropriate inversion:** The child reverses steps or place value. For example,

\[
\begin{array}{c c c c c c c}
43 & 623 \\
-19 & 127 \\
36 & 623 \\
& 1246 \\
& 4361 \\
& 449183 \\
\end{array}
\]
In the first example, the child reversed the subtrahend and the minuend in the ones place, therefore, omitting the borrowing step. In the second example, the child has started the procedure from the left rather than the right.

5) **Incorrect operation:** The child performs an operation other than an appropriate one. For example,

\[
\begin{array}{c}
2 \\
\times 3 \\
\hline
5 \\
\end{array}
\begin{array}{c}
13 \\
- - 1 \\
\hline
14 \\
\end{array}
\]

6) **Incomplete algorithm:** The child omits or discontinues a step.

7) **Identity errors:** The child computes problems containing 0's and 1's in ways suggesting confusion of operations.

8) **Zero errors:** The child has an inadequate concept of zero (or one) or has confused the role of zero and one in the various operations. For example,

\[
\begin{array}{c}
1 \\
- 0 \\
\hline
\end{array}
\begin{array}{c}
3 \\
\times 0 \\
\times 1 \\
\hline
5 \\
3 \\
1 \\
\end{array}
\]

Engelhardt (1977) compared the errors of four achievement groups and concluded the following: 1) the number of items attempted increases with competence, and the number of errors decreases; 2) the absence of errors defined as basic facts, grouping, inappropriate inversion, defective algorithm, and incomplete algorithm, is what distinguishes competent performance, while conversely, incompetent performance is characterized by a high incidence of such errors; 3) in all levels of achievement, basic fact errors were common; and 4) the error type which most dramatically distinguished highly competent performance was the defective algorithm type with the highest group committing almost no such errors.
Summary

The literature has supported several tenets. The first is that fact retrieval and procedural knowledge are two separate modules in arithmetic processing. The second is that there are several components that influence skills in these areas such as various types of memory, visual spatial skills, speed of processing and attention and concentration. These components are all known to be areas of difficulty for students treated with irradiation. Adolescents who have undergone cranial irradiation as part of their treatment for leukemia are at high risk for academic difficulties, particularly in the area of arithmetic. As arithmetic is an important functional skill required for independent adult living, it is important for educators to develop instructional programs that teach directly to the areas of strengths and weaknesses in these students. In order to do this, the neurocognitive characteristics of these adolescents and their effect on various difficulties in arithmetic processing, need to be analyzed quantitatively as well as qualitatively. Adolescents who have been treated for cancer have a variable premorbid medical and academic history. Therefore, the degree to which the student has suffered neuropsychological impairment in the areas identified and the effect of these impairments on fact retrieval and procedural knowledge will vary. The child may have been diagnosed and treated at a developmental stage prior to consolidation of initial arithmetic skills. The child may not only have experienced disruption in his school attendance but also iatrogenic effects of treatment may affect his ability to process new information and his rate of learning. Adolescents diagnosed at the mid-elementary grade level on the other hand, may have already consolidated information learned by rote which is essential for fact retrieval but may have more difficulty with the procedural component.
Although there has been much discussion in the literature regarding the qualitative profiles of errors committed by children thought to have specific difficulties in arithmetic, children who have received irradiation have been described through clinical-inferential rather than through experimental research. The present study, with its focus on adolescents, is designed to replicate and extend some of the previous research on younger children treated for leukemia, in the area of cognitive characteristics. It also attempts to provide information on some aspects of arithmetic processing in adolescents treated for leukemia that have not been investigated in previous studies. The qualitative and quantitative analysis of errors committed by children treated for cancer will be based on the model developed by McCloskey et al. (1985) for assessing fact retrieval and procedural errors. Procedural errors will be further analyzed using a modified typology based on Engelhardt's (1977) categories (see Appendix A).

Objectives and Hypotheses

The following objectives and hypotheses will be addressed in the present study:

1) To clarify the differences between adolescents treated with and without (CRT) for leukemia on measures of verbal and visual-spatial cognitive abilities.

Previous research has described the deleterious effects of cranial irradiation on cognitive abilities in children (Copeland et al., 1985; Mulhern et al., 1991; Ochs et al., 1991; Peckham et al., 1988; Pfferbaum-Levine et al., 1984; Taylor et al., 1987).

It is predicted that adolescents in the CRT group will have lower scores on measures of verbal and visual-spatial abilities as measured by VIQ and PIQ than adolescents in the
non-CRT group. It is further predicted that these abilities would not be significantly different in the non-CRT group relative to test population norms.

2) To determine whether specific deficits occur in areas of information processing such as memory (e.g., working memory, short-term memory, verbal versus nonverbal memory), attention and concentration, visual-spatial organization and speed of processing in adolescents treated for leukemia with and without CRT.

Research by Cousen's at al. (1991) found specific deficits in short-term memory, speed of processing, visual-motor coordination, and sequencing ability in children treated for leukemia with cranial irradiation. Difficulties in various types of memory, attention, visual-motor integration and speed of processing have also been identified by other investigators (Copeland et al., 1985; 1988; Fletcher & Copeland, 1988; Said et al., 1989).

It is predicted that adolescents in the CRT group will have lower scores on measures of visual-spatial processing, processing speed, attention and concentration, and memory than adolescents in the non-CRT group. It is further predicted that these abilities will not be significantly different in the non-CRT group relative to test population norms.

3) To further explore the existence of specific academic skill deficits in the area of arithmetic processing in adolescents treated for leukemia and to describe the nature of these skill deficits.

Previous research in this area has explored a combination of reading, spelling, and arithmetic across a wide age range. Earlier studies have documented difficulties in arithmetic processing in children treated with cranial irradiation (Peckham et al., 1988; Pfferbaum-Levine et al., 1984; Mulhern et al., 1991).
It is predicted that the CRT group will earn lower scores on measures of arithmetic compared to reading and spelling, and that they will have lower scores in arithmetic, reading, and spelling than the non-CRT group and the population norms. It is further predicted that scores on arithmetic will not be different in the non-CRT group for these three skills relative to population norms.

4) To explore the quantitative and qualitative differences among the children treated for leukemia in terms of error rate, error type, attempt rate, and mastery rate.

Previous research has been conducted in the area of error analysis and arithmetic disabilities (Saito, 1992; Yaghoubzadeh et al., 1995).

It is predicted that the CRT group would make more errors overall than the non-CRT group, and that the non-CRT group will earn higher scores on attempt rate and mastery rate than the CRT group. It is further predicted that lower scores on processing speed (PS) will be associated with more errors, fewer attempts and less mastery.

5) To explore whether any specific cognitive deficits are related to certain types of errors made in arithmetic computation.

Previous studies have found an association between types of information processing and types of errors made by children with arithmetic disabilities (Brainerd et al., 1983; Strang and Rourke, 1985; Yaghoubzadeh, 1995).

It is predicted that there will be a relation between types of cognitive deficits found in adolescents treated for leukemia and types of errors made. Specifically, 1) deficits in verbal memory will be associated with basic fact errors; 2) deficits in visual spatial processing will be associated with procedural errors (i.e., inappropriate inversion, regrouping errors); 3) and deficits in attention/concentration will be associated with incorrect operations.
6) To investigate the relationship between factors such as a) age at diagnosis b) time since diagnosis c) time missed from school and errors in fact retrieval and procedural knowledge.

It is predicted that adolescents treated at a younger age (e.g., before the age of 9 years) will have more difficulty with basic fact retrieval as they will have missed some of the basic arithmetic skills in earlier grades. In contrast, it is expected that adolescents who were treated at a later age (e.g., after the age of 9 years) will have more difficulty with procedural knowledge, as they would have consolidated some of the basic facts but missed developing skills in multi-step procedures. Furthermore, it is predicted that time missed from school will be correlated with the overall number of errors (i.e., more time missed from school will be correlated with a higher frequency of errors).
Method

Participants

The participants for this study were selected from a group of 41 adolescents who had been treated for high risk (CRT and IT-MTX) and low risk (IT-MTX without CRT) acute lymphoblastic leukemia (ALL) and were being followed on an out-patient basis by the Hematology/Oncology Division at the Hospital for Sick Children (HSC) in Toronto, Canada. Adolescents were selected if they were between the ages of 14 and 16 years inclusive, attending secondary school, and had English as a primary language or had been educated in English for at least 4 years. All were in first remission and disease free for at least 2 years. Adolescents were excluded if they had a neurological condition in addition to the diagnosis of cancer (e.g., head injury) or an identification of learning disability prior to the diagnosis of leukemia.

Of the 20 eligible adolescents treated with IT-MTX without CRT (non-CRT), 8 (40%) adolescents participated. Of the adolescents who did not participate, 6 (30%) declined to participate, 3 (15%) had moved and could not be contacted, 2 (10%) had a preexisting condition prior to diagnosis of leukemia (e.g., mild head injury and diagnosis of learning disabilities/attention deficit disorder). In the non-CRT group, 1 (5%) adolescent was excluded from the group as the result of a severe language-processing deficit that was also detected in his twin brother. Of the 8 participants, 4 (50%) were female and 4 (50%) were male.

Of the 21 eligible adolescents in the CRT group, 12 (57%) adolescents participated in the study. Of the adolescents who did not participate, 4 (19%) declined to participate, 9
(10%) had moved and could not be contacted, and 3 (14%) were diagnosed as having treatment-induced seizure disorders which may have confounded the results of the cognitive and achievement measures. Of the 12 participants, 7 (58%) were female and 5 (42%) were male.

The oncologists at the Hospital for Sick Children were provided with the names of their patients that were being contacted to ensure that they had no concerns about their participation in the study. Information about the study was sent to potential participants with an enclosed self-addressed post card for the family and adolescent to return if they wished to participate or receive more information. Research consent forms were obtained from the participants prior to each participant’s involvement in the study. In the case of adolescents over 16 years of age, a signed research consent was obtained from the participant. For adolescents under the age of 16 years, consents were obtained from the parents and assents were collected from the participants (see Appendixes B and C). These forms had received prior approval from both the Research Ethics Board of OISE/UT and the Hospital for Sick Children.

Measures

Independent Measures

The participant’s age at diagnosis, type of diagnosis, and treatment protocol were obtained from a review of their Health Record.

Dependent Measures

The adolescent’s cognitive, memory and academic skills was evaluated using the following measures:
1) *Wechsler Intelligence Scale for Children–Third Edition* (WISC-III) (Wechsler, 1991). Psychometric intelligence was assessed with the WISC-III. The WISC-III was designed to assess the intellectual ability of children aged 6 through 16 years and eleven months. The test is administered individually and three composite intelligence quotient (IQ) scores are obtained: Verbal, Performance and Full Scale. All subtests on the WISC-III were included to compute the four factor indexes: Verbal Comprehension, Perceptual Organization, Freedom from Distractibility and Speed of Processing. The reliability and validity and standardization procedures for the WISC-III are well known (Sattler, 1988; Weschler, 1991).

2) *Children’s Memory Scale* (CMS) (Cohen, 1997). Memory and learning were assessed through the administration of the (CMS) using the form developed for ages 9-16 years. All core subtests were administered to obtain the 8 indexes: Verbal Immediate, Verbal Delayed, Visual Immediate, Visual Delayed, General Memory, Attention/Concentration, Learning Index, and Delayed Recognition. The average reliability coefficients for the CMS index scores range from .76 to .91 for ages 10 to 16 years of age. Construct validity for the indexes range from .16 to .79 with correlations being higher within domains than between domains for all indexes.

Correlations between the CMS and the WISC-III were moderate for Verbal IQ and auditory/verbal measures (.57, and .53 respectively), and the Freedom from Distractibility factor was strongly correlated with the CMS Attention/Concentration Index (.73).

3) *Wide Range Achievement Test 3* (WRAT3) (Wilkinson, 1993). Academic achievement was assessed through the Reading, Spelling and Arithmetic subtests of the WRAT3. The WRAT3 has two alternate forms and both forms were randomized for use in
this study. The Arithmetic subtest was administered in a timed and untimed format, using the alternate forms. The written part of the WRAT3 Arithmetic subtest was used for the analysis of errors.

Inter-rater reliability was established by having a graduate student, experienced in coding arithmetic errors, categorize the errors blind to the investigator’s scoring and the medical diagnosis of the student.

Each participant was assessed individually by the primary investigator at the Hospital for Sick Children. The testing was completed in approximately 3 to 3 1/2 hours. The two alternate forms of the WRAT3 Arithmetic subtest (Blue and Tan form) were pseudorandomized in order to obtain a timed and untimed sample for each participant. The timed task was presented after the completion of the WISC-III, while the untimed task was administered at the end of the session.

A brief report was sent to all parents of the adolescents in the study, which included a profile of the adolescent’s abilities and learning needs. If the profile indicated that there were psychological/educational issues that needed to be addressed, the adolescent and family were provided with recommendations for remediation. In several cases, results were shared with families in an interview conducted by the primary and secondary investigators.
Results

This chapter provides the results of the descriptive and the quantitative analyses for this study. Histograms, scatterplots, and descriptive statistics were examined to investigate the distributions and to delineate the overall characteristics of the two groups to determine the appropriate analysis procedures. First, the two groups of participants were compared in terms of their demographic characteristics. Second, the two groups were compared on measures of cognitive, memory, and academic functioning. The alpha level was set a priori at p< .05, for all analyses. Based on directional hypotheses, that the CRT group would achieve lower scores on the measures used in this study, one-tailed t-tests were conducted for the different dependent variables. One-tailed, one-sample t-tests were used to compare the results of each group’s cognitive and academic measures to test norms. As the sample size was small (non-CRT = 8; CRT = 12), in addition to standard statistical techniques, group differences were described by calculating effect sizes for averaged cognitive, memory, and academic scores (effect sizes .20, .50, and .8 correspond to small, medium and large effect sizes; see Cohen, 1992). Only moderate or large effect sizes are reported. Third, arithmetic error rate and type were explored. Fourth, arithmetic error rate and type were correlated with selected neurocognitive measures based on a priori hypotheses about the neurocognitive underpinnings of arithmetic performance. Fifth, age at diagnosis, length of time since diagnosis, and time missed from school, were explored in their relationship to rates and types of arithmetic errors.
Table 1 provides demographic information for the two groups.

Table 1

Demographic Information for non-CRT and CRT Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>non-CRT (n=8)</th>
<th>CRT (n=12)</th>
<th>t-test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Socioeconomic</td>
<td>4.8</td>
<td>4.5</td>
<td>.62</td>
</tr>
<tr>
<td>Age at Diagnosis (years)</td>
<td>15.63</td>
<td>15.55</td>
<td>.81</td>
</tr>
<tr>
<td>Time Since Treatment (years)</td>
<td>8.71</td>
<td>10.38</td>
<td>.14</td>
</tr>
</tbody>
</table>

* p < .05; **p < .01; ***p < .001  Note. None of the above results were significant at p < .05 level.

The socioeconomic status for each child was obtained using the Blishen scale (Blishen, Carroll, & Moore, 1987), which is based on Canadian census data. The highest occupational code was determined for each family. Of the 90% of the families that responded, 15% were classified as professional managers, 30% as semi-professional supervisors, 45% as skilled or semiskilled, and 5% as unskilled. The groups were not different with respect to this measure of SES (non-CRT: M= 4.8, SD= 1.58; and CRT: M= 4.5, S.D. = 1.38).
A chi-square analysis revealed no differences between the two groups with respect to sex \([X^2 (1, 20) = .80, p = .38]\). T-test comparisons revealed no group differences in age at test, age at diagnosis, or length of time since diagnosis.

II Cognitive, Memory and Academic Achievement Measures

Hypothesis #1

*It was predicted that adolescents in the CRT group would have lower scores on measures of verbal and visual-spatial abilities as measured by VIQ and PIQ, than adolescents in the non-CRT group. It was further predicted that these abilities would not be significantly different in the non-CRT group relative to test population norms.*

The means and standard deviations for the WISC-III IQ and factor scores for each group are shown in Table 2.

The CRT group did indeed earn lower WISC-III IQ scores than the non-CRT group. However, one-tailed \(t\)-test comparisons revealed that these differences were not statistically significant with the small number available. As predicted, one-sample \(t\)-tests revealed no significant differences between the non-CRT group and the standardization group. Furthermore, there were no significant differences between the CRT group IQ measures and the standardization group.

The measure of effect sizes for measures used in this study are shown in Appendix D. Effect size was calculated for the IQ measures, comparing the non-CRT and CRT groups to the standardization group and to each other (Cohen, 1992). The difference between CRT group means and population norms for WISC-III FSIQ and VIQ measures were moderate (effect size = .45 for each).
Table 2

Mean Performance and Standard Deviations for the non-CRT and CRT Groups for WISC-III

Index Scores and WRAT3 Achievement Scores

<table>
<thead>
<tr>
<th></th>
<th>non-CRT (n=8)</th>
<th>CRT (n=12)</th>
<th>t-test (between groups)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>FSIQ</td>
<td>99.00</td>
<td>10.93</td>
<td>93.25</td>
<td>19.50</td>
</tr>
<tr>
<td>VIQ</td>
<td>96.75</td>
<td>7.32</td>
<td>93.17</td>
<td>18.01</td>
</tr>
<tr>
<td>PIQ</td>
<td>101.88</td>
<td>14.95</td>
<td>94.17</td>
<td>20.56</td>
</tr>
<tr>
<td>VC</td>
<td>99.50</td>
<td>5.04</td>
<td>95.25</td>
<td>18.03</td>
</tr>
<tr>
<td>PO</td>
<td>103.75</td>
<td>14.94</td>
<td>97.50</td>
<td>20.57</td>
</tr>
<tr>
<td>FD</td>
<td>87.75</td>
<td>13.68</td>
<td>89.92</td>
<td>17.46</td>
</tr>
<tr>
<td>PS</td>
<td>101.50</td>
<td>11.87</td>
<td>93.92</td>
<td>13.48</td>
</tr>
<tr>
<td>Reading</td>
<td>101.00</td>
<td>6.63</td>
<td>92.42</td>
<td>15.88</td>
</tr>
<tr>
<td>Spelling</td>
<td>102.88</td>
<td>8.20</td>
<td>93.92</td>
<td>16.86</td>
</tr>
<tr>
<td>Arithmetic</td>
<td>95.00</td>
<td>6.82</td>
<td>88.67</td>
<td>16.99</td>
</tr>
</tbody>
</table>

*p < .05; **p < .01; ***p < .001
Hypothesis #2
It was predicted that adolescents in the CRT group would have lower scores on measures of visual-spatial processing, processing speed, attention and concentration, and memory than adolescents in the non-CRT group. It was further predicted that these abilities would not be significantly different in the non-CRT group relative to test population norms.

WISC-III

The CRT group did have lower scores than the non-CRT group on the visual-spatial indexes of Perceptual Organization (PO) and Processing Speed (PS) on the WISC-III. However, the CRT group achieved a higher score than the non-CRT group on the Freedom of Distractibility (FD) factor. None of these differences were significant (see Table 2).

When the subjects’ WISC-III factor scores were compared to test norms, both groups achieved significantly lower scores on the FD factor [non-CRT: $t(7) = -2.53, p = .02$; CRT: $t(11) = -2.0, p = .04$].

When compared to population norms, the non-CRT group’s lower score on the FD factor was associated with a large effect size (.82). The CRT group scored lower than the population norms on all factor scores and a moderate effect (.67) was found for both the PO and FD factors.

As noted above, the CRT group scored lower than the non-CRT group on all factors with the exception of FD. The difference for PS was of moderate size (.60).

If there really is no difference between the two groups, probability theory would predict that one group would score higher than the other on approximately half of the tests administered and lower on the other half. This hypothesis was tested using a binomial test which compared mean scores on the WISC-III measures between the two groups and for
each group compared with the population norms. When the two groups were considered in relation to each other, it was found that the non-CRT group scored higher on significantly more tests (17 out of 21 measures) than the CRT group, and this was significant at the p=.001 level. When the non-CRT group was compared to the population norms, the results were not significant. When the CRT group was compared to the population norms, the results were significant at a p=.001 level with the CRT group scoring lower on most tests (19 out of 21 measures).

Memory-CMS

To test the hypothesis that there were significant differences between the CRT and the non-CRT groups on the measures of verbal/nonverbal memory and attention/concentration, mean scores for CMS indexes were compared using one-tailed t-test comparisons and one-sample t-tests. The means and standard deviations for the CMS indexes are shown in Table 3.

The scores for the CRT group were lower than the non-CRT group for Verbal Memory Indexes (Immediate and Delayed), General Memory, and Delayed Recognition. However, these differences were not statistically significant. The results for the two groups were then compared to test norms. For both the non-CRT group and the CRT groups, Visual Immediate Memory [non-CRT: t (7) = -2.15, p = .04; CRT: t (11)= -3.57, p = .01] and Learning [non-CRT: t (7) = -1.93, p = .05; CRT: t (11) = -2.02, p = .04] were significantly below the population norms.

The measures of effect size for the non-CRT and CRT groups when the means of the CMS indexes were compared to the population norms and to each other, are given in Appendix D.
Table 3

**Means and Standard Deviations for the non-CRT and CRT Groups for CMS Index Scores**

<table>
<thead>
<tr>
<th></th>
<th>non-CRT (n=8)</th>
<th></th>
<th>CRT (n=12)</th>
<th></th>
<th>t-test (between groups)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Immediate</td>
<td>102.25</td>
<td>18.90</td>
<td>96.92</td>
<td>21.93</td>
<td>.29</td>
<td>ns</td>
</tr>
<tr>
<td>Verbal Delayed</td>
<td>110.50</td>
<td>17.00</td>
<td>97.50</td>
<td>20.01</td>
<td>.08</td>
<td>ns</td>
</tr>
<tr>
<td>Visual Immediate</td>
<td>89.95</td>
<td>13.35</td>
<td>89.92</td>
<td>9.80</td>
<td>.50</td>
<td>ns</td>
</tr>
<tr>
<td>Visual Delayed</td>
<td>93.13</td>
<td>13.36</td>
<td>94.33</td>
<td>15.48</td>
<td>.43</td>
<td>ns</td>
</tr>
<tr>
<td>General Memory</td>
<td>99.50</td>
<td>19.78</td>
<td>93.00</td>
<td>21.27</td>
<td>.25</td>
<td>ns</td>
</tr>
<tr>
<td>Attention/ Concentration</td>
<td>96.00</td>
<td>15.44</td>
<td>91.33</td>
<td>17.31</td>
<td>.27</td>
<td>ns</td>
</tr>
<tr>
<td>Learning Index</td>
<td>90.88</td>
<td>13.36</td>
<td>91.00</td>
<td>15.42</td>
<td>.49</td>
<td>ns</td>
</tr>
<tr>
<td>Delayed Recognition</td>
<td>102.25</td>
<td>11.31</td>
<td>97.67</td>
<td>13.85</td>
<td>.23</td>
<td>ns</td>
</tr>
</tbody>
</table>

* p < .05; **p < .01; ***p < .001
The non-CRT group scored lower than the population norms on some measures and these were reflected in moderate effect sizes for Verbal Delayed (.70), Visual Immediate (.68), Visual Delayed (.46), and Learning index (.61). The CRT group consistently scored lower than the population norms on the CMS indexes. The effect sizes were moderate for Visual Immediate (.67), General Memory (.46), Attention/Concentration (.58), and Learning index (.60).

The means of the CMS indexes for the two groups were then compared. As noted above, there were no significant differences but the lower Verbal Delayed memory score for the CRT group was associated with a moderate (.70) effect size.

Based on the hypothesis that if there really is no difference between the two groups, one group would score higher than the other on approximately half of the tests administered and lower on the other half, a binomial test was calculated comparing mean scores on the CMS measures. When the two groups were considered in relation to each other, the results were not significant. Nonsignificant results were also obtained when the non-CRT group was compared to the population norms. When the CRT group was compared to population norms, the results were significant at the p=.01 level, with the CRT group scoring lower on all 8 tests.

Hypothesis #3

It was predicted that the CRT group would earn lower scores on measures of arithmetic compared to reading and spelling, and that they would have lower scores in arithmetic, reading and spelling than the non-CRT group and the population norms.
Mean standard scale scores for the WRAT3 Reading, Spelling, and Arithmetic subtests for the two groups are presented graphically in Figure 1. Arithmetic was the lowest score for the CRT group but it was not statistically different from Reading or Spelling. For the non-CRT group, Arithmetic was also the lowest score, and was statistically different from the Reading and Spelling scores.

When the group means were compared to each other, the CRT group earned lower scores on all three achievement subtests, but these differences were not statistically significant (see Table 2). When group means were compared to test norms, results were significant for Arithmetic for both the non-CRT group \( t(7) = -2.07, p = .04 \) and the CRT group \( t(11) = -2.31, p = .02 \).

The effect sizes for group mean and population norm comparisons are presented in Appendix D. The non-CRT group scored higher on Reading and Spelling and lower on Arithmetic than the population norms. The CRT group consistently scored below the population norms on all three measures. The effect size was moderate for Reading (.50) and large for Arithmetic (.75), for both groups.

When the two groups were compared with each other, the CRT group scored below the non-CRT group on all three academic tasks. The effect size was moderate for all three comparisons: Reading (.71), Spelling (.68), and Arithmetic (.49).

The CRT group earned lower scores than the non-CRT group on the untimed arithmetic test, but this difference was not significant.
Figure 1. Mean standard scores for Reading, Spelling, and Arithmetic for non-CRT (n=8) and CRT groups (n=12).
III Arithmetic Processing

Hypothesis #4

It was predicted that the CRT group would make more errors overall than the non-CRT group, and that the non-CRT group would earn higher scores on attempt rate and mastery rate than the CRT group. It was further predicted that lower scores on Processing Speed (PS) would be associated with more errors, fewer attempts, and less mastery.

As predicted, the CRT group did make more errors overall than the non-CRT group, and the non-CRT group did obtain higher scores on attempt rate and mastery rate than the CRT group for both the timed and untimed arithmetic task. However, these differences were not significant using one-tail t-test comparisons. Error rates, attempt rates and mastery rates are displayed in Appendix E.

Because there were no statistical differences between groups on any of the measures used in this study, the treatment groups were collapsed for correlational analysis of selected neurocognitive association with error rate, attempt rate and mastery rate using Spearman non-parametric correlations. Correlations with error rate and mastery rate were significant for most cognitive and memory measures. Unexpectedly, the PS factor was not associated with attempt rate.

Types of Errors

Hypothesis #5

It was predicted that there would be a relation between types of cognitive deficits found in adolescents treated for leukemia and types of errors made. Specifically, deficits in verbal memory would be associated with basic fact errors, deficits in visual spatial
processing will be associated with procedural errors (e.g., inappropriate inversion, regrouping), and deficits in attention/concentration would be associated with incorrect operation errors.

This hypothesis was only partially supported. Given the small sample size and consequently smaller number of errors, statistical analysis could not be carried out for several error categories.

The percentages of errors made by each group in each category for timed and untimed conditions are presented in Appendix F. The most common error among the non-CRT group was defective algorithms (59% for timed, 65% for untimed), followed by basic fact error (13% for timed, 20% for untimed), and regrouping (8% for timed, 3% for untimed).

In the CRT group, the most common error was defective algorithms (67% for timed, 59% for untimed), followed by basic fact error (16% for timed, 28% for untimed), and regrouping (7% for timed, 4% for untimed).

Based on the smaller number of errors, the McCloskey model was used to analyze the error categories. Errors were categorized as either basic fact errors or procedural knowledge errors (including defective algorithm, incomplete operations, regrouping etc.). Spearman nonparametric correlations were carried out to determine the relation between basic fact and procedural knowledge errors and performance on the selected neurocognitive measures.

Correlations for the categories of errors and cognitive and memory measures for both groups are shown in Appendix G. For the non-CRT group, basic fact errors were correlated with Digits Forward, a verbal memory task from the WISC-III ($r = -.79$, $p = .01$), but not with any of the verbal memory tasks on the CMS indexes. Procedural knowledge errors were not
significantly correlated with any of the visual-spatial abilities on the WISC-III, but were correlated with both verbal and nonverbal memory indexes on the CMS.

For the CRT group, basic fact errors were significantly correlated with Digits Forward ($r = .56, p = .03$) only. Procedural knowledge was associated with visual-spatial processing deficits on the WISC-III (PIQ $r = -.55, p = .03$; PO $r = -.56, p = .03$). In this group, there were no correlations between error type and any memory measure.

Comparisons were also made between the number of basic fact and procedural knowledge errors made in timed and untimed conditions for each group. No differences were found for basic facts but the results were significant for procedural errors for the CRT group [$t(11) = 2.171, p = .05$], with more errors on the timed task.

**III Age at Diagnosis, Time Since Diagnosis, Time Missed from School**

**Hypothesis #6**

*It was predicted that adolescents treated at a younger age (e.g., before the age of 9 years) would have more difficulty with basic fact retrieval as they would have missed some of the basic arithmetic skills in earlier grades. In contrast, it was expected that adolescents who were treated at a later age (e.g., after the age of 9 years) would have more difficulty with procedural knowledge, as they would have consolidated some of the basic facts but missed developing skills in multi-step procedures. Furthermore, it was predicted that time missed from school would be correlated with the overall number of errors (i.e., more time missed from school will be correlated with a higher frequency of errors).*

Since age at diagnosis and time since diagnosis were highly correlated ($r = .89, p = .004$), only the age at diagnosis variable was used for analysis.
Age at diagnosis was a strong predictor of WRAT3 arithmetic achievement for the CRT group ($r = .62, p = .02$), with those adolescents diagnosed at an earlier age earning lower scores on arithmetic. However, no significant correlation was found between age at diagnosis and WRAT3 arithmetic for the non-CRT group.

For the CRT participants, age at diagnosis was correlated with error rate, $r = -.57$ ($p = .02$), attempt rate $r = .79$ ($p = .01$), and mastery rate $r = .62$ ($p = .01$) with adolescents diagnosed at an earlier age committing more errors, making fewer attempts and achieving less mastery than adolescents diagnosed at a later age. For the non-CRT participants, age at diagnosis was not significantly correlated with any of the rate measures.

When the participants were grouped by age of diagnosis (before and after age 9), no associations were found with number of basic fact or procedural knowledge errors.

Most parents estimated time missed from school. However, the reports were often qualitative estimates (e.g., “most of grade 1,” “part of grade 3”) and, therefore, were not used in the correlational analyses.
Discussion

The purpose of this study was to examine cognitive, memory, and academic functioning in adolescents treated for leukemia with or without cranial irradiation, and to explore the nature of neurocognitive deficits associated with arithmetic processing. The results of the present study did not identify significant differences between the non-CRT and CRT groups on cognitive, memory, and academic measures. These results were unexpected, given previous studies that have shown significant differences between the two groups (Brown & Madan-Swain, 1993; Butler & Copeland, 1993; Rubenstein, Varni, & Katz, 1990).

As predicted, the non-CRT group was not significantly different from the standardization group on most of these measures. However, the finding of no difference between the CRT group and population norms was not predicted by previous studies (Butler, Hill, Steinherz, Meyers, & Finlay, 1994; Copeland et al., 1985; Rubenstein et al., 1990).

There may be several explanations for these results. First, failure to detect between group differences may be explained by the small number of participants. The power is, therefore, limited. The small sample size diminished the probability of finding significant differences between the groups with the increased possibility that a Type II error could occur.

The measure of effect size that was used to qualitatively describe differences, indicated that there were trends in the predicted directions for between group comparisons. These observed trends suggest that the results may have been significant with increased statistical power. Furthermore, significant differences were found when the mean scores for the two groups were considered in relation to each other and with population norms on the number of measures, using a binomial test. The CRT group achieved lower scores than the non-CRT group and population norms on significantly more tests.
Second, the large variability within the CRT group makes it harder to demonstrate significant differences between groups. Third, an ascertainment bias may have occurred as those adolescents who agreed to participate may have differed from those who did not.

**Cognitive and Memory Functioning**

Previous studies have reported specific deficits in non-verbal intelligence and perceptual abilities (Brown & Madan-Swain, 1993; Brown et al., 1998; Butler & Copeland, 1993; Butler et al., 1994) among children treated for leukemia with cranial irradiation. However, some studies have shown evidence for further specific difficulties in verbal intelligence (Lansky, et al., 1984).

The results in this study present a pattern of higher non-verbal than verbal intelligence, although these differences were not significant. The non-CRT group scored higher on the PIQ than the VIQ (101.88 > 96.75) and higher on the PO factor than the VC factor (103.75 > 99.50). A similar trend was shown in the CRT group: [PIQ vs VIQ: 94.17 > 93.17; and PO vs VC: 97.50 > 95.25].

Descriptive profiles were developed for the individual participants. Thirty-eight percent (3) of the 8 non-CRT subjects had discrepancies of 12 or more points between their Verbal and Performance IQ scores (2 subjects: V > P, 1 subject P > V), whereas in the CRT group, forty-two percent (5) had discrepancies of 12 points or greater (3 P > V, 2 V > P). The frequency of obtaining a VIQ-PIQ discrepancy of 12 or more points in the standardization sample, is 35.8%. Sixty-two percent of the non-CRT group participants and 75% of the CRT group had either verbal or non-verbal subtests that were significantly different from their own average subtest score. It is important to note, that in the CRT group,
the Vocabulary subtest was an area of difficulty in 6 of the 9 cases, and 2 of these participants were functioning within the High Average and Superior range overall. Therefore, individual profiles reflect relative difficulties in both verbal and nonverbal functioning.

Several studies have used the FD factor, which is based on the verbal subtests of Arithmetic and Digit Span as a measure of distractibility. The finding in this study that the FD factor was significantly lower for both groups when compared to the norms, was unexpected. It has been suggested (Brouwers & Poplack, 1990; Brouwers, Riccardi & Poplack, 1984), that irradiation-induced white matter damage is likely to involve demyelination with subsequent attentional disturbance and decreased efficiency in information processing. Brouwers and Poplack (1990) reported that children treated for leukemia with cranial irradiation demonstrate symptoms resembling those of attention deficit/hyperactivity disorder (ADHD), including distractibility and difficulty sustaining attention. Although several studies have found evidence of attention difficulties in children who have received CRT (Butler et al., 1994; Cousens et al., 1991), fewer studies have found the same effect for children who did not receive CRT. Lockwood, Bell, and Colegrove (1999) found significant differences between irradiated and nonirradiated groups on attentional components including sensory selection, attentional capacity and sustained attention, with the irradiated group achieving lower scores on these variables. However, some authors (Brown et al., 1998) have found a modest potential late effect on the FD factor with children who were treated for leukemia with CNS prophylactic chemotherapy alone.

Speed of processing has been cited in the literature as another specific deficit in children treated with CRT (Cousens, Ungerer, Crawford & Stevens, 1991). The present
study does not support this finding when using the PS factor from the WISC-III as a measure of processing speed. Of the two subtests comprising the PS factor (Coding and Symbol Search), Coding was the only subtest that showed a strong trend toward differentiating the two groups. Coding has been cited in some studies as being a specific deficit for children who have received CRT (Pfefferbaum-Levine et al., 1984) and reflects difficulties in the area of working memory and visual-motor integration.

Previous studies that have assessed memory abilities in children treated for leukemia have used a variety of measures. This makes it difficult to compare the results from the present study with existing research. Brouwers and Poplack (1990) administered the Wechsler Memory Scale Revised (WMS-R) and the Rey-Osterrieth figure to assess verbal and nonverbal memory, respectively, in children treated with CRT. They found that a few of these children had significant deficits in verbal memory and verbal learning, and attributed weaknesses in short-term learning to underlying attentional difficulties. Butler et al. (1994) assessed verbal and nonverbal memory in children who had received CRT with IT-MTX or IT-MTX alone, using the Wide Range Assessment of Memory and Learning (WRAML) (Sheslow & Adams, 1990) and WMS-R. The authors found that both groups had better performance on verbal than nonverbal immediate and delayed memory, but the findings were only significant for the CRT group. Using the WRAML, Hill, Ciesielski, and Sethre-Hofstad (1997) assessed survivors of ALL who had received triple intrathecal therapy for CNS prophylaxis. They found mild but consistent deficits in both visual-spatial and verbal single-trial memory tasks. The authors suggested that attention/distractibility was related to poor memory scores.
In the present study, the non-CRT and CRT groups both scored higher on verbal immediate and delayed tasks than nonverbal immediate and delayed tasks. Both groups showed specific difficulties with visual immediate memory and learning over repeated trials. Exploratory analysis was carried out to determine the characteristics of these difficulties. Scores on the visual immediate memory tasks and learning trials for both groups were not associated with the FD factor on the WISC-III. However, a trend was observed for both groups when the CMS Attention/Concentration index was correlated with the Visual Immediate and Learning indexes.

**Arithmetic Functioning**

Most previous studies have documented arithmetic difficulties for children treated with cranial irradiation, but not with IT-MTX alone (Copeland et al., 1985; Deasy-Spinetta et al., 1988; Pfefferbaum-Levine et al., 1984). The prediction that the WRAT3 Arithmetic subtest would be significantly lower than either Reading or Spelling was not supported for the CRT group. Results showed that 33% of the group had scores below Average (standard score <90) for Reading and 42% for Spelling, indicating that these are also areas of difficulty for the CRT group. In contrast, for the non-CRT group, Arithmetic was significantly lower than the other 2 tests. None of the participants had below Average Reading scores and only 13% had below Average Spelling scores. In the present study, 42% of the CRT participants and 13% of the non-CRT group scored below Average on the Arithmetic subtest of the WRAT3. Rourke (1993) has defined an arithmetic disability as a pattern of normal reading and spelling concurrent with markedly impaired arithmetic performance. Siegel and Ryan (1989) have defined arithmetic disability as a WRAT Arithmetic score ≤ 25 percentile and a
WRAT Reading score $\geq 30$ percentile. Using these criteria, none of the CRT participants and only one non-CRT participant [Reading (30%), Spelling (47%) and Arithmetic (12%)], would qualify as arithmetic disabled.

There was no difference between timed and untimed conditions on the WRAT3 when group means were compared. However, within group comparisons identified a significant difference between timed and untimed conditions for the CRT group but not for the non-CRT group. These results must be interpreted with caution. In the CRT group, three out of four participants whose scores increased in the untimed condition were adolescents who obtained Average scores on the timed condition. Two of the participants' scores increased to High Average and one, to Superior. The third participant achieved a score within the Low Average range on the timed condition, and this improved to Average on the untimed task.

Lower scores on all the WISC-III indexes and factor scores predicted difficulties in Arithmetic achievement for the CRT group. It is important to note, that the only trend towards significance for the non-CRT group was the VC factor. For both groups, performance on verbal and non-verbal memory tasks was strongly predictive of achievement on Arithmetic.

The fact that memory performance was more predictive of arithmetic scores than cognitive test scores for the non-CRT group suggests the necessity of administering both cognitive and memory measures to predict arithmetic functioning. Arithmetic processing consists of a complex interaction of abilities. For example, the mean FD factor score was in the Low Average range for both groups (non-CRT: $M = 87.75$; CRT: $M = 89.92$). However, the FD factor was only associated with arithmetic achievement for the CRT group. Furthermore, it has been hypothesized that attention may contribute to memory retrieval
difficulties in arithmetic. Geary (1993) has suggested that if a child’s immediate memory span is short or if there is limited attention allocation, numerical information may not be encoded efficiently and rapid decay of information results. This process of decay may be better measured through memory tasks (e.g., immediate vs delayed memory) than cognitive tasks.

The results of this study indicate that the two most common error types (basic facts and defective algorithms) were similar for both groups in the timed and untimed format. As most categories contained too few errors, the final analysis employed the McCloskey model (basic fact retrieval and procedural knowledge), rather than Englehardt’s classification.

In addition to basic fact retrieval and procedural errors, the participants made some errors that were unclassifiable. For example, the standardized instructions for the WRAT3 direct the participant to reduce all fractions. Even after repetition, several participants failed to reduce, which resulted in errors. On other items, procedures were computed correctly, but inaccuracies were made in copying numbers. These types of errors were random and appeared to be related to lapses in attention or concentration.

Exploration of the association between neurocognitive factors and types of errors revealed variable results given the lack of power to detect statistical significance. However, some patterns did emerge. Lower scores on a rote auditory memory task from the WISC-III were associated with more basic fact errors for both groups. For the CRT group, a trend was also revealed for lower scores on tests of Vocabulary (WISC-III) and Verbal Immediate memory (CMS) being associated with a greater number of basic fact errors. This finding supports the hypothesis (Geary, 1993) that difficulties with retrieval of number facts may be associated with difficulties in long-term semantic memory.
The present study indicates that procedural knowledge errors are related primarily to non-verbal cognitive processes. This is consistent with Rourke's (1993) research that has described the important role of the right hemisphere in mathematical performance that requires adaptive reasoning and/or visual-spatial organization of the elements of the problem. Unexpectedly, scores on working a memory task (Digits Backward) on the WISC-III were not associated with procedural knowledge errors. Siegel and Ryan (1988, 1989) have postulated that children with arithmetic disabilities have a specific working memory deficit in relation to processing numerical information, in simultaneously recalling information and retrieving rules and procedures. Geary (1990) also reported that math-disabled children have relatively poor working memory resources. Again, the small sample size in this study may have decreased the power to detect such correlations.

The findings of this study, employing the dual model of arithmetic processing as reported by Ashcraft (1982) and McCloskey et al. (1985) (i.e. basic facts and procedural knowledge), indicate that arithmetic difficulties for the adolescents in this study are associated with both visual-spatial abilities and verbal abilities.

Results from this study indicate that a younger age at diagnosis is an important predictor of neurocognitive and arithmetic difficulties in children treated with cranial irradiation. For the non-CRT group, age at diagnosis was not a significant predictor. Age at diagnosis did not predict achievement on memory, reading, or spelling tasks for either group.

Age at diagnosis did predict error rates, with younger age at diagnosis being associated with more errors, fewer attempts, and fewer questions answered correctly.
Surprisingly, age at diagnosis did not predict the number of basic facts or procedural knowledge errors committed. However, the small number of errors overall may have mitigated against finding support for this hypothesis.

These results are consistent with most of the literature indicating that children treated with cranial irradiation at a younger age are more vulnerable to late neurocognitive effects (Brown & Madan-Swain, 1993; Copeland et al., 1985; Cousens et al., 1988; Lansky et al., 1984). Furthermore, we found that age at diagnosis is not significantly associated with cognitive and academic functioning in children treated without cranial irradiation (Brown et al., 1998; Copeland et al., 1985; Rubinstein et al., 1990).

Limitations of the Study

The possibility of an ascertainment bias must be considered, as participants were not selected randomly. Participants who were not experiencing school difficulties may have been less likely to agree to participate in a 3-1/2 hour assessment. Conversely, participants who were functioning at a higher cognitive level may have been more motivated to be involved in the challenging nature of these tests. Although the original sample was limited by constraints related to age at testing and time since diagnosis, all eligible participants were invited to participate. Future research would certainly benefit from a larger sample which could well require a multicentre study.

The absence of a control group is another limitation of this study. The use of population norms as a control group limits the generalization of findings. Brown et al. (1998) suggest that a control sample should include children who have another type of cancer or siblings of children with cancer, to control for the cancer experience.
Time missed from school has been found to be a very important factor in how these children progress academically (Brown & Madan-Swain, 1993; Butler & Copeland, 1993; Butler et al., 1994; Lansky, 1984). Future studies should determine the number of days missed from school records rather than relying on parent reports.

Implications for Future Research

There is increasing evidence that gender may be a factor in the nature of the neuropsychological effects of CNS prophylatic treatments (Butler & Copeland, 1993). Although the present study did not investigate gender differences, due to the small sample sizes, the preliminary findings indicate that girls who were diagnosed at an earlier age and treated with CRT are at higher risk for neurocognitive deficits in visual spatial areas. There was no gender effect for the non-CRT group. These initial results support previous research (Mulhern et al., 1991; Waber et al., 1990) which indicates that young girls are especially vulnerable to the effect of CRT. Brown et al. (1998) also reported this pattern in their study of children who received CNS prophylatic chemotherapy without CRT.

Future studies examining arithmetic processing in this population of children should investigate both computation and mathematical reasoning, as they draw on different abilities. The WRAT3 arithmetic task is limited in its ability to measure arithmetic competency in adolescents, as it assesses only mathematical computations. Furthermore, differences were found for the CRT group on timed and untimed procedural errors. An important component of future research would be to provide a more discriminatory analysis of reaction time on arithmetic tasks, by observing the amount of time required to compute clusters of questions with similar processing demands.
The evidence that memory is a strong predictor of arithmetic functioning suggests that memory measures should be an integral part of the research into late effects. From a methodological standpoint, it is crucial that there be uniformity in the measures used. However, unlike measures traditionally used to assess cognitive functioning (e.g., WISC-III, WPPSI-R), there are fewer consistently used memory measures.

**Implications for Remediation**

This study found no difference between the two groups on timed and untimed conditions for WRAT3 Arithmetic. There were differences found within the CRT group based on total performance and also for number of procedural errors made, with more errors in the timed condition. However, providing more time in which to compute math facts may not provide an advantage for students who have difficulties in computation. The ability to compute more facts is based on a pre-existing knowledge base in addition to the ability to retrieve this knowledge. That these children did not attempt more problems in the untimed condition, and the lack of association between processing speed and attempt rate, indicates that the time constraint was not a factor. We observed that most of these adolescents finished before the time limit. In most instances where time did make a difference, the child was already doing well in math and could continue to draw on his fund of arithmetic knowledge, when given more time.

The finding that arithmetic functioning relies on both verbal and nonverbal abilities, suggests that a multisensory approach might be used for presenting mathematical information. That is, when teaching algorithms or procedures, it may be beneficial to provide verbal support to visual presentation. Providing remediation for older adolescents is
difficult and several of the participants in this study had only basic math literacy. Encouraging these adolescents to use a calculator to support their computations to compensate for inadequate basic fact retrieval is a more practical remediation than having them try to learn their times tables, which depends on an efficient memory system and automaticity.

**Summary**

The findings from this study indicate that both the non-CRT and CRT groups demonstrated generally average performance on most tasks. Although the CRT group achieved lower scores on most measures relative to the non-CRT group, these differences were not significant. Both groups performed more poorly on measures of attention, immediate visual memory, multitrial learning tasks, and arithmetic compared to test norms. Adolescents in this study showed relative difficulties in both language and non-language areas. Furthermore, difficulties in arithmetic are related to both verbal and non-verbal abilities in cognitive and memory functioning with verbal abilities being associated with basic fact retrieval and visual spatial abilities being associated with procedural knowledge. Younger age at diagnosis was a strong predictor of neurocognitive and academic difficulties for the CRT group. The present study is a pilot project and should be considered exploratory. However, further research on the impact of treatment for leukemia on attention functioning and language and non-language abilities, will be important to enhance our understanding of how these adolescents learn and what intervention methods might be most effective.
References


Appendix A

Error Categories
Error Categories

1) **Basic fact error**: An error is classified as a basic retrieval error if the child employs a simple number sentence that is untrue (e.g., 1+4=6; 2x5=15). For example,

```
  72
x4
218   Error: 4x7=21
```

2) **Incorrect operation**: The child performs an operation other than an appropriate one. This may be due to the child misreading the sign. For example,

```
  4
+3   15
 1  - 2
 1   17
```

3) **Incomplete operation**: The child performs the correct operation with an appropriate procedure, but does not complete the operation. For example,

```
  598
x23
1794
```

4) **Place value error**: The child performs an error in computation because he/she does not understand the positional value in the numerical system. For example,

```
  174
  685
  131
  81810
```

5) **Regrouping error**: The child does not use correct carrying and borrowing procedures in computation. For example,

```
  38
x4
122
```
6) **Inappropriate inversion:** The child performs a computation that involves reversing the steps. A common example is subtracting the minuend from the subtrahend, or starting the computation from the wrong place. For example,

\[
\begin{array}{c}
532 \\
634 \\
102
\end{array}
\]

7) **Mix of operations:** The child applies various operations in one question. For example,

\[
\begin{array}{r}
36 \\
15 \\
41
\end{array}
\]

8) **Defective algorithm:** The child responds with a systematic but incorrect procedure but the error is not explainable by error types 4-7. For example,

\[
\begin{array}{c}
2 \times 4 = 8 \\
3 \times 3 \neq 6
\end{array}
\]

9) **Unclassifiable error:** The child makes an error that cannot be classified according to the above mentioned error types.

Appendix B

Consent Form for Ages 16 Years and Over
Consent Form
(Age 16 or Older)

Title of Study: Arithmetic Processing in Adolescents Treated for Leukemia

Investigators:
Karen Ghelani
Master of Applied Developmental Psychology Student
Ontario Institute for Studies in Education

Dr. Brenda Spiegler
Department of Psychology
Hospital for Sick Children
416-813-6784

Purpose of Research:
The purpose of this study is to obtain a better understanding of the kinds of school problems experienced by adolescents who have had leukemia. We want to learn more about how adolescents who have had leukemia solve math problems. We also want to find out whether having had radiation as part of treatment is associated with a different outcome.

Description of Research:
You will be asked to come to the Psychology Department at the Hospital for Sick Children once, for about 3 1/2 hours. You will be doing different types of activities including answering some questions and doing some puzzles. You will also be asked to do reading, spelling, arithmetic and memory activities. Breaks will be provided when needed. The results of these measures will be confidential and stored in a locked cabinet within the Department of Psychology.

Your health record at the Hospital for Sick Children will be reviewed to obtain information about your medical history. Your school will be contacted to obtain the number of days you missed during the time you were treated for leukemia.

Potential Harms (Injury, Discomforts or Inconvenience):
Taking the time to complete the tests could be an inconvenience. You could feel a bit awkward if you have difficulty answering some of the questions, but the examiner will give you every support and encouragement. There are no other known harms associated with participation in this study. Any concerns that arise during the course of the testing or interview, will be dealt with directly.
Potential Benefits:
We hope that the information collected from this project will help teachers understand how adolescents, who have been treated for leukemia, do on arithmetic tasks.

This information we collect from you will also provide you and your family with a unique profile of your abilities and learning needs. You will be provided with a written report.

Confidentiality:
Confidentiality will be respected and no information that discloses your identity will be released or published without your consent. For your information, the test results will be retained in the Department of Psychology. The research consent form and the written report will be inserted in your health record. The results of the tests described above will be used for research purposes only in the context of this study. We would need your permission and signed consent to send these test scores to another professional involved in your care. We recommend that the results of these tests be interpreted by a registered psychologist or physician. Psychological test scores can only be sent, with your permission, to another psychologist.

Participation:
Participation in this research is voluntary. If you choose not to participate, you and your family will continue to have access to quality care at the Hospital for Sick Children. If you choose to participate in this study you can withdraw from this study at any time. Again, you and your family will continue to have access to quality care at the Hospital for Sick Children.

Consent: (Subjects 16 years and older)
I acknowledge that the research procedures described above have been explained to me and that any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising the quality of medical care at the Hospital for Sick Children for me and for other members of my family. As well, the potential harms and discomforts have been explained to me and I also understand the benefits of participating in the research study. I know that I may ask now, or in the future, any questions I have about the study or the research procedures. I have been assured that records relating to me and my care will be kept confidential and that no information will be released or printed that would disclose personal identity without my permission.

I hereby consent to participate:

Name of Patient and Age

Signature (if 16 yrs. and over)

Dr. Brenda Spiegler
Who may be reached at 416-813-1500
Name of person who obtained consent

Signature

Date

Signature

Date
Appendix C

Information Form for Ages 14-15 Years of Age
and Research Consent Form for Parents
Information Form
(For subjects 14-15 years)

Title of Study: Arithmetic Processing in Adolescents Treated for Leukemia

Investigator: Karen Ghelani
Master of Applied Developmental Psychology Student
Ontario Institute for Studies in Education

Dr. Brenda Spiegler
Department of Psychology
Hospital for Sick Children
416-813-6784

Why are we doing this study?
Some adolescents who have had leukemia have difficulties with different types of school work when their treatment is over. We want to learn more about how adolescents who have had leukemia solve math problems.

What will happen during the study?
If you agree to participate, you will be asked to come to our office at the Hospital for Sick Children. You will be doing different types of activities including answering some questions and doing some puzzles. Some of the things that we ask you to do will be easy and some will be hard. It should take around 3 1/2 hours altogether to finish these tests but you can take a break in the middle if you get tired.

Are there good things and bad things in the study?
Some of the activities that you do will be quite easy for you and others may be more difficult. On some activities you may have to concentrate for a long time. But the person giving you the tests will do everything possible to put you at ease and you will be given a break during the activities. The test results might help you and your family understand how you learn most easily. We don’t think that there are any bad things about the study and we don’t think that you will be bothered by any of the questions.

Who will know what I did in the study?
If you are part of this study your name and address will not be given to anyone. Only your parents and the people who are directly involved with the project will know that you participated. Your test results will be shared with you and your parents. If your parents ask us to send a report about the test results to your school, we will do that as well.
Can I decide if I want to be in the study?
If you do not want to be part of this study it is O.K. No one will be upset or disappointed. If you say yes now but change your mind, that will be O.K. too. Your guardian, mother, or father is also reading some information about this study. They will talk to you about it. Ask them questions if you do not understand what you have read or heard. They will help you to understand. Please ask the person giving the tests any questions that you may have. They will also help you to understand.

Assent:
I was present when ______________________ read this form and gave his/her verbal assent

______________________________
Signature

______________________________
Date

______________________________
Name of person who obtained assent

______________________________
Signature

______________________________
Date
Research Consent Form
(Age Less Than 16)

Title of Study: Arithmetic Processing in Adolescents Treated for Leukemia

Investigators:
Karen Ghelani
Master of Applied Developmental Psychology Student
Ontario Institute for Studies in Education

Dr. Brenda Spiegler
Department of Psychology
Hospital for Sick Children
416-813-6784

Purpose of Research:
The purpose of this study is to obtain a better understanding of the kinds of school problems experienced by adolescents who have had leukemia. We want to learn more about how adolescents who have had leukemia solve math problems. We also want to find out whether having had radiation as part of treatment is associated with a different outcome.

Description of Research:
You and your child will be asked to come to the Psychology Department at The Hospital for Sick Children once, for about 3 1/2 hours. Your child will be doing different types of activities including answering some questions and doing some puzzles. Your child will also be asked to do reading, spelling, arithmetic and memory activities. Breaks will be provided when needed. The results of these measures will be confidential and stored in a locked cabinet within the Department of Psychology.

Your child’s health record at The Hospital for Sick Children will be reviewed to obtain information about his/her medical history. Your child’s school will be contacted to obtain the number of days your child missed during the time they were treated for leukemia.

Potential Harms (Injury, Discomforts or Inconvenience):
Taking the time to complete the tests could be an inconvenience. Your child could feel a bit awkward if they have difficulty answering some of the questions, but the examiner will give them every support and encouragement. There are no other known harms associated with participation in this study. Any concerns that arise during the course of the testing or interview, will be dealt with directly.
**Potential Benefits:**
We hope that information the information collected from this project will help teachers understand how adolescents, who have been treated for leukemia, do on arithmetic tasks.

This information we collect from your child will also provide you and your family with a unique profile of your child’s abilities and learning needs. You will be provided with a written report.

**Confidentiality:**
Confidentiality will be respected and no information that discloses the identity of your child will be released or published without your consent unless required by law. For your information, the test results will be retained in the Department of Psychology. The research consent form and the written report will be inserted in your child’s health record. The results of the tests described above will be used for research purposes only in the context of this study. We would need your permission and signed consent to send these test scores to another professional involved in your child’s care. We recommend that the results of these tests be interpreted by a registered psychologist or physician. Psychological test scores can only be sent, with your permission, to another psychologist.

**Participation:**
Participation in this research is voluntary. If you choose not to participate, you and your family will continue to have access to quality care at the Hospital for Sick Children. If you choose to participate in this study you can withdraw from this study at any time. Again, you and your family will continue to have access to quality care at the Hospital for Sick Children.

**Consent: (Parents of Subjects under 16 years of age)**
I acknowledge that the research procedures described above have been explained to me and that any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising the quality of medical care at The Hospital for Sick Children for my child and other members of my family. As well, the potential harms and discomforts have been explained to me and I also understand the benefits of participating in the research study. I know that I may ask now, or in the future, any questions I have about the study or the research procedures. I have been assured that records relating to my child and my child’s care will be kept confidential and that no information will be released or printed that would disclose personal identity without my permission.

I hereby consent for my child ________________________________ to participate:

__________________________________
Name of Parent
The person who may be contacted about the research is: Dr. Brenda Spiegler who may be reached at 416-813-1500.

Name of person who obtained consent

__________________________
Signature

__________________________
Date
Appendix D

Measure of Effect Size for Cognitive, Memory, and Academic Measures
Measure of Effect Size for WISC III Scores for non-CRT and CRT Groups Relative to Test Norms

<table>
<thead>
<tr>
<th>Group</th>
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*Compared with a mean=100 and a standard deviation=15
** Effect Sizes .2, .5 and .8 correspond to small, medium and large effect sizes
Measure of Effect Size: WISC III Scores for non-CRT and CRT Groups When Compared to Each Other

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** Effect Sizes .2, .5 and .8 correspond to small, medium and large effect sizes.
Measure of Effect Size for CMS Scores for non-CRT and CRT Groups Relative to Test Norms

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*Compared with a mean=100 and a standard deviation=15

** Effect Sizes .2, .5 and .8 correspond to small, medium and large effect sizes
Measure of Effect Size for CMS for non-CRT and CRT Groups Compared to Each Other

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** Effect Sizes .2, .5 and .8 correspond to small, medium and large effect sizes
### Measure of Effect Size for WRAT3 Achievement for non-CRT and CRT Groups Relative to Test Norms

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*Compared with a mean=100 and a standard deviation=15

** Effect Sizes .2, .5 and .8 correspond to small, medium and large effect sizes

### Measure of Effect Size for WRAT3 Achievement for non-CRT and CRT Groups Compared to Each Other

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** Effect Sizes .2, .5 and .8 correspond to small, medium and large effect sizes
Appendix E

*Attempt Rate, Error Rate, Mastery Rate*
### Mean Error Rates, Attempt Rates and Mastery Rates for non-CRT and CRT Groups

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Appendix F

Percentage of Errors Made for Each Error Type
### Percentage of Error Types for non-CRT and CRT Groups

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Appendix G

Correlations Between Error Type and Cognitive and Memory Measures
## Correlations for Types of Errors and WISC-III Indexes for non-CRT Group

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***p<.001  **p<.01  *p<.05
Correlations for Types of Errors and CMS Indexes for non-CRT Group

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***p<.001 **p<.01 *p<.05
## Correlations for Types of Errors and WISC-III Indexes for CRT Group

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### Full - Scale IQ
- .02 & -.27

### Verbal IQ
- -.30 & -.36

### Performance IQ
- -.19 & -.55

### VC
- .10 & -.12

### PO
- -.33 & -.56

### FD
- -.03 & -.22

### PS
- -.01 & -.38

### Verbal

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### Non - Verbal

| Picture Completion | -.12 | -.55 |
| Coding             | .23  | .18  |
| Picture Arrangement| -.09 | -.56 |
| Block Design       | -.45 | -.42 |
| Object Assembly    | -.10 | -.50 |
| Symbol Search      | -.21 | -.51 |

***p<.001  **p<.01  *p<.05
### Correlations for Types of Errors and CMS Indexes for CRT Group

<table>
<thead>
<tr>
<th>CMS Indexes</th>
<th>Basic Facts</th>
<th>Procedural Knowledge</th>
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<td>Attention / Concentration</td>
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***p<.001 **p<.01 *p<.05