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AN INVESTIGATION OF THE LONG-TERM NEUROPSYCHOLOGICAL OUTCOME OF PRENATAL TERATOGENIC EXPOSURE:

FETAL ALCOHOL SYNDROME AND MATERNAL PKU SYNDROME

A Thesis Submitted to the Faculty of

Graduate Studies and Research

in Partial Fulfillment of the Requirements

for the Degree of Doctor of Philosophy

in the Department of Psychology

University of Saskatchewan

Saskatoon, Saskatchewan

By

Susan R. Brock

Spring, 1999

UNIVERSITY OF SASKATCHEWAN

College of Graduate Studies and Research

SUMMARY OF DISSERTATION

Submitted in partial fulfillment .

of the requirements for the

DEGREE OF DOCTOR OF PHILOSOPHY

by

Susan R. Brock

Department of Psychology

University of Saskatchewan

Spring 1999

Examining Committee:

Dr. A. Leis	Dean's Designate, Chair, College of Graduate Studies & Research
Dr. J. Cheesman	Chair of Advisory Committee, Department of Psychology
Dr. J. Nanson	Supervisor, Department of Psychology
Dr. D. Scott	Department of Psychology
Dr. M. Crossley	Department of Psychology
Dr. B. Habbick	Professor Emeritus, Department of Community Medicine and Epidemiology, Royal University Hospital

External Examiner:

Dr. Julie Conry
Assistant Professor, Department of Educational Psychology
University of British Columbia
Vancouver, British Columbia

An Investigation of the Long-term Neuropsychological Outcome of Prenatal Teratogenic Exposure: Fetal Alcohol Syndrome and Maternal PKU Syndrome

Previous research has shown a relationship between prenatal teratogenic exposure and impaired cognitive functioning. However, data regarding the long-term outcome of prenatal teratogenic exposure are minimal. The present study investigated the long-term neuropsychological functioning (specifically attention and memory) of adults prenatally exposed to alcohol or phenylalanine, and examined whether there was evidence to suggest that there are effects specific to individual teratogens.

Using a battery of attention and memory measures the performance of 17 adults diagnosed with Fetal Alcohol Syndrome (FAS) and 13 adults with Maternal Phenylketonuria Syndrome (MPKUS) was assessed. In order to examine the pattern of deficits associated with prenatal teratogenic exposure, an age and IQ matched control group was assessed. Attention was broadly assessed using Mirsky et al.'s (1991) neuropsychological model of attention. The memory and learning tests administered included a number of well standardized measures of verbal learning, verbal and visual recall, delayed recall, and recognition.

Paired comparisons between the FAS group and age and IQ matched controls indicated a unique pattern of attention and memory deficits consistent with previous research with children and adolescents. Specifically, adult individuals with FAS appear to have deficits in acquisition of new material, delayed recall of verbal material and in response inhibition. Paired comparisons between the MPKUS group and IQ matched controls indicated that the pattern of attention and memory deficits seen in adults with MPKUS is difficult to distinguish when the effect of IQ is removed.

A randomized block design using IQ as the blocking variable and group (FAS, MPKUS, or Controls) as the treatment variable was utilized to examine the question of whether the two prenatal teratogen groups differ from one another and from Controls in terms of attention and memory ability. Ten blocks of three participants (FAS, MPKUS

and Control) matched on IQ were formed. The randomized block analyses revealed few differences between the groups and failed to reveal a number of the differences found in the paired comparisons between the prenatal teratogen groups and the IQ matched Control group. Possible reasons for these differences are discussed.

BIOGRAPHICAL

December, 1960	Born in California, U.S.A.
October, 1989	Bachelor of Arts (Hon.), Psychology University of Saskatchewan
May, 1992	Master of Arts, Clinical Psychology University of Saskatchewan

HONOURS

Roeher Institute Student Research Grant, 1993-1995
University of Saskatchewan Graduate Scholarship, 1991-1992
University of Saskatchewan Graduate Scholarship, 1990 - 1991
Natural Sciences and Engineering Research Council of Canada University Undergraduate Student Research Award, Summer, 1989
University of Saskatchewan Honours Scholarship, 1988 - 1989

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Head of the Department of Psychology
University of Saskatchewan
Saskatoon, Saskatchewan S7N 0W0

ABSTRACT

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DEDICATION

In loving memory of my grandfather, Frank Anderson whose belief in me has been a continual driving force throughout my life.

To my grandmothers, Muriel Anderson and Katherine Brock, you are an ongoing inspiration to all that know you and I love you dearly.

To my son Ryan who supported me throughout my education journey and who many times did without my time and attention in order that I could reach my goal. Thank you Ryan, the pride you have expressed in me has meant more than I can express.

To Mark, who came along in the middle of my journey and managed to survive internship and endless evenings and weekends of "I have to work". You were always supportive and never once complained. Thanks for waiting.

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LIST OF ABBREVIATIONS

ACH ..... Acetaldehyde

ADD ..... Attention Deficit Disorder

ADHD ..... Attention Deficit Hyperactivity Disorder

ADV ..... Average Daily Volume

ANOVAS ..... Analyses of Variance

CNS ..... Central Nervous System

CPT ..... Continuous Performance Test

CVLT ..... California Verbal Learning Test

CVLT-C ..... California Verbal Learning Test for Children

FAE ..... Fetal Alcohol Effects

FAS ..... Fetal Alcohol Syndrome

FHD ..... Frequent Heavy Drinking

HD ..... Huntington's Disease

IQ ..... Intelligence Quotient

MPKUS ..... Maternal PKU Syndrome

MRI ..... Magnetic Resonance Imaging

PDH ..... Pyruvate Dehydrogenase Complex

PEA ..... Prenatal Exposure to Alcohol

PKU ..... Phenylketonuria

RAVLT ..... Rey Auditory Verbal Learning Test

SES ..... Socioeconomic Status

SNK ..... Student Newman Keuls

TLCT ..... Talland Letter Cancellation Test

WAIS-R ..... Wechsler Adult Intelligence Scale-Revised

WCST ..... Wisconsin Card Sorting Test

WRAT-3 ..... Wide Range Achievement Test-Third Edition

1 An Investigation of the Long-term Neuropsychological Outcome of Prenatal Teratogenic Exposure: Fetal Alcohol Syndrome and Maternal PKU Syndrome

1.1 Introduction

Behavioural teratology is the study of the behavioural effects of teratogenic exposure. Teratogens are substances known to affect offspring in an adverse manner as a result of prenatal exposure. There are four outcomes of teratogenic exposure: functional deficits (teratogenesis), growth deficiency, malformation, and death. Functional deficits are usually defined in terms of central nervous system (CNS) deficits. Vorhees (1986) proposed that for teratogens that cause all four types of teratogenic outcomes, there is a dose/response curve for each outcome (See Figure 1.1), as well as a dose/effects relationship among outcomes.

The most commonly used teratogen is alcohol. Other known human teratogens include phenylalanine, anticonvulsants, benzodiazepines, anticoagulants, and thalidomide. To date, the behavioural teratology of alcohol has received the most attention in the teratogen literature. Although existing prospective studies and animal models have delineated the early effects of maternal alcohol consumption on fetal and child development; empirical data on adult outcomes are minimal (Hanson, Streissguth, & Smith, 1978; West et al., 1990).

The effects of prenatal phenylalanine exposure on the development of young children have been broadly described; however, little scientific evidence has been published regarding the development of these children in terms of specific strengths

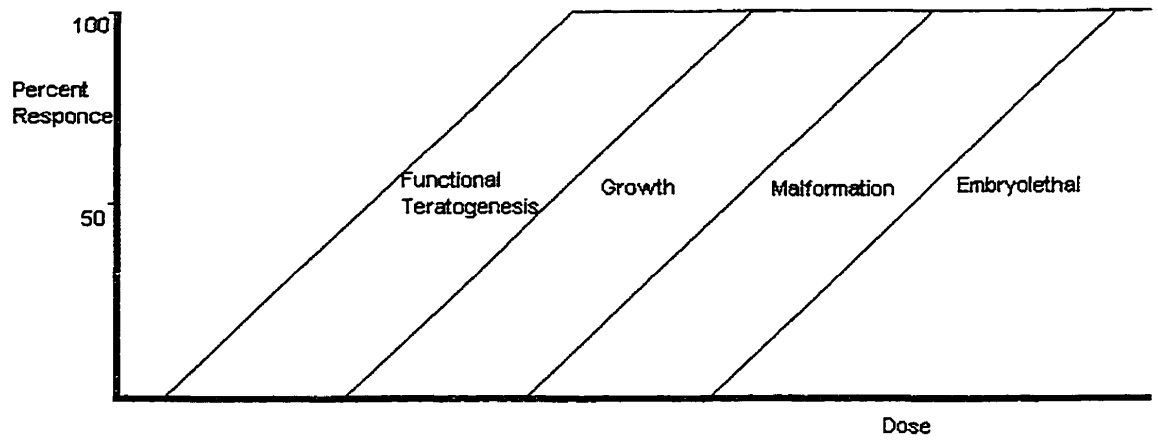


FIGURE 1.1 VORHEES DOSE/RESPONSE CURVE.

Idealized dose/response curves for the major manifestations of teratogenesis. The slope and spacing of the curves are dependent on the agent under investigation. The positions of the curves are only valid in their ordinal relationship to one another and if and only if the agent in question is capable of producing all four types of embryo toxicity shown (from Vorhees, 1986).

and deficits. Until recently, there was no animal model of phenylalanine's prenatal influence. Therefore, there is limited information available regarding the teratogenic properties of phenylalanine.

The existing literature on other prenatal teratogens, such as anticonvulsants, anticoagulants, and benzodiazepines, is based on clinical reports because of the low base rate of these disorders. Therefore, only the effects of alcohol and phenylalanine will be examined in the present study.

Data concerning the complete developmental trajectory of prenatal teratogens are minimal. In order to attribute a pattern of deficits to a specific prenatal teratogen, it is necessary to demonstrate that it is significantly different from the pattern of deficits that results from other prenatal teratogens. Based on a review of the relevant literature on prenatal teratogens, the pattern of deficits resulting from exposure to various teratogens appears more similar than different (e.g., Mason, Jardine, & Gibbin, 1992; St. Clair & Schirmer, 1992; Viggedal, Hagberg, Laegreid, & Aronsson, 1993). The majority of the information available pertaining to these teratogens is based on clinical observation rather than empirical investigation. Therefore, it is difficult to determine whether the few differences between various patterns of deficits can meaningfully differentiate different types of prenatal teratogenic exposure.

The present study investigates the pattern of attention and memory abilities in adults who were prenatally exposed to alcohol or phenylalanine, and it examines whether there are effects specific to individual teratogens.

2 Fetal Alcohol Syndrome

2.1 History and Description

The term Fetal Alcohol Syndrome (FAS) was proposed by Jones, Smith, Streissguth, and Myrianthopoulous (1974) to describe a pattern of malformations observed in children born to alcoholic mothers. Although the terminology was new at the time, knowledge of the effects of drinking during pregnancy was by no means novel. References to alcohol's harmful effects on the fetus can be found throughout history. One of the earliest documented studies was carried out in 1899 by a British physician who noted that the neonatal mortality rate in alcoholic women was two and one-half times that of non-alcoholic women (as cited in Streissguth & LaDue, 1987).

The first carefully conducted empirical study of the effects of prenatal alcohol exposure was not carried out until 1968. A French pediatrician, Paul Lemoine, reported growth deficiencies, behavioural disturbances, and physical malformations in 120 children of alcoholic women (Lemoine, Harrousseau, Borteyru, & Menuet, 1968).

Widespread international recognition and acceptance of alcohol (independent of any other agent) as a direct cause of birth defects did not occur until 1974. At this time Jones and his colleagues published two papers describing their observations of 11 children of alcoholic women; all of these children shared a similar pattern of malformations (Jones, Smith, Ulleland, & Streissguth, 1973; Jones et al., 1974). The authors proposed a link between "maternal alcoholism and aberrant morphogenesis in the offspring" (Jones et al., 1973, pg. 1000). Following the publication of these

influential papers, Clarren and Smith (1978) delineated the clinical characteristics necessary to make a diagnosis of FAS. These characteristics included a history of maternal alcoholism, mental retardation/developmental delay and/or microcephaly, prenatal and postnatal growth retardation (height and weight below the fifth percentile for age), and facial malformations. Facial malformations include short palpebral fissures, epicanthal folds, flattened midface, short upturned nose, long smooth philtrum, low nasal bridge, minor ear abnormalities, micrognathia, and thin vermilion of the upper lip (see Figure 2.1).

Besides those characteristics delineated by Clarren and Smith (1978), there are other characteristics, although not diagnostic, which are commonly seen with FAS. These include other types of CNS dysfunction, such as seizure disorders, hyperactivity, and attention deficits, as well as hearing loss, cardiac defects, and hand anomalies. FAS is considered to be the third most prevalent known cause of mental retardation, with only Down's Syndrome and spina bifida being more prevalent (National Institute on Alcohol Abuse and Alcoholism, 1993).

Streissguth and Ladue (1987) described the effects of prenatal exposure to alcohol as a "continuum of disabilities," with FAS representing the most severe end of the continuum and a less severe consequence of prenatal exposure to alcohol being termed Fetal Alcohol Effects (FAE). A diagnosis of FAE is made when the child has few physical malformations but manifests a subnormal intelligence quotient (IQ) as well as the behavioural and CNS disturbances associated with FAS, such as hyperactivity, attention deficit, poor judgement, and delayed learning. It is important to

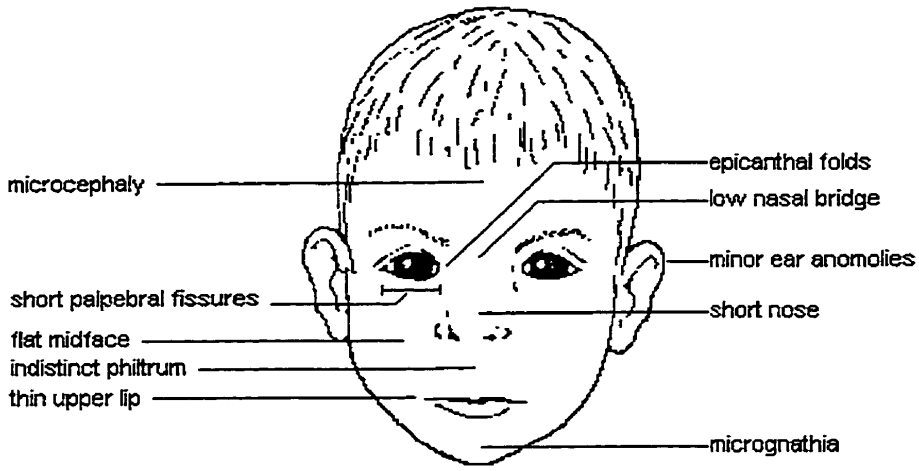


FIGURE 2.1 FACIAL DYSMORPHOLOGY IN FAS.

Facies in FAS particularly characteristic of the prepubertal child. Features on the left side are the most definitive, Those on the right side are less differentiating. Microcephaly (small head circumference) is not a facial feature per se, but a central nervous system characteristic. (Epicanthal folds: small fold of skin covering inner corner of the eye; philtrum: zone between nose and mouth; micrognathia; abnormal smallness of the jaws; palpebral fissures: eye openings.) Source: Little & Streissguth, 1982.

note that a woman does not necessarily have to be an alcoholic during pregnancy in order to bear a child with FAS or FAE.

Alcohol is a teratogen that can cause all four types of outcome (i.e., functional deficits, growth deficiency, malformation, and death). In humans we see an increased risk of spontaneous abortion, stillbirths, malformations, resorption, growth deficiency, and CNS deficits related to prenatal exposure to alcohol. Animal studies show face and limb malformations, resorption, growth deficiency, and decreased litter size. CNS deficits are also frequently observed, particularly hippocampal damage, cerebellar damage and changes in size and weight of the brain (Abel, 1981; Streissguth & LaDue, 1985). The behavioural teratology of alcohol in animal studies replicates that shown in humans, including increased offspring activity, developmental delay, poor nursing ability, poor response inhibition, and decreased learning (Meyer & Riley, 1986).

There is extensive evidence from both animal and human studies that ethanol rapidly crosses the placental and blood-brain barriers of the fetus and reaches approximately the same levels of concentration as those found in the mother (Corrigan, 1976; Jones et al., 1973). Data from both clinical and animal studies have revealed that defective growth and morphogenesis is directly related to the level of maternal blood alcohol rather than to the amount of alcohol ingested (Jones et al., 1973; Sandor, 1981).

Rosett, Ouellette, Weiner, and Owens (1978) have proposed that the most damaging morphologic effects of FAS are caused by high concentrations of alcohol in the blood at critical periods of fetal development. It is generally recognized that the first trimester in particular, the period from 4-10 weeks gestation (period of embryogenesis-establishment of the embryonic body) is most critical for the induction

of anatomic abnormalities (Ernhart, Sokol, Martier, Moron, Nadier, Ager, & Wolf, 1987). Ernhart and her colleagues (1987) found that maternal drinking early in the first trimester explained considerably more variance in the craniofacial and other anomalies than either late first trimester or second trimester maternal alcohol use. During the second half of the gestation period, nerve cells in the neocortex are generated and migrate to the appropriate brain regions. Alcohol exposure appears to influence the timing and pattern of nerve cell generation, both delaying the process and altering the number of cells that are produced. In addition, cell migration patterns are altered so that unusual cell formations occur in many areas in the brain, including the hippocampus, cerebellum, sensory nucleus, and neocortex (Coles, 1994).

Third trimester-equivalent effects have been studied extensively by West and Goodlett (1990) using a rat model. There is a period of rapid brain development that occurs, in part, during the third trimester in humans (prenatally) and in rats (postnatally). Exposure to alcohol during this period results in reduced brain weight and head circumference, and reduced numbers of cells in certain regions of the hippocampus and cerebellum (West & Goodlett, 1990). The hippocampus is known to affect learning and memory and the cerebellum to affect motor ability. That these anatomical changes are related to abnormal behaviour later in life is suggested by findings demonstrated by physically normal animals that were exposed to alcohol during the third trimester. The animals demonstrated learning deficits, more activity than controls, and an inhibitory response deficit that is compatible with the clinical reports of impulsiveness, distractibility, and attentional deficits seen in FAS children (Riley, Lochry, & Shapiro, 1979; Riley, Lochry, Shapiro, & Baldwin, 1979).

In an attempt to examine the effects of third trimester alcohol exposure in humans, Day, Goldschmidt, Robles, Richardson, Taylor, Geva, and Stoffer (1991) carried out a prospective study that used two measures of maternal drinking: average daily volume (ADV) and frequent heavy drinking (FHD). They found significant inverse relationships between both prenatal FHD and ADV and offspring growth at 18 months (i.e., higher alcohol intake was associated with decreased growth). They also found a significant inverse relationship between ADV during the second and third trimester and weight, height, and head circumference at 18 months. In a more recent study, Day and colleagues have reported a relationship between ADV and lowered IQ and achievement at age two years (Day et al., 1991).

Neuroanatomical studies that report structural damage in the hippocampus of animals prenatally exposed to alcohol suggest a possible anatomical basis for behavioural effects: it has been found that experimental prenatal lesions of the hippocampus produce much the same effects as prenatal alcohol exposure (Barnes & Walker, 1981; West, Hodges, & Black, 1981). There is also some initial evidence from magnetic resonance imaging (MRI) studies that suggests a possible anatomical basis for behavioural effects in humans with FAS (Mattson, Riley, Jernigan, Ehlers, Delis, Jones, Stern, Johnson, Hessilink, & Bellugi, 1992; Mattson, Jernigan, & Riley, 1994).

Mattson et al. (1994) obtained MRIs from two adolescents with a clinical diagnosis of FAS, and from two adolescents who had a known history of heavy prenatal exposure to alcohol (PEA) but lacked sufficient characteristics to warrant the clinical diagnosis of FAS. Mattson et al. found that all four children were microcephalic; the volume of each adolescent's brain was about 25 percent smaller than

the brain of a healthy child of the same age. The volume of the cerebellar area was also smaller than that of an average healthy child by approximately 20 percent. In addition, the basal ganglia were also reduced in size. Mattson et al. controlled for the overall reduction in the brain volume of their participants by examining the volume of each brain part in proportion to the overall volume of the brain. Even after this adjustment, the basal ganglia were still smaller in size than those of both normal and mentally retarded control participants. Mattson et al. also found reduced corpus callosum in the FAS and PEA children compared to normal children matched for age and gender. Lastly, the volume of the diencephalon was reduced in all four children. However, after controlling for the overall reduction in brain size, only the two children with FAS showed a reduction in the proportional size of the diencephalon; although the children with PEA showed a reduction in the size of their diencephalon, the ratio remained within the normal range for healthy control subjects.

Mattson et al. (1994) used their data to argue for a connection between the behavioural and cognitive characteristics associated with prenatal alcohol exposure, such as memory deficits, and specific structural defects in the brain. To relate brain structure to function they used the example of Huntington's disease (HD), which is an inherited disorder associated with damage to the basal ganglia that causes motor abnormalities as well as memory problems or dementia. On the (CVLT), a test of auditory memory involving five presentations of a list of 16 words taken from four semantic categories, HD patients demonstrated limited ability for learning and immediate recall of a word list. The HD patients also displayed perseverative errors, were insensitive to proactive interference, and performed better when asked in a yes/no

format whether certain words appeared on the list as opposed to an unassisted recall format. The CVLT for children has been given to children with FAS, and the results show a similar pattern of performance to individuals with HD, suggesting that smaller basal ganglia size may effect FAS children's memory (Mattson et al., 1994; Streissguth, Barr & Sampson, 1990; Streissguth et al., 1994). For example, the basal ganglia play a role in our ability to remember where things are in space, in our goal-directed behaviour, and in our ability to successfully transfer from one activity or task to the next. Streissguth, Aase, Clarren, Randels, LaDue, & Smith (1991) have reported memory deficits specifically in the area of spatial memory in their subjects with FAS. There are also both clinical and empirical reports of children with FAS having difficulty learning the consequences of their actions and being perseverative (Nanson, 1993; Streissguth et al., 1991).

The three regions of the corpus callosum that Mattson et al. (1994) found to be reduced in prenatally alcohol-exposed children are, in healthy people, thought to contain nerve fibers from several parts of the brain. These include the frontal region, involved in complex integration of other brain systems; the posterior parietal region, involved in visual and spatial functioning; the temporal region, involved in memory; and the occipital region, involved in vision.

The three reduced regions of the corpus callosum in individuals with FAS are also reduced in children with Attention Deficit Hyperactivity Disorder (ADHD), which is a cluster of symptoms consisting of excessive motor activity, inattention, distractibility, and impulsivity (Hynd, Semrud-Clikeman, Lorys, Novey, Eliopulos, & Lyytinen, 1991). That these regions are reduced in both FAS and ADHD children

suggests that there may be some common dysfunction in brain development underlying both disorders. That is, the fact that both disorders include symptoms of hyperactivity and difficulty with behavioural inhibition may indicate that both have deficiencies related to the frontal region of the brain. Thus, there is clear evidence of structural changes in the brain as a result of prenatal alcohol exposure, and emerging evidence linking behavioural deficits to this damage.

2.2 Cognitive Development in Children with FAS

One of the main criteria on which a diagnosis of FAS is made is central nervous system deficits; in particular, subnormal IQ. The majority of studies report the average intelligence score of FAS children to be 68, with the average verbal score being about 10 points lower than the performance score, which is typically attributed to the Native Ancestry of the majority of the participants (Streissguth et al., 1991). There have, however, been exceptions to these findings. Shaywithz, Cohen, and Shaywithz (1980) reported on a sample of 15 children born to alcoholic mothers. These children exhibited physical signs of FAS, as well as hyperactivity, impulsivity, restlessness, short attention span, and distractibility, yet had intelligence scores within the normal range. Further, there have been other studies that have reported IQ scores in the low average range (e.g., Male, Nanson, & Block, 1995; Streissguth & Randels, 1991). The most frequently reported problems in individuals with FAS are attention and memory deficits. Problems with judgment, comprehension, and abstraction that significantly hamper psychosocial adjustment have also been reported (Streissguth & Randels, 1991).

Parents and caretakers report impaired daily living and socialization skills, as well as increasing difficulties as children reach adolescence and early adulthood. Both parents/caretakers and clinicians describe these children as naive and gullible, as well as seemingly unable to learn from past experiences. In Streissguth et al.'s (1991) long-term follow-up study of individuals with FAS, major psychosocial and life-long adjustment problems were noted even in those individuals who were of borderline (70-79) or higher IQ. In particular, they were found to have extreme difficulty with abstractions such as time and space, cause and effect, and generalizing from one situation to another. It was also noted that the severity of deficits in individuals with FAS is often masked by their ability to carry on superficial conversation.

In summary, the literature has suggested that prenatal exposure to alcohol can result in deficits, which range along a continuum from mild to severe. The severity of these deficits has been shown to correlate with dose and timing of exposure. Research on the cognitive development of children with FAS suggests that attention and memory deficits exist even when IQ is in the normal or low average ranges.

2.3 Prevalence Rates

It is commonly cited that approximately one third of children born to alcoholic mothers will have FAS (e.g., Niccols, 1994; Streissguth, Sampson, Carmichael-Olson, Bookstein, Garr, Scott, Feldman, & Mirsky, 1994). Data from the Collaborative Perinatal Project estimates the incidence of chronic alcoholism during pregnancy to be between .42 and 1.23 cases per 1,000 pregnancies (Hanson, Jones, & Smith, (1976). However, this range may be an underestimate because those women who drink the most are unlikely to give an accurate account of their alcohol consumption (Erb &

Andresen, 1978). Moreover, those women who drink the most alcohol have also been shown to smoke more and to have a poorer diet than women who drink less, which may compound the effects of alcohol on the fetus thereby limiting what conclusions may be drawn (Rosett et al., 1978).

The prevalence rate of FAS for all live births (including those of alcoholic and nonalcoholic mothers) has been reported to be one in 750. This rate was determined from systematic, retrospective studies of newborns conducted in France (Dehaene, Crepin, Delahousse, Querleu, & Blane-Garin, 1981), the United States (Hanson et al., 1978), and Sweden (Olegard, Sabel, Aronsson, Sandin, Johansson, Carlsson, Kyllerman, Iversen, & Hrbek, 1979). However, prevalence figures vary quite dramatically depending on the population in question. For example, a surveillance study conducted by Wong (unpublished) between 1973 and 1980 in British Columbia found an incidence rate of FAS ten times higher for the Native population than for the rest of the population (4.7 per 1000 versus .4 per 1000). Another surveillance study, based on hospital discharge records of FAS cases collected from 1236 United States hospitals, found that the incidence of FAS among Blacks was seven times higher than among Whites, and the rate among Native Americans was 30 times higher than among Whites (Chavez, Corder, & Becerra, 1988).

The prevalence rates cited in the previously mentioned studies were based on retrospectively gathered data. In the area of FAS, retrospective data collection typically involves the use of infants' hospital discharge records to determine the presence or absence of FAS, or it involves choosing a particular population (e.g., a Native reserve) and assessing all of the children for the presence or absence of FAS. Studies of this

type have been criticized on several levels, ranging from their lack of consistent diagnostic criteria to the lack of random sampling. The most consistent criticism of retrospective research, however, has been that one finds what one is looking for. Hence, retrospective studies likely provide the least conservative view of the prevalence of alcohol-related birth defects.

In contrast to retrospective studies, prospective studies provide the most conservative estimates of alcohol-related birth defects. Prospective studies of FAS typically follow a large number of women throughout their pregnancies. Questions concerning alcohol intake, smoking, diet, etc. are embedded in larger more general questionnaires dealing with issues surrounding pregnancy. These questionnaires are administered to mothers at several points throughout the pregnancy. Physicians who are blind to maternal alcohol intake make subsequent examination and diagnosis of the offspring.

Based on a review of 15 prospective studies, Abel and Sokol (1991) estimated the incidence of FAS in the western world to be .33 cases per 1000. However, in Cleveland hospitals, a prospective study of 8331 consecutive pregnancies found a prevalence rate of 20.8 cases of FAS per 1000 which results in an incidence of 3.00 per 1000 for the entire population (Sokol, Ager, Martier, Debanne, Ernhart, Kuzma, & Miller, 1986). This incidence rate is approximately 10 times higher than the .33 cases per 1000 cited as the incidence rate for the western world. Sokol et al. (1986) concluded that the most critical determinant of the number of cases of FAS cited is likely to be the population characteristics of the study site.

Prospective studies, although more methodologically rigorous than retrospective ones, probably provide an underestimate of actual incidence due to their reliance on prenatal clinics to recruit participants. It is likely that the heaviest-drinking women do not seek out regular prenatal care and thus would not be included in studies of this type. The use of self-report questionnaires may also lead to under-reporting or denial by the expectant mothers of their actual alcohol intake during pregnancy. Further, it is unclear the extent to which poor diagnostic reliability of FAS influences prevalence numbers (Little & Wendt, 1991). Given these problems, the true incidence rate of FAS probably lies somewhere between the numbers cited by retrospective studies and those found in prospective studies.

Besides the debate regarding the incidence rate, whether or not FAS affects one sex of offspring more than the other also remains unclear. There has been some suggestion that there is a greater preponderance of females with FAS than males (e.g., Coles, Brown, Smith, Platzman, Erickson, & Falek, 1991; Qazi and Masakawa, 1976). Moreover, Nanson (1992; 1993) has consistently found females with FAS to function at higher levels than males, which may suggest a higher incidence of fetal miscarriage of males. This gender difference in level of functioning has also been reported in the Fragile X and Attention Deficit Hyperactivity Disorder populations with males being more affected (Wright-Talamante, Cheema, Riddle, Luckey, Taylor, & Hagerman, 1996). However, the issue is far from clear as the majority of studies reviewed did not report sex ratios or sex differences.

3 Maternal Phenylketonuria Syndrome

3.1 History and Description

Maternal phenylketonuria (MPKU) refers to fetal damage that occurs during pregnancy in women with classic phenylketonuria (PKU). The offspring of women with PKU are described as having maternal PKU syndrome (MPKUS). PKU is a hereditary, autosomal recessive metabolic disorder. It is identified by an elevated level of plasma phenylalanine and by the presence of phenylpyruvic acid in the urine. PKU is caused by a deficiency of the enzyme phenylalanine hydroxylase; this enzyme is used to metabolize phenylalanine, a large neutral amino acid in food. Because this enzyme is missing, phenylalanine builds up in the bloodstream and eventually causes severe mental retardation.

In the mid-1950s, it was demonstrated that initiating a diet low in phenylalanine beginning early in infancy resulted in the prevention of the neurological and intellectual deterioration typically associated with PKU (Bickel, Gerrard, & Hickman, 1954; Woolfe, Griffiths, & Moncrieff, 1955). In 1963, an assay, based on bacterial inhibition, was developed to identify newborns with PKU (Guthrie and Susii, 1963). This identification method was implemented in mass screening programs throughout Europe and North America in the mid- 1960s.

Initially, it was believed that dietary treatment need be continued only until the child reached six years of age in order to ensure normal cognitive development. The belief was based on the notion that the brain had completed its myelination process by

six years of age and, hence, high levels of phenylalanine could no longer produce brain damage. Indeed, there are now many adolescents and young adults who, having received early dietary treatment, demonstrate average intelligence quotients (IQs). However, more recent research has shown that although these individuals have average IQs, those who have discontinued dietary treatment have high blood phenylalanine levels and show evidence of subtle intellectual and neurological deterioration (Koch, Azen, Freidman, & Williamson, 1982). On the basis of this information, most clinics dealing with PKU now promote indefinite continuation of dietary therapy.

A low phenylalanine diet has been found to be crucial for women with PKU who are considering pregnancy. The first report of offspring damage appeared in an article by Dent in 1957. He described three retarded women with untreated PKU who had each given birth to a retarded child. Unfortunately, little attention was paid to these observations because, prior to the initiation of widespread newborn screening programs, most women with PKU were severely mentally retarded and thus were less likely to bear children. Similar observations were reported again in 1963 (Mabry, Denniston, Nelson, & Choon, 1963), and over the next decade many more studies across North America and Europe revealed that the offspring of women with untreated PKU were severely damaged (e.g., Hsia, 1970; Howell & Stevenson, 1971; Lenke & Levy, 1980; Perry, Hansen, Tischler, Richards, & Sokol, 1973). These studies found that at least 90% of such offspring were mentally retarded, 75% had microcephaly, 50% had intrauterine growth retardation, and 25% had congenital abnormalities. Thirty percent of the pregnancies in mothers with untreated PKU resulted in spontaneous abortions or miscarriages.

Both animal and human research have shown that a fetal-maternal plasma gradient for phenylalanine exists across the placenta (Kerr, Chamove, Harlow, & Waisman, 1968; Thomas, Parmley, Stevenson, & Howell, 1971). This not only means that phenylalanine crosses the placenta during pregnancy, but also that the level of blood phenylalanine in the mother is magnified by the time it reaches the fetus. To prevent the prenatal damage associated with maternal PKU, blood levels of phenylalanine must be maintained within a certain range beginning prior to conception (Hanley, Clarke, & Schoonheyt, 1987).

Early identification and dietary treatment of individuals with PKU has resulted in a group of women with average intelligence that is now in their childbearing years. The majority of these women discontinued dietary treatment in childhood and thus have uncontrolled blood phenylalanine levels. Unless rigorous dietary control aimed at lowering their blood phenylalanine level is initiated prior to conception and maintained throughout pregnancy, these women are at risk for bearing severely retarded offspring. However, even with dietary control the blood levels of phenylalanine in mothers with PKU are significantly higher than in normal women and thus all children born to mothers with PKU are considered to have MPKUS (Lenke & Levy, 1980).

3.2 Cognitive Development in Children with MPKUS

To date, all of the research on MPKUS has described school-aged children and has consisted mainly of global IQ testing. These studies have demonstrated deficits in IQ ranging from mild to severe. Clinical reports suggest that individuals with MPKUS appear to have attention deficits and hyperactivity; however, systematic investigations of these areas of functioning are lacking.

In summary, phenylalanine is a prenatal teratogen shown to have similar effects on offspring as alcohol (e.g., lowered IQ, physical malformations). A maternal diet, low in phenylalanine may reduce the severity of these effects.

3.3 Prevalence Rates of PKU and MPKUS

Neonatal screening programs in the United States report one per 10,000 infants born each year are diagnosed with PKU. The Quebec Network of Genetic Medicine involves newborn screening of a mixed ethnic population of approximately six million citizens with a birth rate of 17 per 1,000; it cites a live birth frequency of 1 per 21,000 infants born each year with PKU (Cartier, Clow, Lippman-Hand, Morissette, & Scriver, 1982). As noted previously, all offspring born to mothers with PKU are considered to have MPKUS (Lenke & Levy, 1980).

4 Models of Attention and Memory

Prior to discussing the assessment of attention and memory in individuals with either FAS or MPKUS, the models on which these assessment techniques are based will be reviewed. There is overlap in the literature between conceptualizations of attention and memory processes. It is difficult to clearly separate these two functions because attentional processes are an integral part of memory. Furthermore, there continues to be debate over how, or if, we can clearly separate these two functions for the purpose of assessment (e.g., Cowan, 1995). With this in mind, the following two sections highlight some of the major models of attention and memory, with particular focus on those which have been previously applied to research on prenatal teratogens.

4.1 Attention

Traditionally, research in the area of attention has been divided into two major approaches, the psychological-testing approach and the information-processing approach. The psychological-testing approach has depended on factor-analytic techniques to identify cognitive components of attention, whereas the information-processing approach has employed theoretically based experimental tasks to assess cognitive abilities. Although the psychological-testing approach has been useful in predicting external criteria such as clinical diagnosis, it has been criticized for its lack of a theoretical basis and its narrow analysis of human cognitive abilities (Posner, 1978; Pribram & McGuinness, 1975; Schmidt, Trueblood, Merwin, & Durham, 1994). On the other hand, although the information-processing approach is theoretically based,

it has been criticized for its lack of ecological validity and clinical applicability (Mirsky Anthony, Duncan, Ahearn, & Kellam, 1991; Schmidt et al., 1994; Shum, McFarland, Bain, & Humphreys, 1990).

Whereas attention research has historically been split into studies of sustained or selective attention, current conceptualizations define attention as an integrated system of processes that register information into the central nervous system (Schmidt et al., 1994). This multicomponent view stems from information-processing studies that have demonstrated a link between attention and a variety of functions, such as selectivity, focusing, vigilance, switching attention, distractibility, and attention to memorial processes such as rehearsal, retrieval, and coding (e.g., Parasuraman & Davies, 1984; Posner, 1978; Shiffrin, 1988). Many formal models of attention have arisen out of this type of research (e.g., Kahneman & Treisman, 1984; Posner & Rafal, 1987; Pribram & McGuinness, 1975; Schneider & Shiffrin, 1977; Shum et al., 1990). There have also been recent attempts to develop models integrating cognitive theories of attention with the more traditional psychological-testing approach in an attempt to address the behavioural, theoretical, and statistical concerns raised about each approach (e.g., Mirsky, 1987; 1988; 1989; Mirsky et al., 1991; Shum et al., 1990; Sohlberg & Mateer, 1989).

Using exploratory factor-analysis, Shum et al. (1990) examined the construct validity of eight attention tests in a population of 125 university control subjects, 45 community control subjects, and 37 closed-head-injury patients. They concluded that a three-factor solution of attention, consisting of a visual-motor scanning component, a

sustained-selective processing component, and a visual-auditory spanning component, best fit the data.

Shum, McFarland, and Bain (1994) then attempted to integrate their results into an information-processing model. Using a cognitive correlates method, they examined whether the three-factor structure of attention could be predicted by attention processes operationalized in terms of the stages of information processing. Results indicated that individuals' performances on the three attentional components - visual-motor scanning, sustained-selective processing and visual-auditory spanning - were significantly predicted by six indices derived from an information-processing task (i.e., visual-spatial reaction-time test). From these data, Shum and colleagues concluded that the interpretation of processes measured by the components of attention could be facilitated by their significant relationships to other measures of attention anchored to information-processing theory. The authors also suggested that this convergence between the psychological-testing approach and information-processing approach strengthened the construct validities of the psychological tests of attention.

A second model that has attempted to address the criticisms leveled against the psychological-testing and information-processing approaches was proposed by Mirsky et al. (1991), who presented a theoretical model of attention based on research in cognitive psychology and neuropsychology. They proposed three "elements" or "components" of attention, each of which represent significant aspects of the regulation of information processing. The first element, "focus-execute", represents the ability to select target information from an array for enhanced processing. This function has been highly researched in neuropsychology, particularly in studies examining the symptom

of visual neglect, and in cognitive psychology, in studies of automatic selection and the relationship of eye movements to visual selection. The second element, "sustain-vigilance", represents the ability to maintain focus and alertness over time. Vigilance tasks have a long history in the cognitive psychology literature, dating back to the Second World War when it was noted that sustained attention deteriorates over time. The third element, "shift", represents the ability to change attentive focus in a flexible and adaptive manner. Although cognitive psychology has focused mainly on the speed of shifting visual attention through space, the term 'attention for action' has been used recently in reference to the hypothesis that attention is involved not only in selecting relevant input, but in linking input with relevant output systems (Mirsky et al., 1991). In neuropsychology, an inability to change inappropriate linkage is referred to as perseveration, a symptom traditionally linked to frontal lobe dysfunction (Luria, 1966).

Mirsky and colleagues (1991) conducted a principal components analysis on a battery of eight tests administered to a heterogeneous sample of 203 individuals (76 normal; 81 eating disorder; 14 epileptic; 8 schizophrenia; 15 affective disorder; 9 head injury). Each of these tests is routinely used in neuropsychological assessment and/or psychological experiments on attention and information processing. Results partially supported the three-factor structure proposed by Mirsky and his colleagues; however, two tasks involving numerical manipulation (arithmetic and digit span) loaded on a fourth factor rather than on the proposed "focusing" factor. This fourth factor was labeled "encode", as the two tasks require the ability to sequentially register, recall, and mentally manipulate numeric information.

Using both animal and human data, Mirsky linked these four functions to different specialized brain regions organized into a larger attentional system. The "sustain" element of attention is viewed as particularly dependent upon the brain stem and thalamic portions of the attention system (e.g., Bakay-Pragay, Mirsky, & Nakamura, 1987; Moruzzi & Magoun, 1949; Lindsey, Bowden, & Magoun, 1949). The "shift" element of attention has been localized to the prefrontal cortex (e.g., Bakay-Pragay et al., 1987; Milner, 1963). The "focus-execute" and "encode" elements of attention have been hypothesized to involve the temporal cortex, hippocampus, and amygdala (Hermann & Wyler, 1988; Penfield & Jasper, 1954; Roth, Connell, Faught, & Adams, 1988).

Using equivalent and modified tests from the adult test battery, Mirsky et al. (1991) replicated this factor structure in a sample of 435 public school children. These results were also replicated in five independent studies with samples of adolescent inpatients with various psychotic disorders: adults with psychotic disorders, normals ranging in age from 5 to 90, and schizophrenics and their siblings (Kendler, Ochs, Gorman, Hewitt, Ross, & Mirsky, 1991; Kremen, Seidman, Faraoin, Pepple, & Tsuang, 1992; Pogge, Stokes, & Harvey, 1994; Steinhauer, Zubin, Condray, Shaw, Peters, & Van Kammen, 1991; Tatman, 1992).

Both Mirsky's (1991) and Shum's (1994) models have been criticized by Schmidt et al. (1994) on methodological grounds. Schmidt et al. argue that Mirsky and colleagues failed to address some basic parametric statistical assumptions underlying factor analysis, namely the normality of variable distributions and the independence of variables. In particular, they note that the measures defining the "sustain" factor are not

independently derived - because they are all drawn from visual subtests of the Continuous Performance Task (CPT), they would be expected to load on the same factor.

The issue of independent measures on the "sustain" factor has been partially addressed in replications of Mirsky's model using the auditory form of the CPT, which loaded on the same factor as the visual form (Kremen et al., 1992; Tatman, 1992). Further, in a study by Steinhauer et al. (1991), the Span of Apprehension Test -which is generally regarded as a vigilance task - loaded on the same factor as scores from the CPT.

Schmidt et al. (1994) also point out that Mirsky's "shift" factor consists of a single measure (i.e, Wisconsin Card Sorting Task (WCST), which measures an individual's ability to shift conceptual categories based on feedback), and that single-variable factors are not interpretable. Mirsky et al. (1991) have taken initial steps towards addressing this limitation by adding the Reciprocal Motor Programs Test (RMPT) to their battery. Preliminary data on 42 subjects (26 normal controls, 7 schizophrenic patients, and 9 head-injury patients) found scores on the RMPT to be significantly correlated with the number of categories achieved on the Wisconsin Card Sorting Test (WCST). Further, a reduced principal components analysis based on these 42 subjects found that the RMPT loaded 0.89 on the same component as the WCST. Mirsky also cites an unpublished study by Bilder (1990) in which the same relationship was found between WCST and RMPT scores in a sample of head-injured patients.

Schmidt et al. (1994) also criticize Shum et al. (1990) for their inattention to basic statistical issues, such as normality of variable distributions and assessment of

sampling adequacy, and for their adoption of a strictly empirical approach (as opposed to a theory driven one). Schmidt and colleagues state that none of the attention factors identified by Shum et al. correspond to constructs from cognitive science models or current understanding of brain-behaviour relationships. However, Shum did address this concern in his 1994 cognitive correlates study, in which he demonstrated a statistically significant relationship between his three-factor structure of attention and a cognitive visual-spatial reaction-time model of attention.

There is a strong resemblance between Mirsky et al.'s (1991) and Shum et al.'s (1990) factor structure for attentional processes. There are similarities between Mirsky's "focus-execute", "sustain", and "encode" factors and Shum's "scanning", "sustaining", and "spanning" factors. It is likely that the differences between the two models would be eliminated if the same tests were used to generate the models. For example, Shum and colleagues did not include the WCST or any other measure of shift response set flexibility, whereas Mirsky et al.'s (1991) fourth factor measuring flexibility of "shift" consisted only of the WCST. However, the psychometric properties of Mirsky's model, combined with its theoretical base and clinical utility, make it a stronger candidate for use in clinical research than Shum's model.

4.2 Memory

Historically, psychological models of memory and memory assessment were based on the dual concept of short- and long-term memory (Kolb & Whishaw, 1996). Hebb's 1949 (as cited in Kolb & Whishaw, 1996) concept of cell assemblies has shown the possible implications of structural differences for the brain to the memory process.

Hebb (1949) developed a neurological model of short-term and long-term memory. He proposed that short-term memory was the reverberation of the closed loop of a cell assembly and that long-term memory resulted from repeated reverberation of the closed loops of the cell assembly, which resulted in a long-lasting structural change in the nervous system.

Hebb's (1949) theory provided an explanatory link between what is known about the physiological properties of the nervous system and behavioural or psychological events. Hebb's theory of synaptic modification as the basis of memory has more recently led to the use of the term *Hebb synapse* to label synapses that undergo change during learning. Although the nature of the synaptic change in information storage is uncertain, several areas of research have shown that synaptic changes may accompany behavioural change (Greenough & Chang, 1985 as cited in Kolb & Whishaw, 1996).

Although the distinction between short- and long-term memory is widely accepted, the way that each is viewed has varied widely. William James (1890 as cited in Kolb & Whishaw, 1996) described short-term memory as primary memory, or information that occupies one's current attention. This description differs from Hebb's description of short-term memory in that it places less emphasis on the duration of memory storage and more emphasis on the roles of attention and conscious processing in memory (Squire, 1987).

Long-term memory is typically divided into declarative and procedural processes, and the majority of information available regarding these processes is based on studies of amnesic patients (Cohen & Corkin, 1981; Squire & Cohen, 1984).

Declarative memory is typically defined as memory for facts that are acquired through learning and are accessible to conscious recollection. Declarative memory can be further divided into episodic and semantic memory. Episodic memory refers to memory for past events in an individual's life, whereas semantic memory refers to knowledge of the world, such as facts, concepts, and vocabulary (Squire, 1987). Procedural memory refers to memory for skills and other cognitive operations. In both retrograde and anterograde amnesia procedural memory is spared because the acquired information is embedded in procedures (i.e., skill that can only be expressed through performance, such as riding a bike).

The concept of short and long-term memory evolved from experimental paradigms of memory. Much of the theoretical support for the model was provided through studies of the now famous patient H.M. who became amnesic following bilateral temporal lobe insults (Scoville & Milner, 1957). It was discovered that although H.M. had normal short-term memory abilities, he was unable to retain any information even after brief distractions or periods of delay. As a result of this discovery, the model of short and long-term memory was further developed to include the notion of neuroanatomically separate structural and functional storage systems, with transfer occurring between them through the process that Hebb (1949) termed consolidation (Scoville & Milner, 1957).

Experimental investigation of the dual model has challenged the premise of two distinct, separable systems (e.g., Craik & Watkins, 1973; Wickens, 1972). The main properties of the two systems - rate of information decay, capacity of storage, and type of preferred encoding - have not been consistently separable (e.g., Posner & Snyder,

1975a, 1975b; Treisman, 1977). This has resulted not only in a lack of agreement about how to define short and long-term memory, but also about how to theoretically differentiate the two (Squire, 1987). Although the terms short-term and long-term memory continue to be frequently used in discussions of memory, particularly from a clinical perspective, it is important to recognize that this terminology is most useful in describing behavioural categories, not structure to function relationship.

A more current view postulates a working memory - long-term storage system as a modification of the short-term - long-term memory view (Baddeley, 1990). Working memory is defined as a system that holds a limited amount of information for a brief time period until it can be processed (Baddeley, 1990). Working memory has also been described as involving computational modeling of higher cognitive processes, such as language, reasoning, and problem solving (e.g., Carpenter, Just, & Shell, 1990; Just & Carpenter, 1992). From this perspective, working memory includes not only information that has to be retrieved at a later time, but also the intermediate products of mental computations involved in higher cognitive processes.

Baddelely's (1990) working memory model comprises a central executive that is responsible for processing information and two slave systems, the phonological loop, which processes auditory information, and the visuospatial sketchpad, which processes visual and spatial information. These slave systems have limited capacity; hence concurrent visual or spatial processing will selectively interfere with short-term memory for visual information by competing for processing resources in the visuospatial sketchpad.

Based on a large body of research, Baddeley and colleagues describe the phonological loop component of working memory as a system for supporting language learning (Baddeley, Gathercole, & Papagno, 1998). Research has demonstrated a link between phonological loop function and word learning in a variety of participant populations (Baddeley et al., 1998). The phonological loop is specialized for the retention of verbal information over short periods of time. It is made up of a phonological store that holds information in phonological form and a rehearsal process that acts to retain decaying representations in the phonological store while more permanent memory representations are being constructed (Gathercole & Baddeley, 1993).

The central executive component of working memory is hypothesized to represent an alliance of executive processes that are dependent on different anatomical locations, and therefore are differentially disruptable (Baddeley et al., 1998). There is growing evidence to suggest that executive functioning is fractionated into subprocesses associated with different anatomical locations within the frontal lobes, and this has included evidence for separable encoding and retrieval function (Baddeley, Della Sala, Papagno, & Spinnler, 1997). Baddeley (1996) has proposed at least three other executive functions while Burgess and Shallice and (1996) suggest no fewer than eight executive subprocesses.

Applications of Baddeley's model have been useful in the study of short-term memory and working memory operation in clinical, experimental, and neuropsychological populations. This model has also contributed to current developmental models of learning disabilities (Swanson & Alexander, 1997;

O'Shaughnessy & Swanson, 1998). Swanson (1996) examined whether age-related and individual differences in working memory reflect a domain-specific or common central executive system. In support of a central executive system he found that children's verbal and visual-spatial working memory was significantly correlated, with and without age partialled out, and that they were correlated with diverse achievement and intelligence measures. He also examined whether age-related differences in children's working memory are primarily related to processing efficiency or capacity. A comparison of three age groups (7, 10, & 13 years old) on working memory performance tests under initial, cued, and maintenance conditions supported the general capacity model, in that age-related performance differences in working memory, were found on all conditions and not isolated to specific processes. The maintenance measures predicted the variance better in age-related performance than process measures. Although individual differences in working memory indicated two independent processes, these processes had similar correlations to achievement within age groups. Overall, the results supported a central executive system supporting Baddelely's (1986) proposal of two distinct store regions concerned with auditory-verbal and visual-spatial information and a single executive system reponsible for processing information.

Research in the area of working memory is ongoing, and the debate as to exactly what working memory entails continues to generate research.

From a cognitive perspective, memory is viewed as a multidimensional information-processing system that incorporates various levels of processing rather than as a store-based mechanism (Cermak, 1982; Craik & Lockhart, 1972). Typically,

consolidation, and retrieval. From this perspective, attentional capacity is seen as a logical component of any memory model because it is this capacity that initially allows information to access the system. Encoding refers to the level of analysis that an individual performs on the material to be remembered, and is significantly related to later recall or recognition ability. Storage refers to the transfer of a temporary memory to a location in the brain for permanent storage or for access through consolidation. From this perspective, consolidation is the process of integrating new memories into the individual's existing cognitive/linguistic schema or framework. Retrieval refers to the search for or activation of memory traces, as well as the ongoing monitoring of the accuracy of memories retrieved from storage.

From a neuropsychological perspective, much of what is understood about memory has come from the study of patients with anterograde amnesia, temporal lobe damage, and other types of brain damage. Based on both human and animal research, Petri and Mishkin (1994 - as cited in Kolb & Whishaw, 1996) have proposed a neural model of memory, which is divided into explicit (episodic) and implicit (procedural) memory. Results from their studies suggest that the limbic structures are involved in explicit memory. Experimental studies with monkeys and rats have implicated the rhinal cortex in object memory, the amygdala in emotional memory, the hippocampus in spatial memory, and the prefrontal cortex in memory for verbal (left temporal) and nonverbal material (right temporal). These structures have reciprocal connections between the medial thalamus, the basal forebrain, and sensory areas of the neocortex. The basal ganglia, which receive projections from all regions of the neocortex and send projections through the globus pallidus and ventral thalamus to the premotor cortex, are

implicated in implicit memory. Animal studies have demonstrated that damage to the basal ganglia result in impaired ability to learn motor skills, to make appropriate responses to cues and to complete association tasks (Kolb & Whishaw, 1996).

It is clear that the classic idea of a specific brain structure being responsible for memory is no longer appropriate. Current conceptualizations of memory discuss it as a multidimensional complex process of neuronal connectivity involving ongoing synaptic change with memory stored in both cortical and subcortical structures (Kolb & Whishaw, 1996).

5 Assessment of Attention and Memory

5.1 Assessment of Attention

In the past, the behavioural syndrome of attention has often been treated as a global concept, with little of the behavioural, theoretical and statistical sophistication and rigor seen in research on memory and learning. Research in the cognitive and experimental realms has resulted in attention being viewed as a set or group of processes. Many tasks used to assess hypothesized attention deficits, such as reaction time tasks, dual task paradigms, and vigilance tasks, originated in experimental psychology. Because hyperactivity and inattention are commonly seen in individuals with FAS, the tasks used to assess attention in these individuals are frequently those used to assess Attention Deficit Hyperactivity Disorder (ADHD) and Attention Deficit Disorder (ADD). In particular, vigilance tasks are frequently used in research with hyperactive children, and have generally been shown to yield reliable differences between these children and normal age-matched controls (Douglas & Parry, 1983). Vigilance tasks have been popular tools in attention research since their development during the Second World War, primarily because of their ecological validity. They require individuals to attend in a manner that closely resembles the real-world demands for sustained attention present in both school and work activities. Various vigilance tasks have been developed, each employing different types of stimuli and requiring different types of responses. Increasingly, the most commonly used vigilance task in

clinical research is the Continuous Performance Test (CPT) (Rosevald, Mirsky, Bransome, & Beck, 1956).

Neuropsychological assessment of attention continues to expand through the implementation of information gained from cognitive and experimental studies of attention into clinical test batteries (Mirsky et al., 1991). The Laboratory of Psychology and Psychopathology-National Institute of Mental Health (LPP-NIMH) Attention Battery (Mirsky, 1987; 1988; 1989; Mirsky et al., 1991; Mirsky, Lochhead, Jones, Kugelmass, Walsh & Kendler, 1992; Mirsky, Fantie, & Tatman, 1995) is one example of a factor analytically based model with a strong theoretical basis that has drawn from cognitive and experimental research as well as from clinical neuropsychology. It has been utilized with a spectrum of clinical populations, including individuals with FAS (Mirsky et al., 1991; Mirsky, 1992; Streissguth et al., 1994).

5.2 Assessment of Memory

Memory is multifaceted, hence a thorough assessment of memory must include measures of immediate memory span (verbal and spatial), measures of new learning in which the individual has the opportunity to be exposed repeatedly to information, and recall and recognition tasks - which allow for the separation of retrieval problems from other types of impairment (Lezak, 1994; Solhberg & Mateer, 1989).

Verbal and nonverbal memory tasks are common and important components of memory assessment. The distinction between verbal and nonverbal memory was proposed by Milner and her colleagues (1970), who noted that patients who had undergone left temporal lobectomies had impaired memory for words or letters, but not

designs, whereas patients who had undergone right temporal lobectomies had impaired memory for designs, but not words or letters. Performance on measures of verbal and nonverbal memory is thought to be reflective of the patient's underlying capacity to analyze verbal versus nonverbal information. The patient with verbal memory deficits often has a widespread problem with language comprehension or production, whereas the patient who performs poorly on nonverbal memory tests often has perceptual, spatial, or constructional impairments. The problem may originate in the manner in which individual patients analyze and encode the material presented to them (Sohlberg & Mateer, 1989). However, caution should be taken in assumptions regarding the manner in which patients analyze or encode information. Apparent verbal or nonverbal dissociations may be misleading as nonverbal tasks may be being verbalized and verbal tasks may be processed and encoded nonverbally.

Research in the area of verbal memory with individuals who were prenatally exposed to alcohol has typically used the Rey Auditory Verbal Learning Test (Rey, 1941) or the California Verbal Learning Test for Children (CVLT-C) (Delis, Kramer, Kaplan, & Ober, 1987) to assess verbal skills. The Rey Complex Figure (Rey, 1941) and the Figural Memory component of the Wechsler Memory Scale- Revised (Wechsler, 1987) has been frequently used to assess nonverbal memory (i.e., perceptual, spatial, and constructional abilities).

Another difficulty is the identification and separation of memory problems from attention deficits. Problems in focused, sustained, selective, alternating, or divided attention prohibit the effective registration of information for subsequent information processing or recall (Lezak, 1994).

5.3 Process-Specific Approach

The criterion of a good neuropsychological test has traditionally been its ability to accurately predict the presence of brain dysfunction. The ability to accurately measure behavioural deficits, and thus infer brain dysfunction, is frequently the only means by which a diagnosis of prenatal teratogenic exposure can be determined. Historically, there have been two major approaches to neuropsychological assessment, the statistical-psychometric approach and the theoretical-clinical approach.

The statistical-psychometric approach relies on statistical techniques to define constructs such as organic impairment and deficit, assigning diagnoses on an actuarial basis (Sohlberg & Mateer, 1989). Statistical criteria are the basis of the various tests selected for assessment, with the most important variable being a test's ability to differentiate brain-injured from non-brain-injured individuals on a greater than chance basis.

According to Sohlberg and Mateer (1989), the consequence of a solely statistical approach to test selection has been an atheoretical view of brain-behaviour relationships. In other words, tests that are designed, constructed, and validated for the main purpose of predicting and even localizing brain damage tend to give a limited view and understanding of the overall pattern of deficits (e.g., cognitive, motor, behavioural) associated with the damage.

In contrast, the theoretical-clinical approach to neuropsychological assessment is qualitative and practically based. This approach addresses questions concerning brain-behaviour relationships, specifically, the type and degree of functional impairment experienced by the individual in question. Assessment based on this

approach also seeks to identify which functions have been spared and if they can be utilized to promote recovery and adaptation. To accomplish these goals, the theoretical-clinical approach incorporates both quantitative and qualitative (e.g., behavioural descriptions) procedures into the assessment process, thereby providing an individualized understanding of the behavioural effects associated with a particular pattern of brain disturbance. Luria (1966) developed a well-known model based on this view. He believed that all cognitive functions were dependent on multiple brain areas, each acting as part of a dynamic system. Using qualitative methods, he delineated the functional deficits involved in various brain systems. The major drawback of the theoretical-clinical approach is a lack of standardized evaluations across clinicians and across age ranges, which leads to difficulties in quantifying what was actually measured and in conducting longitudinal study.

To address the limitations of both the statistical-psychometric and the theoretical-clinical approaches, Kaplan (1983) proposed that features of both be combined into what is termed the Process-Specific Approach. This approach is based on the premise that although cognitive systems work together, separate aspects of cognitive function can be differentially impacted through brain damage or disease. A process-specific assessment battery should consist of tests designed to assess general intellect, executive function, attention and concentration, memory, language, perceptual and perceptual-motor function, and reasoning/problem solving (Sohlberg & Mateer, 1989).

6 Attention and Memory Deficits Associated with FAS and MPKUS

Animal models have demonstrated relationships between abnormal behaviours, particularly in terms of attention and memory behavioural deficits, and specific structural defects in the brain (NIAAA, 1990; 1993). There are considerable data from animal studies to support the observation that a difference in brain development is one outcome of prenatal exposure to alcohol (Bauer-Moffett & Altman, 1977; Clarren, Alvord, Sumi, Streissguth, & Smith, 1978; Majewski, 1981; Pierce, Goodlett, & West, 1989; Phillips & Cragg, 1982; Riley, Barron & Hannigan, 1986).

6.1 Attention Deficits

There are considerable data from animal studies to suggest that deficits in attention are associated with prenatal exposure to alcohol (e.g., Riley, 1990; West et al., 1990). The most common finding in animals exposed prenatally to alcohol was an increase in activity followed by deficits in avoidance performance (e.g., moving from one compartment to another in order to avoid shock) compared to control animals. These attention deficits and hyperactivity have been linked to alterations in norepinephrine and to dopamine depletion (e.g., Clarren, Astley, Bowden, Lai, Rudeen, Shoemaker, & Bunt-Milam, 1990).

Data from human research also suggest that deficits in attention are a consequence of prenatal alcohol exposure (e.g., Nanson & Hiscock, 1989; Streissguth, Barr, Sampson, Parrish-Johnson, Kirchner, & Martin, 1986; Streissguth & al., 1994). Nanson and Hiscock (1989) demonstrated that children diagnosed with FAS/FAE and

those classified with attention deficit disorder (ADD) exhibit similar attention deficits and behavioural problems.

Streissguth and colleagues (1990; 1994) used Mirsky et al.'s (1991) neuropsychological model of attention (see Table 6.1) to examine the attention capabilities in their Seattle population-based sample of children prenatally exposed to alcohol across the full spectrum of maternal use (Streissguth, Barr, Sampson, Bookstein, & Darby, 1989). In their 14 year follow-up study, Streissguth et al. (1994) found that the 'focus' and 'sustain' components of attention were the most strongly related to prenatal alcohol of all of the attention measures comprising Mirsky's model of attention. The 'shift' and 'encoding' components of attention were only moderately correlated with prenatal alcohol exposure at the 14-year follow-up.

On the Talland Letter Cancellation Test (TLCT – Talland, 1965), a paper and pencil test of the 'focusing attention' component, the scores most correlated with prenatal alcohol exposure were total number correct and false alarms. Standard deviation of reaction time scores on the Continuous Performance Test (a vigilance task and measure of the 'sustaining attention' component) for all three visual tasks, X, AX, DX, were highly correlated with degree of alcohol exposure. The number of false alarms and the ratio of false alarms to total presses for the AX task were also highly salient for alcohol, with more alcohol exposure leading to a more variable response rate, and failure to withhold a response when X was not preceded by A.

The WCST (Heaton, 1981 - a measure of the 'shift' component of attention) Total Number of Categories and the Other Response score (extraneous, non-category

Table 6.1 Mirsky et al.'s Four Factor Model of Attention Test Battery

Factor 1 FOCUS-EXECUTE (perceptual-motor speed)	Talland Letter Cancellation, Trails A & B, Digit Symbol Modalities, Stroop
Factor 3 SUSTAIN (vigilance)	Continuous Performance Task (CPT)
Factor 2 SHIFT (flexibility)	Wisconsin Card Sorting Task (WCST)
Factor 4 ENCODE (numerical-mnemonic)	Wechsler Adult Intelligence Scale-Revised (WAIS-R) Arithmetic & Digit Span Wide Range Achievement Test-Revised (WRAT-3) Arithmetic (written)

responses) were only moderately salient for prenatal alcohol exposure as was the WISC-R Digit Span subtest (a measure of the 'encoding' component of attention). At the seven year follow-up (Streissguth, Barr, & Sampson, 1990), the WISC-R Digit Span subtest was one of the measures most sensitive to prenatal alcohol effects; however, data on a smaller sample of 14-year-old adolescents using a more complex measure of 'encoding' (WISC-R Arithmetic subtest) did reveal prenatal alcohol effects. The authors concluded that increasingly complex measures are needed to detect the long-term effects of prenatal alcohol exposure in older children, which is consistent with experimental studies that have found that increasingly difficult tasks are needed to detect long-term effects of early alcohol exposure in older animals (West, Goodlett, Bonthius, & Pierce, 1989).

Similar findings were reported by Carmichael Olson, Feldman, Streissguth, and Gonzales (1992) in a study comparing adolescents with FAS to psychometric norms when available or with the Seattle population-based cohort (464 adolescents - median age 14.3). They also found that when compared with the normative sample, adolescents with FAS demonstrated deficits in the focusing, encoding, and shifting components of attention proposed by Mirsky et al. (1991) and were similar to the population-based sample on the sustaining component of attention. Another study examining sustained attention found deficits in nonretarded adults with FAS using the APT, a measure of auditory attention (Kerns, Don, Mateer, & Streissguth, 1997). Using standardized scores for comparison, individuals in both the average and below average IQ groups showed deficits in sustained attention, and none of the eight

participants in the below average group were able to complete the sustained attention task.

6.2 Memory Deficits

The hippocampus has been identified as particularly susceptible to the damaging effects of alcohol (see Table 6.2). The literature on memory deficits associated with known brain lesions in humans and animals emphasizes the important role of the hippocampus in overall memory functioning. Research has demonstrated that the hippocampus is critical for the registration of new memories (Mahut & Moss, 1984; Zola-Morgan, 1984). The frontal lobes also play an active role in certain aspects of memory, including allocation of attention, organization of memories, and retrieval of the temporal order of information from memory (Lezak, 1994). Thus, the type of memory loss that results from various brain diseases or traumas is highly dependent on the nature of the injury or illness.

Researchers exploring the long-term behavioural effects of prenatal alcohol exposure in rats have also found behavioural deficits that are consistent with damage to the hippocampus (e.g., Goodlett, Leo, O'Callaghan, Mahoney, & West, 1993; Reyes, Wolfe, & Savage, 1989; Riley et al., 1986; Riley,1990; West et al., 1990). These authors conclude that the deficits seen in the radial arm maze and the Morris-maze performance by fetal alcohol rats are consistent with the hypothesis that prenatal alcohol exposure causes significant impairments in the working, reference, and spatial memory of adult rats. However, these studies have shown that working memory is most profoundly affected by prenatal exposure to alcohol.

Table 6.2 Hippocampal Effects of Prenatal Alcohol Exposure - Animal Literature

Barnes & Walker, 1981	Reduced number of neurons.
Abel, 1985	Reduced complexity and fewer spines in dendrites of the pyramidal cells.
Weinberg & Jerrells, 1991	Pyramidal cell death, decreased numbers of dendritic spines, aberrent mossy fibre terminal subfields, and altered lesion-induced sprouting.
Reyes et al., 1985; 1989	Elevations in y-glutamyltranspeptidase activity.
Farr et al., 1988; 1990	Decreased numbers of glutamate receptor binding sites.
Savage et al., 1989	Decrease in histochemically detectable hippocampal mossy fibre zinc.

Those memory deficits identified in animals exposed prenatally to alcohol have also been observed in humans with FAS. In a longitudinal clinical study of nine adolescents and three young adults with FAS, participant performance was especially poor on the Stepping Stone Maze, a computer adaptation of Milner's (1965) test of hippocampal function assessing spatial memory (Streissguth et al., 1991). Procedural learning (i.e., memory for skills and other cognitive operations) was unimpaired among the FAS patients; however, their declarative learning performance (i.e., memory for facts acquired through learning) was poorer than in the comparison group.

Another long-term study of 20 children with FAS assessed verbal learning and memory ability (Mattson, Riley, Delis, Stern, & Jones, 1991; Mattson, Stern, Jones, Delis, & Riley, 1996) using the CVLT-C (Delis, Kramer, Kaplan, & Ober, 1987). When compared with children matched for age, sex, and race, there was evidence of mild defects in immediate memory in the FAS group. Children with FAS learned fewer words over the first five learning trials, and their recall of a distractor list was also impaired. It was further noted that their retention span over delayed intervals was severely impaired even when their reduced learning was considered, and that they displayed moderately elevated intrusion rates on the recall trials. Recognition performance was also impaired in children with FAS. Although these children gave a normal number of correct positive responses, their discriminability (i.e., ability to correctly reject those words not on the learned list of words) was severely impaired.

Mattson et al. (1996) also observed that the memory performance of FAS children with average IQs showed deficits on the CVLT-C compared to same-age normal control participants. The learning strategies used by children with FAS on the

CVLT-C indicated a trend toward a passive, more haphazard learning style than that of controls. Evidence for this learning style lies in decreased recall from the recency region of the word list, a high level of inconsistency in responding across trials, as well as more serial than semantic clustering of words.

A similar pattern of impaired learning and relatively unimpaired retention with average IQ was demonstrated in a study of non-retarded adolescents and young adults with FAS (Kerns et al., 1997). Kerns et al. divided their sample into two groups - those with average IQ and those with below average to borderline IQ. On the CVLT, both groups demonstrated a lower level of learning, such that they were unable to acquire the expected average amount of words even with repeated trials and the below average IQ group also demonstrated a shallow slope of learning. However, whereas the average IQ FAS group demonstrated good recall of what was learned over both short and long delays, the below average IQ group demonstrated marked difficulty with long delay free recall. Compared to normative scores, both groups also demonstrated a number of free recall intrusions and impaired recognition scores. Although they were able to recognize words that they had recalled, they showed little recognition of words they had not previously recalled from the list suggesting that their difficulty lies in their ability to acquire and encode new material.

In another, more in-depth study, Mattson et al. (1992) carried out neuropsychological testing, MRI, and EEG assessments of two adolescents with FAS. Both children showed severe deficits in verbal fluency, naming, visual-motor integration, and memory for motor sequences. Additionally, they both showed mild to moderate difficulty with immediate memory span for digits, abstract thinking, and

immediate memory for a story. Performance on the CVLT-C was compared with two control groups of children, one group matched for chronological age and one matched for mental age (using Verbal IQ scores). When compared with children of similar chronological age, both FAS subjects showed impaired immediate and delayed recall of the learned word list and excessive perseverations and intrusions. On the recognition task, the subjects showed poor discrimination and an increase in false-positive responses. When compared with eight 5-year-old male controls (to equate mental age), both FAS subjects demonstrated relatively normal learning and recall. However, they still exhibited excessive intrusions and poor recognition discrimination, including an increase in false-positive responses. It is interesting to note that children with ADHD exhibit similar difficulty with learning and recall, but not with recognition or false-positive responses. Mattson et al. concluded these data support their hypothesis that learning and memory deficits in children with FAS may lie at the encoding and storage level, distinguishing them from the attentional deficits commonly reported among children with ADHD.

Streissguth et al. (1994) reported on adolescent attention/memory performance and its relationship to prenatal alcohol exposure in a Seattle population-based, longitudinal, prospective study involving 464 participants, substantial covariate controls, and "blind" examiners. The majority of the mothers were married, middle class, and were considered at low risk for adverse pregnancy outcome. Streissguth et al. (1994) oversampled their sample for heavier maternal alcohol use, with half of the mothers being heavy drinkers and approximately half, infrequent drinkers or abstainers. These results indicated a significant relationship between prenatal alcohol exposure and

attention/memory deficits in a dose-dependent fashion (i.e., higher the alcohol intake by mother during pregnancy, the more attention/memory deficits observed in children). The number of drinks of alcohol consumed per sitting was the strongest predictor of deficits, and fluctuating attentional states, problems with response inhibition, and poor spatial learning shared the strongest association with prenatal alcohol exposure. These attention/memory deficits appear to be the adolescent sequelae of deficits observed earlier in development (Mattson et al., 1991).

In sum, there is accumulating evidence to suggest that prenatal alcohol exposure results in widespread attentional deficits and in long-term deficits in memory, particularly in the areas of acquisition and encoding.

7 Current Status of Research in FAS and MPKUS

To establish the effects of prenatal teratogens, such as alcohol and phenylalanine, researchers must first be able to clearly differentiate the consequences of the prenatal teratogens. They must also attempt to partial out the effects of a variety of clinical and environmental problems that often occur in the children of alcoholics. This task can be partially accomplished by using control groups that are matched as closely as possible on variables such as chronological age (CA), IQ, socioeconomic status, and living arrangements.

The following two sections outline the current directions of neuropsychological investigations into FAS and MPKUS and the potential impact on future research of a recent debate concerning specific teratogens versus general teratogenic exposure.

7.1 FAS Research

Research on FAS has reached a point at which investigators are examining highly specific areas (e.g., cellular, structural) in an attempt to provide an in-depth understanding of specific deficits associated with prenatal alcohol exposure, and in an attempt to discover a means of minimizing the damage to the fetus. According to West et al. (1990), the next step in FAS research must be to conduct detailed human neuropsychological studies that will provide insights into the types of functional deficits produced by prenatal alcohol exposure. Such in-depth neuropsychological studies in the adult FAS/FAE populations could help determine whether existing functional deficits are consistent with damage found in specific neocortical systems.

These cortical regions could then be empirically examined in primate models using neuroanatomical and neurochemical methods, or using functional imaging techniques in both primates and humans. According to West et al., only by integrating neuropsychological and psychosocial studies of humans with the neuroanatomical, neurochemical, and behavioural studies of animals can we hope to uncover the basis of brain damage in humans with FAS or FAE.

7.2 MPKUS Research

There have been no in-depth neuropsychological studies in the area of MPKUS. Although research is underway on the effects on offspring of controlling phenylalanine levels during pregnancy, there is no information, aside from clinical reports, concerning the pattern of cognitive strengths and weaknesses in individuals with MPKUS. To clearly demonstrate the impact of dietary treatment during pregnancy on the long-term outcome of the offspring, it is necessary to first have knowledge of the complete developmental trajectory of untreated MPKUS. Thus, neuropsychological data outlining the patterns of strengths and weaknesses associated with MPKUS would provide much-needed information.

7.3 Specific Teratogen versus General Teratogenic Exposure

In a paper presentation at the Research Society on Alcoholism Meeting (1994), Nanson argued that the logical and scientific basis of diagnosing FAS from behaviour in the absence of physical markers of the syndrome is premature. As noted previously, a review of the literature on prenatal teratogenic exposure indicates that there may be more behavioural similarities than differences between the effects of various teratogens (e.g., alcohol, phenylalanine, and benzodiazepines). Whereas, Streissguth and Ladue

(1985) have argued that the behaviours of individuals with FAS/FAE are caused by their prenatal exposure to alcohol, Nanson (1994) argued that coexistence does not prove causality. According to Nanson, to demonstrate that a pattern of behavioural deficits are causally linked with a particular syndrome, one must demonstrate that the deficits are distinct and different from those seen in prenatal exposure to other teratogens.

Although several theories (e.g., nutritional deficiency, fetal hypoxia, and acetaldehyde (ACH) embryo toxicity) have been proposed to account for the deficits seen in individuals with FAS, none have been proven to be a causal agent. Further, according to several prominent researchers in the area, it is unlikely that there is a single causal mechanism accounting for the observed damage (e.g., Riley, 1990; West et al., 1990). From this perspective, Nanson (1994) proposed that the effects of prenatal teratogenic exposure, rather than being dependent upon the presence of a particular agent, occur along a continuum, with the pattern of deficits dependent primarily on the timing of the prenatal exposure, the length of exposure, and characteristics of the mother (e.g., metabolism, diet, etc.). Research has demonstrated that prenatal alcohol exposure alters the generation, proliferation, and migration of cerebral cortical neurons in rats (Miller, 1992, 1993; West, Goodlett, Bonthius, Hamre, & Hamre, 1990). What is not yet clear is whether other teratogens such as phenylalanine have the same effect. The lack of animal models of other teratogens, as well as a lack of comparative studies between those models that are available, has limited this area of research.

Similar to West et al. (1990), Nanson (1994) sees the need for a research paradigm in FAS that would begin to differentiate between function and structure.

However, Nanson believes that we must first be able to demonstrate the unique nature of FAS, independent of other prenatal teratogenic exposures. Nanson proposed that in order to demonstrate the uniqueness of FAS we must be able to demonstrate a double dissociation of function between it and other disorders. Nanson argues for the development of a research paradigm differentiating prenatal alcohol exposure from other prenatal teratogens at the levels of facial dysmorphology, behaviour, and brain morphology.

As discussed earlier, the behavioural and physical effects of prenatal exposure to various other teratogenic agents appear similar to those of alcohol. In a paper detailing the initial data collected from a prospective, collaborative study of MPKUS, Rouse, Lockhart, Matalon, Azen, Koch, Hanley, Levy, de la Cruz, and Friedman (1990) comment that the "facial features of maternal PKU syndrome are reminiscent of those of fetal alcohol syndrome" (pg. 290). Lipson, Yu, O'Halloran, and Williams (1981) have also commented on the similarities between FAS and MPKUS and argued that the facial dysmorphology seen in FAS was striking but not unique. More recently, Abel, Martier, Kruger, Ager, & Sokol (1993), have shown that dysmorphologists can - in the absence of information regarding exposure history - reliably identify the facial dysmorphology of FAS from newborn photographs and knowledge of birth weight. However, there have not been studies attempting to reliably differentiate FAS from other forms of teratogenic exposure in the absence of exposure history.

McKay, Petrova-Benedict, Thoene, Bergen, Wilson and Robinson (1986) proposed that there is a common mechanism underlying FAS, MPKUS, and another metabolic disorder, pyruvate dehydrogenase (PDH) complex. Individuals with PDH

deficiency are characterized by pre- and postnatal growth deficiency, mental retardation, hypotonia, and in some cases, facial dysmorphology. Robinson, MacMillan, Petrova-Benedict, and Sherwood (1987) described this facial dysmorphology as similar to that seen in individuals with FAS. Although some of the dysmorphism is similar to that described in FAS - namely micrognathia, microphthalmia, narrow palpebral fissures, a wide nasal bridge, and ventricular septal defects — other features are different from the dysmorphia usually thought to be pathognomonic of FAS.

Robinson and colleagues (1987) have proposed that there is a common metabolic pathway in-utero that is disrupted in all three aforementioned disorders (FAS, MPKUS, PDH). Acetaldehyde is a product of alcohol metabolism that is present at elevated levels in alcoholics, and acetaldehyde from maternal circulation inhibits pyruvate dehydrogenase in the fetus. In MPKUS, high maternal levels of phenylalanine also inhibit pyruvate dehydrogenase in the fetus. In PDH complex, the endogenous low activity of pyruvate dehydrogenase in the fetus may cause the same malformations. Thus, Robinson proposes that low PDH activity is the final common pathway in-utero that results in all three disorders.

Enloe (1980) has proposed a contrasting theory specific to the properties of alcohol. He proposes that a reasonable biochemical explanation for the damage that occurs when the developing brain is exposed to alcohol can be based on alcohol's ability to absorb water. In the developing fetus the brain receives a rich supply of maternal blood. Consequently, if the mother's blood alcohol level is high, the developing brain is bathed in alcohol-laden blood. The dehydrating effect of alcohol

withdraws fluid from the developing brain cells, leaving them dead or functionless. This would ensure that a child prenatally exposed to alcohol would not have the same amount of brain tissue as a non-exposed child. Some evidence for Enloe's theory has been provided by autopsy studies of infants who have died due to alcohol-related birth defects and by recent MRI studies of children diagnosed with FAS, which demonstrate a reduction in brain mass (e.g., Mattson et al., 1994). Moreover, this theory helps to explain why we see varying levels of CNS damage in children who were prenatally exposed to alcohol. It suggests that the type and extent of CNS damage are dependent on the level of alcohol exposure and on the timing of that exposure during brain development (Enloe, 1980).

According to Nanson (1994), if FAS is a unique diagnostic entity, it should be possible to differentiate it from MPKUS and other forms of teratogenic exposure at multiple levels, including but not limited to dysmorphology. She suggests that there are a limited number of ways in which teratogens can disrupt the development of facial structure, thus leading to similar, overlapping forms of facial dysmorphia in affected individuals. Because, the central nervous system develops throughout the entire pregnancy, it is especially vulnerable to teratogens. Mothers of MPKUS individuals, because of the endogenous nature of PKU, continuously expose their unborn offspring to some level of phenylalanine. Most mothers of FAS individuals are chronic alcoholics, with their unborn offspring being exposed to fluctuating levels of alcohol (high levels to no exposure) throughout their pregnancy. As a result, there may be behavioural characteristics unique to a specific teratogen, even if the dysmorphia proves to be indistinguishable from other disorders.

If, as Streissguth and LaDue (1985) have argued, there is a behavioural phenotype (behavioural manifestation of the disorder) in FAS, it should be possible to define objective behavioural markers that differentiate FAS from other forms of mental retardation and developmental abnormalities. Nanson (1994) argues that in order to state that FAS has a unique behavioural phenotype, research must move beyond simply cataloging the problems noted in individuals with FAS, and beyond simple comparisons that demonstrate differences between individuals with FAS and normal controls. She suggests that if a double dissociation of FAS and MPKUS could be demonstrated at the behavioural level, the stage would be set for studies linking behavioural anomalies with neuroanatomic and neuroradiologic findings in these disorders.

8 The Present Study

The literature review discussed studies of children with FAS and children with MPKUS, providing an initial understanding of the pattern of deficits seen in these populations - specifically, in the areas of attention and memory. The literature review also provided an overview of the debate regarding the distinctiveness of these two types of prenatal teratogenic exposure. The present study provides empirical data regarding the attention and memory functioning of adults prenatally exposed to alcohol or phenylalanine, and examines whether there are effects that are specific to the individual teratogens.

First, following West's (1990) call for further investigation into FAS, the present research provides an understanding of the pattern of strengths and weaknesses in the areas of attention and memory through an examination of the long-term neuropsychological functioning of adults with FAS and MPKUS. The present study also provides information about the developmental trajectory of untreated MPKUS, providing information for evaluation of the efficacy of current prenatal dietary treatment programs.

Second, following Nanson's (1994) discussion of specific versus general prenatal teratogenic exposure, the present study provides preliminary data as to whether the pattern of deficits seen in individuals with FAS are unique and distinguishable from the pattern of deficits seen in individuals with MPKUS. Demonstration of the pattern of similarities or differences between the two groups - at the behavioural level - will

provide direction for ongoing investigations of the impact of prenatal exposure to alcohol and phenylalanine.

In summary, the two goals of the current study were: to obtain much needed descriptive data on the long-term neuropsychological functioning of individuals with FAS or MPKUS, and to determine if the two groups differ in their pattern of strengths and deficits.

8.1 Research Questions and Hypotheses

The following hypotheses and questions were addressed:

1. *Can adult individuals with FAS or MPKUS be differentiated from CA and IQ matched Controls with regard to attention and memory abilities?*

First, based on the literature to date, it is expected that adults with FAS will demonstrate poorer performance than the CA- plus IQ-matched Control group in terms of verbal memory, including the ability to learn new information, and immediate, delayed, and recognition memory ability. Second, based on the literature to date, it is expected that adults with FAS will demonstrated poorer performance than the CA- plus IQ-matched Control group in terms of capacity to focus, sustain, shift, and encode attention as defined by Mirsky et al.'s model of attention.

Because empirical data regarding the adult outcome of prenatal teratogenic exposure are lacking the following questions are exploratory in nature. First, how do adults with MPKUS differ from a CA- plus IQ-matched Control group in terms of verbal memory, including ability to learn new information, immediate and delayed recall, and recognition memory ability? Second, how do adults with FAS or MPKUS differ from a CA- plus IQ-matched Control group in terms of visual memory, including immediate and delayed recall? Third, how do adults with MPKUS differ from a CA-

plus IQ-matched Control group in terms of capacity to focus, sustain, shift and encode attention as defined by Mirsky et al.'s model of attention?

2. *Are the relative effects of alcohol and phenylalanine different?*

The following questions are exploratory in nature and are based on clinical observations, performance of participants at a younger age, and the differential exposure pattern of the two prenatal teratogens. First, do adults with FAS differ significantly from adults with MPKUS in terms of verbal and visual memory, including the ability to learn new information, immediate and delayed recall, and recognition memory ability? Second, do adults with FAS differ significantly from adults with MPKUS in terms of capacity to focus, sustain, shift and encode attention as defined by Mirsky et al.'s model of attention?

9 Method

9.1 Participants

Seventeen adults who received a diagnosis of FAS in childhood according to criteria set out by Clarren and Smith (1978) and 13 adults with MPKUS, whose mothers had PKU and did not receive dietary treatment during pregnancy, participated in the present study. All FAS participants were recruited from the pool of individuals with FAS that are followed through the Kinsmen Children's Centre of the Royal University Hospital in Saskatoon, a multidisciplinary clinic for individuals with mental handicaps and other developmental disorders. The MPKUS participants were recruited through the Kinsmen Children's Centre (8 participants) and from the Clinic for Inborn Errors of Metabolism of the Children's Hospital in Boston (4 participants). Participants were 16 years of age or older, had an IQ of 50 or more on the Wechsler Adult Intelligence Scale-Revised, had no known neurological impairments caused by conditions other than prenatal exposure to alcohol or phenylalanine, and English was their first language.

The Control group participants were recruited from the Saskatchewan Community Living Association (a community organization for the mentally handicapped), Cosmopolitan Industries (a sheltered workshop for the mentally handicapped), Saskatchewan Abilities Council (a functional rehabilitation and vocational training centre for individuals with cognitive and/or physical disabilities) and Children's Hospital in Boston. Additional inclusion criteria for this group included:

no neurological impairments other than any general developmental delay present at birth (e.g., no hydrocephalus, no metabolic disorders, no brain injury or illness), no known history of excessive prenatal alcohol exposure, and English was their first language.

The Control group participants consisted of 29 individuals who were matched on chronological age (CA) and IQ to the FAS and MPKUS individuals. Age was matched within 18 months and IQ was matched within five points. A Control group was included in order to examine the pattern of attention and memory deficits associated with prenatal exposure to alcohol or phenylalanine while controlling for the influence of IQ. Approximately half of the Control group participants carried a diagnosis of mental retardation of unknown etiology. The remaining Control participants were recruited from an adult basic education program and from a vocational retraining program and scored within the low average to average IQ range. Four Control participants were recruited from the Children's Hospital in Boston as matches for the four participants with MPKUS recruited from there.

9.2 Measures

The symbiotic nature of attention and memory necessitates a multifaceted assessment. Therefore, the test battery used in the present study will be guided by Kaplan's concepts (i.e. a combination of statistical-psychometric and theoretical-clinical testing) to achieve the broadest scope of assessment.

9.2.1 Intelligence Quotient (IQ)

The Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1981) was used to determine the Full Scale IQ of all participants. The WAIS-R is a

standardized instrument containing 11 subtests that assess Verbal and Performance abilities, and covers an age range from 16 years, 0 months to 74 years, 11 months. The WAIS-R IQ scales (Verbal, Performance, and Full Scale) have an internal consistency of .98 or higher over the entire age range covered by the scale.

9.2.2 Structured Interview

A structured community assessment interview was utilized with participants and/or their caregivers to collect demographic material concerning family structure, socioeconomic status (SES), education, and employment (Crossley, Inch, Keegan, & Murdoch, 1992; see Appendix A).

9.2.3 Attention

The attention-demanding tasks selected from Mirsky et al.'s (1991) attention battery for the present study are listed below. These tasks were chosen because they had the highest factor loadings both in Mirsky's original factor analysis of attentional components and in subsequent replications. In addition, these tasks have been frequently used in previous research on FAS.

The first task is Talland Letter Cancellation (TLC; Talland, 1965; see Appendix B), a paper and pencil test of perceptual-motor speed/accuracy with tasks of varying levels of complexity. It is used to measure the ability to "focus" attention and screen out distractions. In each trial, the participant scans rows of upper- and lowercase letters to find and cross out as many of an assigned target as possible in 60 seconds. Either single or double spaces separate the letters. On trials 1 and 2 (Capitals), participants must draw a line through all capital letters. During trials 3 and 4 (Spaces), participants draw a line through the letters immediately before and after each double space,

ignoring the letter's case. On trials 5 and 6 (Both), participants cross out both types of targets previously assigned (i.e., capitals and spaces). Scores include mean number of hits, false alarms and errors of omission. However, pilot testing indicated that lower functioning individuals were unable to complete all of the trials due to their inability to recognize letters. Therefore, the Underlining Test (Rourke, Bakker, & Strang, 1983; see Appendix C), a similarly designed test, utilizing geometric shapes and numbers instead of letters, was added. The Underlining Test consists of five trials, three involving underlining a specific shape and two involving underlining a specific number. Both the TLCT and the Underlining Test provide practice trials, ensuring that all participants understand the task. Although the Underlining Test is a similar test, it may not necessarily load on the same factor as the TLCT. Therefore, in order to ensure that the 'focus' component of Mirsky's attention battery was reliably assessed, the Trail Making Test was included as it had the second highest factor loading for this component and unlike the Stroop Test did not require reading.

The Trail Making Test (Reitan & Davidson, 1974; Reitan & Wolfson, 1985) requires motor speed and focused attention while examining visuomotor coordination and speed of processing in the sequencing of both numbers and letters. Part A of the task calls simply for sequencing overlearned material, while Part B requires conceptual alternation and behavioural inhibition (Reitan & Wolfson, 1985).

The third task is the Continuous Performance Test (CPT; Rosevald, Mirsky, Bransome, Sarason, & Beck, 1956; see Appendix D), a computerized vigilance test used as a measure of brain damage. This measure of attention involves responses to visually-presented letters or numbers, with reaction time and accuracy as the outcome

measures. The CPT is used to measure the ability to "sustain" attention over time. Participants are required to press a response key for certain target stimuli ("press as fast as possible whenever you see the letter X" or "press for the X only if it is preceded by the letter a", or "press when you hear the high tone"). The version used runs on software operated by a DOS based laptop computer that communicates with a separate Stimulus\Response Unit. It is used with a 4.2 minute X-task, a 8.6 minute AX-task, a 5.5 minute DX-task (degraded X stimuli), and a 4.2 minute auditory tone task. The X task reflects a highly automatic vigilance test that is dependent almost exclusively on sensory-perceptual processing, whereas the AX task has a clear memory component linked to the participant's distinguishing between target and nontarget Xs. The AX task also assesses the participant's ability to inhibit the previously established task of pressing for each X. The DX task letters appear as dense clusters of tiny dots against a background of similar dots. This task requires more perceptual effort because participants must extract a meaningful gestalt from a nebulous display. The Auditory task stimuli consist of three tones of distinctly different pitches (Mirsky, Fantie, & Tatman, 1995). All tasks are preceded by a practice phase during which participants are provided with feedback until such time as they are responding to the critical stimuli. Vigilance scores include mean percentage of correct responses, mean percentage of commission errors, mean percentage of omission errors, and mean reaction time.

The fourth task is the Wisconsin Card Sort Test (WCST; Heaton, 1981; see Appendix E), a concept-identification task that according to Mirsky (1991), measures the ability to "shift" attention. It is primarily used to assess perseverative and abstract thinking, and is also used clinically as a measure of frontal lobe function. It provides

objective measures of overall success and identifies particular sources of difficulty on the task. The WCST involves stimulus and response cards printed with various shapes differing in number and color. Participants are required to sort the cards according to different principles (shape, number or color) and to alter their approach as unannounced shifts in the sorting principle occur during test administration. Normative data are available for subjects aged 6.5 to 89 years.

The fifth and sixth tasks are the WAIS-R Arithmetic Subtest, a test of numerical reasoning and auditorily-processed mental computation, the WAIS-R Digit Span Subtest, a test of attention and short-term memory and the Wide Range Achievement Test-Third Edition (WRAT-3) Arithmetic subtest, a timed, written arithmetic achievement test. Both are well-standardized age-normed tests that load on what Mirsky (1991) termed the "encoding" factor of attention.

9.2.4 Memory and Learning

Memory and learning were examined using the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987), the Rey Auditory Verbal Learning Task (RAVLT; Rey, 1941, 1964; Wiens, Crossen, & McMinn, 1988), and the Rey Complex Figure (Rey, 1941). The RAVLT was chosen over the CVLT as pilot testing indicated that lower functioning individuals were unfamiliar with 'spices', a subcategory of words within the larger list, resulting in them being unable to recall any words from that category on either free or cued recall.

The WMS-R is a standardized battery of eight tests designed to assess various aspects of memory, including memory for verbal, visual, meaningful, and abstract material, as well as immediate and delayed recall of material. The WMS-R covers an

age range from 16 years, 0 months to 74 years, 11 months. It provides three summary scores: Attention/Concentration, General Memory, and Delayed Recall. General memory can be further subdivided into two additional indices measuring Verbal Memory and Visual Memory. Reliability coefficients for the indices range from .70 to .90.

The RAVLT assesses verbal learning and memory ability, as well as recognition memory. The tasks probe ability to learn, immediate and delayed recall, and recognition memory using a list of 15 nouns presented over five trials. After the fifth trial an interference list of 15 words is presented, followed by a free recall of the first list. After a 30-minute delay involving nonverbal testing, free recall is again assessed followed by a recognition task of the first list of words. The test has modest test-retest reliability (Spreen & Strauss, 1991).

The Rey-Osterrieth Complex Figure assesses visuospatial constructional ability and visual memory. Participants are first instructed to copy a geometric figure. Following a period of delay, typically 30 minutes after completion of the copy, participants are asked to reproduce the figure from memory. There are strict scoring criteria based on the correctness of details and their placement in the copied figure. The copy score is a measure of visual-constructional ability, and the delayed recall score is a measure of the amount of information retained over time. Using the scoring criteria developed by Taylor (1979), interrater reliability for the Rey-Osterrieth Complex Figure is above .95. Normative data is available from Canadian samples of healthy adults, ages 16-44 (Spreen & Strauss, 1996).

9.3 Procedure

Ethics approval for the present study was obtained from the University of Saskatchewan, Saskatoon District Health, and from the Children's Hospital in Boston (see Appendix F).

All participants were recruited through a letter either from the Kinsmen Children's Centre or from Boston Children's Hospital that outlined the study and requested participation (see Appendix G). A letter describing the study was also sent to parents/caregivers of individuals in these three groups (see Appendix G). All individuals received a small honorarium and reimbursement for any travel expenses incurred to take part in the study. Testing was carried out at the Kinsmen Children's Centre and in participant's homes. Consent forms were obtained from each individual and their caregiver where appropriate (see Appendix H). The test battery required approximately five hours to complete (see Appendix I for order of test presentation). There were scheduled breaks throughout the day of testing.

All participants were tested individually. Three investigators were involved in the administration of the selected measures. The primary investigator first met with the individual (and their caregiver if appropriate) to answer any questions and to obtain signed consent for participation in the experiment (see Appendices H through J).

10 Results

10.1 Demographic Information

The following demographic information is provided as background information and for purposes of replication. All participants provided information concerning their current medications. Participants acknowledging use of medication associated with cognitive change (e.g., Ritalin, Cylert) were not included in this study.

Control group participants were matched to the participants in both teratogen groups (17 FAS-Control matches and 12 MPKUS-Control matches) based on their chronological age (within 18 months) and WAIS-R Full Scale IQ score (within 5 IQ points). Table 10.1 provides the mean Full Scale, Performance, and Verbal IQ scores for each of the four groups.

The FAS group ranged in age from 16 to 34 years and the MPKUS group ranged from 16 to 37 years (see Table 10.2). There were no significant differences in age among the four groups, $\underline{F}$ (3, 55) = 2.15, p = .10. Table 10.3 lists the distribution of males and females among the four groups. Gender distribution did not differ significantly among the groups, $\chi^2(3) = 0.98$, p = .80. The FAS group appeared to differ from the other three groups in terms of racial composition; however, because chi-square is invalid when the expected cell number is less than five (Howell, 1992), this statistic was not computed. There were 12 Natives in the FAS group (replicating the Saskatchewan population sampled in an epidemiological study by Habbick et al., 1996)

Table 10.1 WAIS-R IQ by Group

Test & Subscale	FAS (n=17)	MPKUS (n=12)	FAS-C (n=17)	MPKUS-C (n=12)
WAIS-R				
Full Scale IQ	73.47 (13.0)	66.76 (18.0)	73.12 (11.3)	67.33 (17.0)
Verbal IQ	70.06 (10.8)	65.69 (16.3)	74.29 (10.7)	68.58 (17.1)
Performance IQ	80.71 (17.1)	73.46 (17.8)	75.06 (13.6)	71.08 (15.7)

Table 10.2 Age Distribution by Group

Age	FAS (n=17)	MPKUS (n=12)	FAS-C (n=17)	MPKUS-C (n=12)
Mean	21.4	24.8	21.7	26.0
Median	19.0	26.0	19.0	28.5
Mode	18.0	26.0	18.0	16.0

Table 10.3 Gender Distribution by Group

Gender	FAS (n=17)	MPKUS (n=12)	FAS-C (n=17)	MPKUS-C (n=12)	TOTAL (n=59)
Male	9 (52.9%)	5 (41.6%)	10 (58.8%)	5 (41.6%)	30 (50.8%)
Female	8 (47.0%)	7 (58.3%)	7 (41.1%)	7 (58.3%)	29 (49.2%)

and four in the FAS-C group (more race-matched controls were not available). The remainder of the participants were Caucasian (see Table 10.4).

Table 10.5 outlines the current employment status of the four groups[a]. The groups varied as more of the MPKUS and their matched controls were employed in sheltered workshop environments, whereas more of the FAS individuals and their matched controls were involved in school or pre- employment training. Only two participants were engaged in full-time regular employment (one FAS and one MPKUS). One MPKUS participant (who was a full-time high school student) was working part-time.

Table 10.6 outlines the groups' living arrangements.[b] Although more of the FAS participants resided in single family homes with adoptive or foster families, this difference was largely due to the number of individuals in the FAS group under 20 years of age (9 FAS versus 4 MPKUS).

10.2 Education Outcome Information

Table 10.7 lists the education status of the four groups. At the time of the study nine of the FAS participants, four of the FAS-C participants, two MPKUS, and one MPKUS-C were still in school.

[a] The employment section of the demographics questionnaire was not complete for one FAS-C individual.
[b] The living arrangement section of the demographics questionnaire was not complete for one MPKUS individual and two FAS-C individuals.

Table 10.4 Race Distribution by Group

Race	FAS (n=17)	MPKUS (n=12)	FAS-C (n=17)	MPKUS-C (n=12)	TOTAL (n=59)
Native	12(70.6%)	----	4 (23.5%)	----	16 (27.1%)
Caucasian	5 (29.4%)	12(100%)	13 (76.5%)	12 (100%)	43 (72.9%)

Table 10.5 Employment by Group

Employment	FAS (n=17)	MPKUS (n=12)	FAS-C (n=16)	MPKUS-C (n=12)	TOTAL (n=58)
Full-Time	1 (5.9%)	2 (15.4%)	-----	-----	3 (5.2%)
Part-Time	-----	3(15.4%)[a]	1 (6.2%)	1 (8.3%)	4 (6.9%)
Casual	-----	-----	-----	1 (8.3%)	1 (1.7%)
Sheltered Workshop	3 (17.6%)	6 (53.8%)	4 (18.8%)	7 (58.3%)	20 (34.5%)
Pre-Employment Training	1 (5.9%)	-----	8 (50.0%)	2 (16.7%)	11 (19.0%)
Unemployed	3 (17.6%)	1 (7.7%)	-----	-----	4 (6.9%)
Student	9 (52.9%)	1 (7.7%)[a]	4 (25.0%)	1 (8.3%)	15 (25.9%)

[a] One full-time student was working part-time—not included in part-time percentage.

Table 10.6 Living Arrangements Distribution by Group

Living Arrangements	FAS (n=17)	MPKUS (n=12)	FAS-C (n=15)	MPKUS-C (n=12)	TOTAL (n=56)
Alone	-----	-----	-----	1 (8.3%)	1 (1.8%)
Parents[a]	9 (52.8%)	3 (25%)	4 (26.7%)	5 (41.7%)	21 (37.5%)
Spouse &/Or Children	-----	1 (8.3%)	1 (6.7%)	-----	2 (3.6%)
Relatives	2 (11.8%)	-----	2 (13.3%)	-----	4 (7.1%)
Supervised Group Home	4 (23.5%)	6 (50.0%)	7 (46.7%)	5 (41.7%)	19(34.0%)
Independent Group Home	1 (5.9%)	-----	-----	-----	1 (1.8%)
Semi-Independent Group Home	1 (5.9%)	2 (16.6%)	1 (6.7%)	1 (8.3%)	8 (14.3%)

[a] * Biological, adoptive and foster parents

Table 10.7 Education by Group Outcome Data

Education	FAS (n=17)	MPKUS (n=12)	FAS-C (n=17)	MPKUS-C (n=12)	TOTAL (n=59)
Partial Primary	7 (41.2%)	6 (50.0%)	2 (11.8%)	3 (25.0%)	19(32.2%)
Completed Primary	-----	1 (8.3%)	1 (5.9%)	2 (16.6%)	4 (6.8%)
Partial Highschool	8 (47.1%)	4 (33.3%)	6 (35.3%)	7 (58.3%)	26(44.1%)
Complete Highschool	1 (5.9%)	-----	8 (47.1%)	-----	9 (15.2%)
Technical Training	1 (5.9%)	1 (8.3%)	-----	-----	2 (3.4%)

10.3 Data Analysis

10.3.1 Dependent Variables

The data from the tests administered were scored in accordance with the standard instructions provided with each test. The dependent variables chosen from each measure and the component of interest are discussed below (see Table 10.8).

A total of four attention-demanding tasks were selected from Mirsky's attention battery for the present study. The dependent variables from the TLCT include the mean number of correct responses, the mean number of omissions, and the mean number of commissions.

The dependent variables taken from the Underlining Test include mean time across tests, mean number of commission errors, mean number of omissions, mean rate, and mean hits.

The dependent variables taken from the Trail Making Test were time in seconds for both Trails A and Trails B.

The dependent variables from the CPT include mean reaction time, percent correct, percent omission errors, percent commission errors, β, and d' for the X task, the AX task, the degraded X task, and the auditory Tones task. β is a measure of the individual's error response bias relative to the total number of errors. d' prime is a measure of how able the individual was to discriminate between critical and non-critical stimuli relative to the total number of critical stimuli (see Appendix J for computational information on CPT variables).

Table 10.8 Data Analysis Design

Area of Interest	Components	Corresponding Tests & Dependent Variables Selected for Analysis
Attention	Focus	TLCT - Mean Number Omissions, Commissions, and Correct Underlining Test - Mean Number Omissions, Commissions, and Correct Trail Making Test - Trails A & B Time
	Sustain	CPT - Mean Reaction Time, Percent Correct, Percent Omission Errors, Percent Commission Errors, d' & β for the X, AX, DX, and Auditory Tones Tasks
	Shift	WCST - Categories Completed, Percent Correct; Percent Perseverative Errors, Failure to Maintain Set
	Encode	WAIS-R Arithmetic & Digit Span; WRAT-3 Arithmetic
Memory	Ability to Learn	RAVLT - Learning Index; Total # of Perseverations; Total # of Intrusions
	Verbal Memory (Immediate)	WMS-R - Logical Memory I; Verbal Paired Associates I RAVLT - Immediate Recall Trial; Percent Recall (A6/A5); Proactive Interference (B1/A1)
	Verbal Memory (Delayed)	WMS-R-Logical Memory II; Verbal Paired Associates II RAVLT - Delayed Recall Trial; Forgetting Index (A7/A6)
	Recognition	RAVLT - Recognition and Signal Detection of Recognition Performance
	Visual Memory (immediate)	WMS-R - Visual Reproduction I; Visual Paired Associates I
	Visual Memory (Delayed)	Rey Complex Figure - Delayed Recall WMS-R - Visual Reproduction II; Visual Paired Associates II

The dependent variables from the WCST include number of categories/sets completed; percentages of perseverative errors, failure to maintain set, and percent correct.

The dependent variables from the WAIS-R include the raw scores from the Arithmetic and Digit Span subtests.

The dependent variables from the WMS-R include the raw scores of the eight subscales (Logical Memory I & II; Verbal Paired Associates I & II; Visual Paired Associates I & II; and Visual Reproduction I & II) that comprise the Visual, Verbal, and Delayed Memory indices. The decision to utilize raw subscale scores was made, as indices could not be calculated for a number of individuals due to floor effects (see Table 10.9).

The dependent variables from the RAVLT include the following: Learning Index (Trial A5 - Trial A1), Immediate Free Recall (Trial A6), Delayed Free Recall (Trial A7), Intrusion and Perseveration scores, Percent Recall, a measure of retroactive interference is the ratio of number of words recalled following a distractor list versus number of words recalled prior to the distractor (Trial A6: Trial A5), Proactive Interference, a ratio of number of words learned on Trial 1 list A versus number of words learned on List B (Trial A1: Trial B1), Forgetting Index (A7/A6), which compares the immediate recall score with a delayed (20 minutes) recall score, and Signal Detection of Recognition Performance (p(A), which corrects the recognition score formulated as 0.5 (1 + HR - FP) and varies between 0 (random) and 1 (perfect performance). See Appendix K for computational information.

Table 10.9 Floor Effects for WMS-R Indices Across Groups

WMS-R MEMORY INDICES

Group	Verbal Memory	Visual Memory	Delayed Memory
FAS	1	2	4
MPKUS	2	4	5
Control	5	5	6

The dependent variable from the Rey-Osterrieth Complex Figure is participants' raw score on delayed recall of the figure.

10.3.2 Sample Characteristics

The original data set, group by IQ, is shown in Figure 10.1. The question of interest in the current study was whether individuals with FAS or MPKUS could be differentiated from CA and IQ matched Controls with regard to attention and memory abilities. To examine this question, paired data sets for the FAS group and the CA and IQ matched Control Group and the MPKUS group and the CA and IQ matched Control Group were set up to test planned comparisons.

There were 17 FAS and CA and IQ matched controls appropriate for analysis (matched within five IQ points). Figure 10.2 outlines the FAS paired data set. Figure 10.3 outlines the MPKUS paired data set. In the MPKUS group, one individual was dropped as his IQ was below 50, leaving 12 MPKUS and CA and IQ matched pairs appropriate for analysis (matched within five IQ points).

A second question of interest was whether the two teratogen groups differ from one another and from Controls in terms of attention and memory ability. This question was explored using a randomized block design with IQ as the blocking variable and group (FAS, MPKUS, or Control) as the treatment variable. A randomized block design, which reduces sampling variability between the groups, was chosen in order to reduce the variability attributable to IQ, thereby, reducing the overall measure of error (McClave, Dietrich, & Sincich, 1997).

The blocked data set is shown in Figure 10.4. Within each block, IQ was matched within five points. Due to the small sample size of the MPKUS group, 29

FIGURE 10.1 GROUP DATA BY IQ

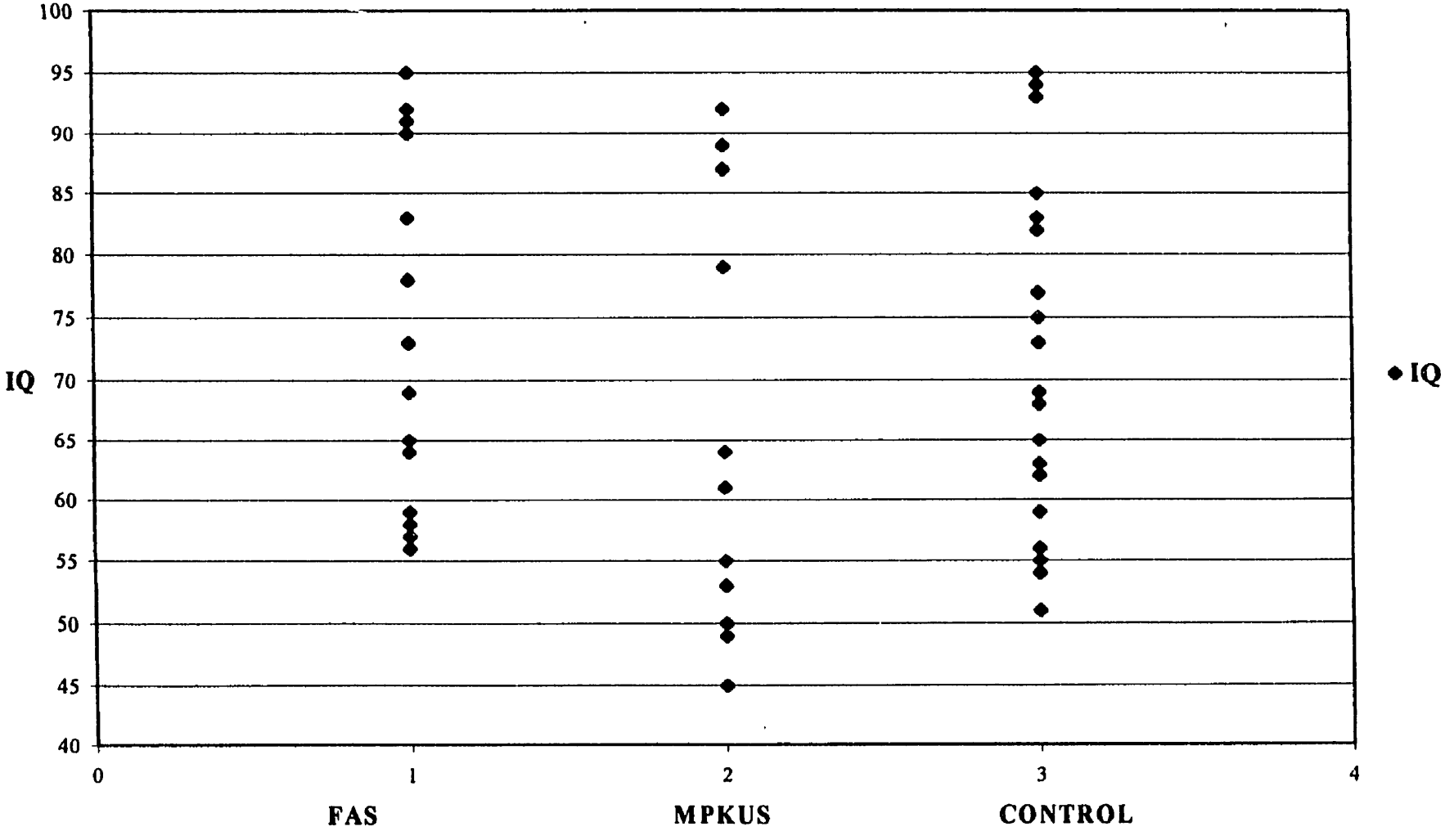


FIGURE 10.2 FAS & CONTROL MATCHED PAIRS BY IQ

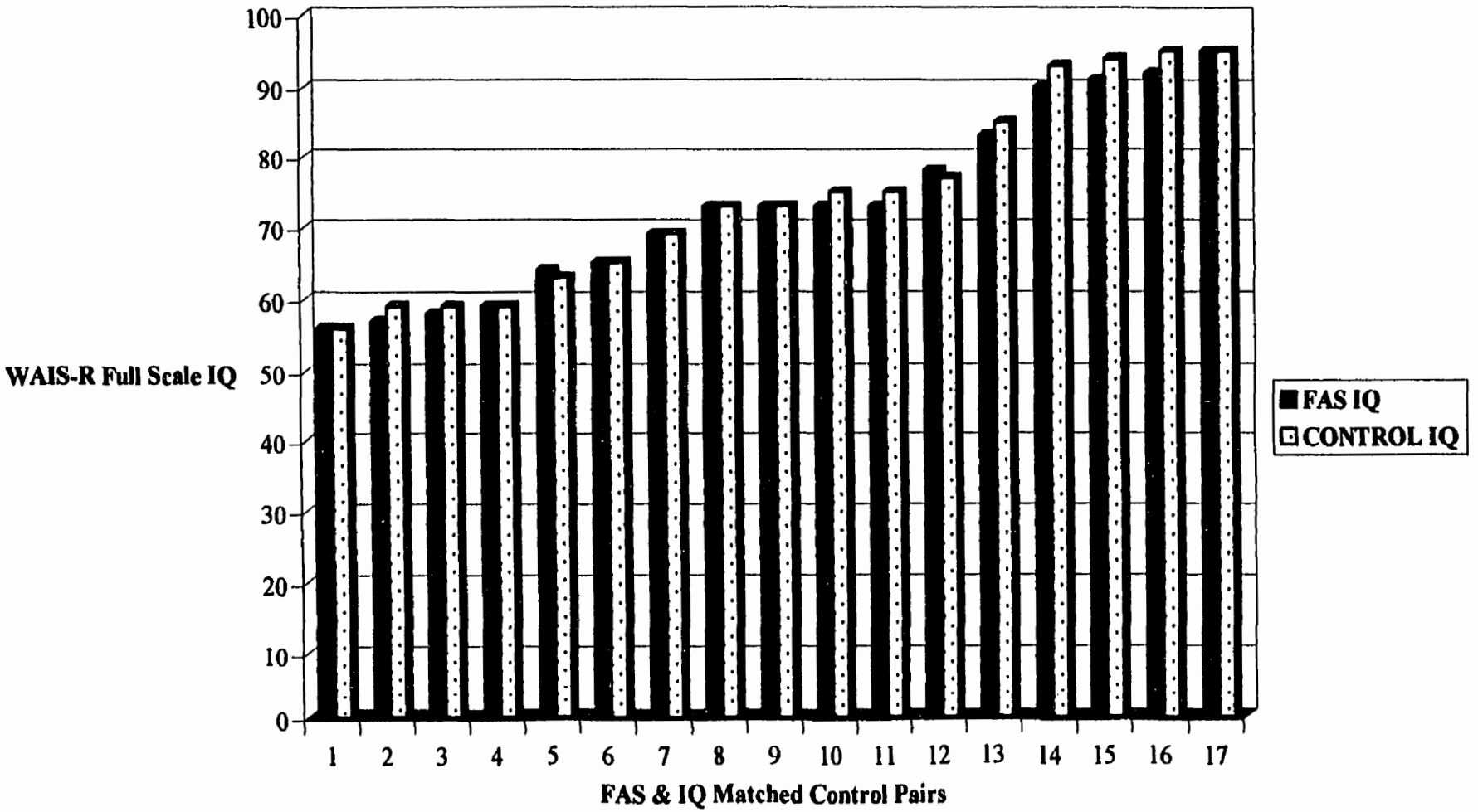


FIGURE 10.3 MPKUS & CONTROL MATCHED PAIRS BY IQ

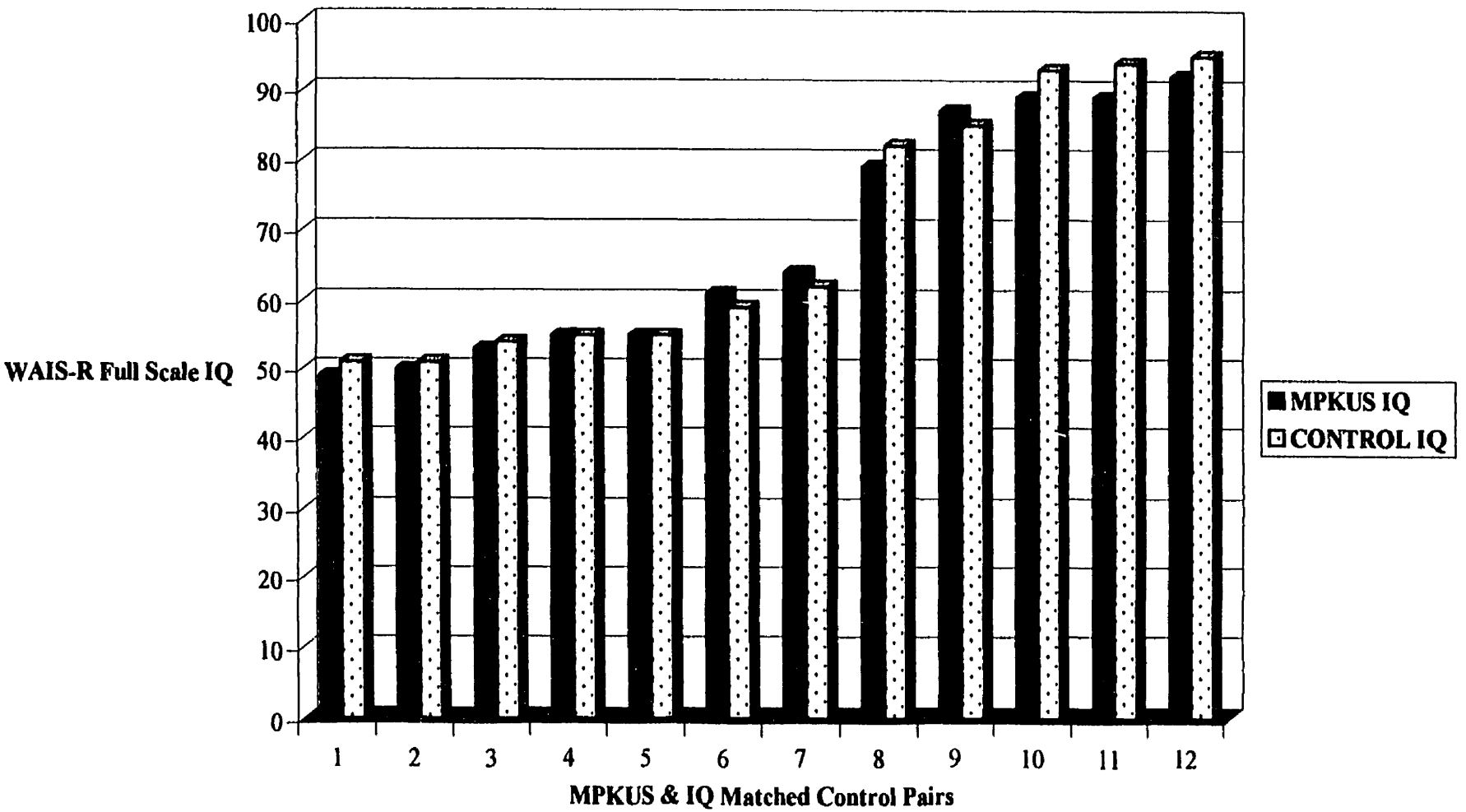
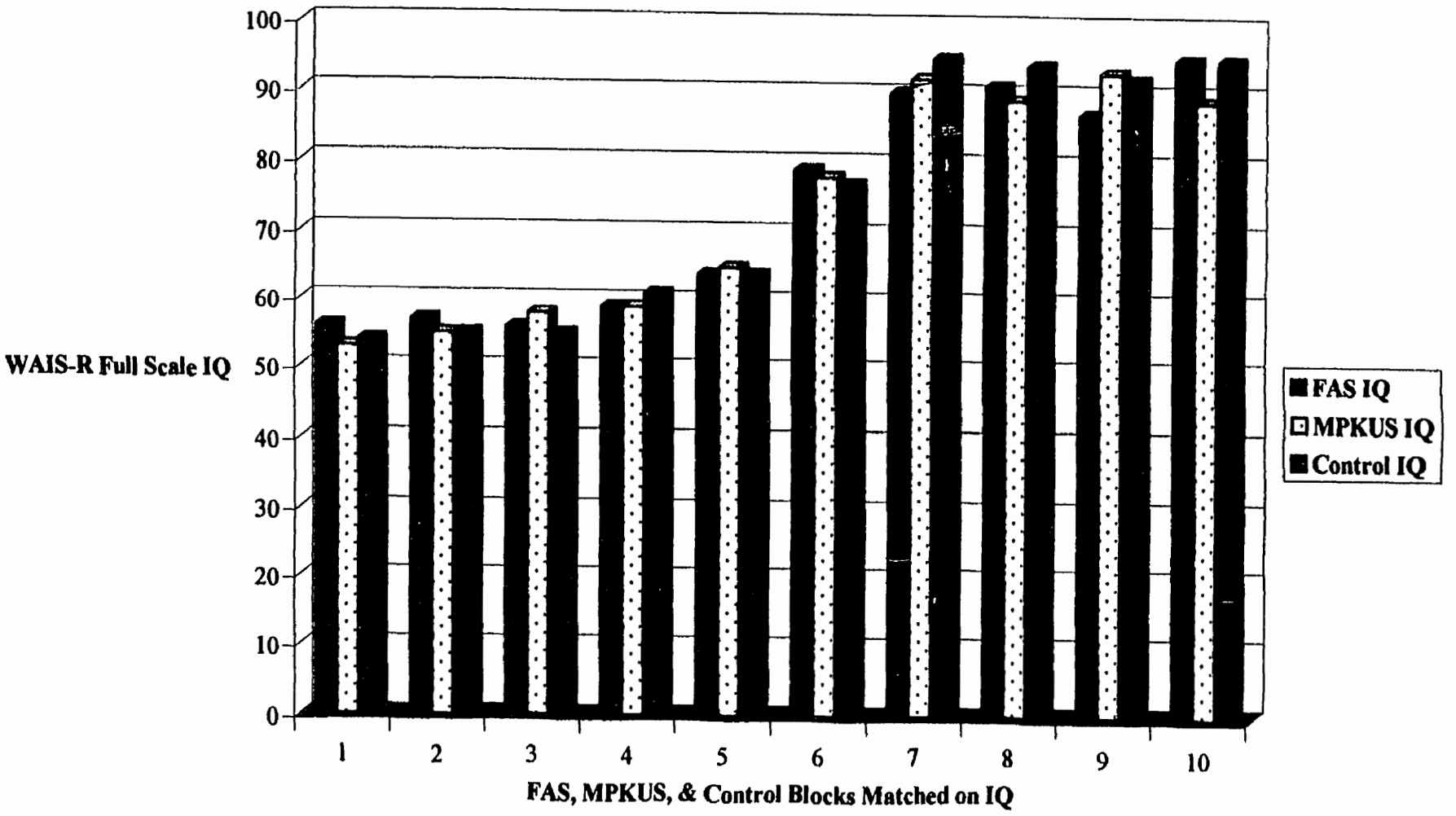


FIGURE 10.4 BLOCKED DATA SET BY IQ



individuals from the FAS and CA and IQ matched Control groups were eliminated from this analysis in order to have equal group numbers and to limit the range of IQ within blocks to five points or less. Hence, there were 10 IQ matched blocks appropriate for the randomized block analysis (not matched on age).

Within the 10 blocks appropriate for analysis, there were a number of data points missing due to the participant(s) not responding to the question asked or not completing the requested task. A randomized block analysis requires data in each cell. Therefore, to correct for the empty cells resulting from floor effects, a score was calculated for each empty cell by taking the lowest score in the sample for the variable(s) in question and subtracting one point. The block analyses were then run with the 10 triplets and then re-run not using the corrected data from participants with empty cells, to determine if the added data point resulted in a significant outcome. Data point subtraction is commonly used in clinical research in the area of mental retardation to deal with missing data due to floor effects. The rationale behind this method of data correction is that the lack of data due to floor effects is important information as the individuals who were unable to complete the various tasks would likely score somewhere below the lowest score in the sample (Widerman, 1998). This method of data correction is currently being utilized on the International MPKUS study to account for missing data due to floor effects. Table 10.10 outlines the number of missing data points for each variable in the current study. Any differences between the randomized block designs with the added data points and those without will be discussed in section 10.6.

Table 10.10 Missing Data Points Across Tests and Groups

TEST	FAS (n=10)	MPKUS[a] (n=10)	Control (n=10)
Rey Complex Figure		1	
CPT X task	1[b]	1	
CPT AX task		1	
CPT DX task		1	
CPT Tones	1[b]	1	
WCST		2	
Underlining		2	
Trails	1	2	
RAVLT Subtests		1	
WMS-R Subtests		1	

[a] All missing data points are from two participants.

[b] Missing data due to computer error - not floor effects.

10.4 Analyses

The initial analysis plan included paired samples t-tests for the FAS and MPKUS paired data sets on each of the dependent measures and parametric analyses of variance (ANOVAs) for the randomized block data set on each of the dependent measures. The ANOVAs were followed by Student Newman Keuls (SNK) post-hoc comparisons to identify the pattern of significant differences between groups. The SNK comparison procedure was chosen over other more conservative procedures because of the exploratory nature of the present study.

A review of the dependent variable distributions indicated that some of the derivational assumptions of both the paired samples t-test and ANOVA appeared to have been violated. However, ANOVA in particular, has routinely demonstrated robustness to modest violations (Howell, 1992). Further, it has been argued that the assumptions required for parametric tests are overly restrictive and that these tests are remarkably unaffected by violations of distribution assumptions (Howell, 1992). However, the view of a robust ANOVA is not universal, and these opponents recommend use of nonparametric statistics (Wilcox, 1998).

Nonparametric tests arguably have greater power than parametric tests when derivational assumptions are violated (Blair & Higgins, 1985). These tests rely on neither parameter estimation nor distribution assumptions, and are more sensitive to medians than to means. Another advantage of nonparametric tests is they employ ranked data and are therefore not as affected by the presence of outliers. In contrast, extreme scores in a data set render the parametric test less powerful by inflating the variance and biasing the mean in the direction of the outlier. The major disadvantage of

nonparametric tests is their lower power relative to the corresponding parametric test. However, this occurs only when derivational assumptions have not been violated; if they are, the parametric value is inconclusive and lacks power.

Due to the violations of derivational assumptions of parametric tests, in particular, homogeneity of variance and normality, and the threat of inaccurate parameter estimation from small group sizes, the Wilcoxon Signed Rank Test for the paired samples experiment, and the Friedman F_r Test, for the randomized block design, were computed.

10.5 Paired Samples Analyses Results

The outcome from the paired samples t-tests are discussed within the framework of the attention and memory components of interest (see Table 10.8). Results for the FAS group and CA and IQ matched Control group analyses will be presented first, followed by results for the MPKUS group and CA and IQ matched Control group.

Tables 10.11 through 10.14 show the parametric and nonparametric results for all significant planned comparisons between the FAS and CA and IQ matched Control groups and between the MPKUS and CA and IQ matched Control groups. When both t and z were significant, the t value was interpreted because it is the more powerful test. If only the t statistic is significant and the derivational assumptions were violated, then it will not be interpreted. When only z is significant, it will be interpreted. A complete listing of both the significant and nonsignificant results are tabled in Appendix L.

Table 10.11 TLCT, Underlining Test and CPT Parametric and Nonparametric Comparisons of FAS Group and CA and IQ matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
TLCT	n=16	n=16		
Mean # Omissions	5.56 (4.54)	7.87 (7.50)	-1.143 (.271)	-1.862 (.063)
Mean # Commissions	3.63 (4.83)	1.28 (1.23)	-1.933 (.072)	-2.386 (.017)
CPT	n=15	n=15		
X Task Percent Commission Errors	4.83 (7.98)	.600 (.66)	2.089 (.055)	2.589 (.010)
X Task d'	96.12 (17.68)	107.87 (13.86)	-2.212 (.043)	-1.541 (.123)
X Task β	-.047 (.39)	-.408 (.53)	2.309 (.036)	2.244 (.025)
	n=17	n=17		
AX Task Percent Commission Errors	5.55 (6.69)	3.35 (6.90)	.977 (.343)	1.178 (.074)
AX Task β	-.197 (.42)	-.213 (.53)	2.759 (.014)	2.249 (.025)
Tones Task Percent Commission Errors	7.65 (9.80)	4.77 (7.75)	.986 (.341)	1.791 (.073)

Note. Below each of the group names are the number of observations for each comparison, the mean and standard deviations in parentheses for each dependent variable, the t value with two-tailed significance level in parentheses, and the z value (using Wilcoxin's Signed Rank test) with two-tailed significance in parentheses.

Table 10.12 WCST and WAIS-R Arithmetic and Digit Span Subtests Parametric and Nonparametric Comparisons of FAS Group and CA and IQ matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
WCST	n=16	n=16		
Categories Completed (Sets)	3.47 (2.34)	2.05 (2.22)	1.888 (.070)	1.740 (.082)
% Perseverative Errors	22.00 (10.43)	31.35 (18.54)	2.839 (.012)	2.438 (.015)
% Correct Responses	59.14 (10.50)	46.68 (18.49)	2.710 (.015)	2.533 (.011)
WRAT-3	n=17	n=17		
Arithmetic Subtest	22.11 (9.40)	25.70 (2.42)	-1.908 (.075)	-1.682 (.093)
WAIS-R	n=16	n=16		
Arithmetic Subtest	4.00 (3.08)	4.88 (2.82)	2.252 (.039)	2.025 (.043)
Digit Span Subtest	6.64 (3.99)	8.35 (5.20)	-1.550 (.141)	-1.666 (.096)

Note. Below each of the group names are the number of observations for each comparison, the mean and standard deviations in parentheses for each dependent variable, the t value with two-tailed significance level in parentheses, and the z value (using Wilcoxin's Signed Rank test) with two-tailed significance in parentheses.

Table 10.13 RAVLT and WMS-R Parametric and Nonparametric Comparisons of FAS Group and CA and IQ matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
RAVLT	n=17	n=17		
Learning Index	4.41 (2.47)	6.00 (2.71)	-2.057 (.056)	-1.909 (.056)
Intrusion Errors	14.52 (14.52)	5.05 (3.96)	2.590 (.020)	2.528 (.011)
Proactive Interference (B1/A1)	2.69 (1.34)	1.42 (.75)	-1.707 (.107)	-2.664 (.096)
Immediate Recall (A6)	6.70 (3.03)	9.41 (3.20)	2.718 (.015)	2.287 (.022)
% Recall (A6/A5)	74.40 (32.80)	96.73 (30.50)	-2.376 (.030)	-2.215 (.027)
Delayed Recall (A7)	5.82 (3.18)	8.94 (3.52)	-3.253 (.005)	-2.629 (.009)
WMS-R	n=17	n=17		
Logical Memory II	9.58 (6.82)	14.70 (8.34)	-2.466 (.025)	-2.199 (.028)
Verbal Paired Associates II	5.95 (1.34)	7.00 (1.45)	-3.816 (.002)	-2.835 (.005)

Note. Below each of the group names are the number of observations for each comparison, the mean and standard deviations in parentheses for each dependent variable, the t value with two-tailed significance level in parentheses, and the z value (using Wilcoxin's Signed Rank test) with two-tailed significance in parentheses.

Table 10.14 CPT, WCST and RAVLT Parametric and Nonparametric Comparisons of MPKUS Group and CA and IQ matched Control Group

Test & Subscale	MPKUS	Control	t (2 tailed)	z (2 tailed)
CPT	n=11	n=11		
Tones Task Percent Correct	36.11 (37.30)	54.29 (32.25)	-1.484 (.169)	-1.956 (.050)
Tones Task Percent Omission Errors	60.19 (38.33)	35.74 (31.19)	1.834 (.097)	2.045 (.041)
Tones Task d'	136.73 (32.71)	106.63 (10.35)	3.404 (.007)	2.223 (.026)
WCST	n=10	n=10		
Failure To Maintain Set	.500 (.97)	2.10 (2.02)	-3.042 (.014)	-2.384 (.017)
RAVLT	n=11	n=11		
Recognition	12.27 (2.05)	14.27 (1.48)	-2.507 (.031)	-2.084 (.037)

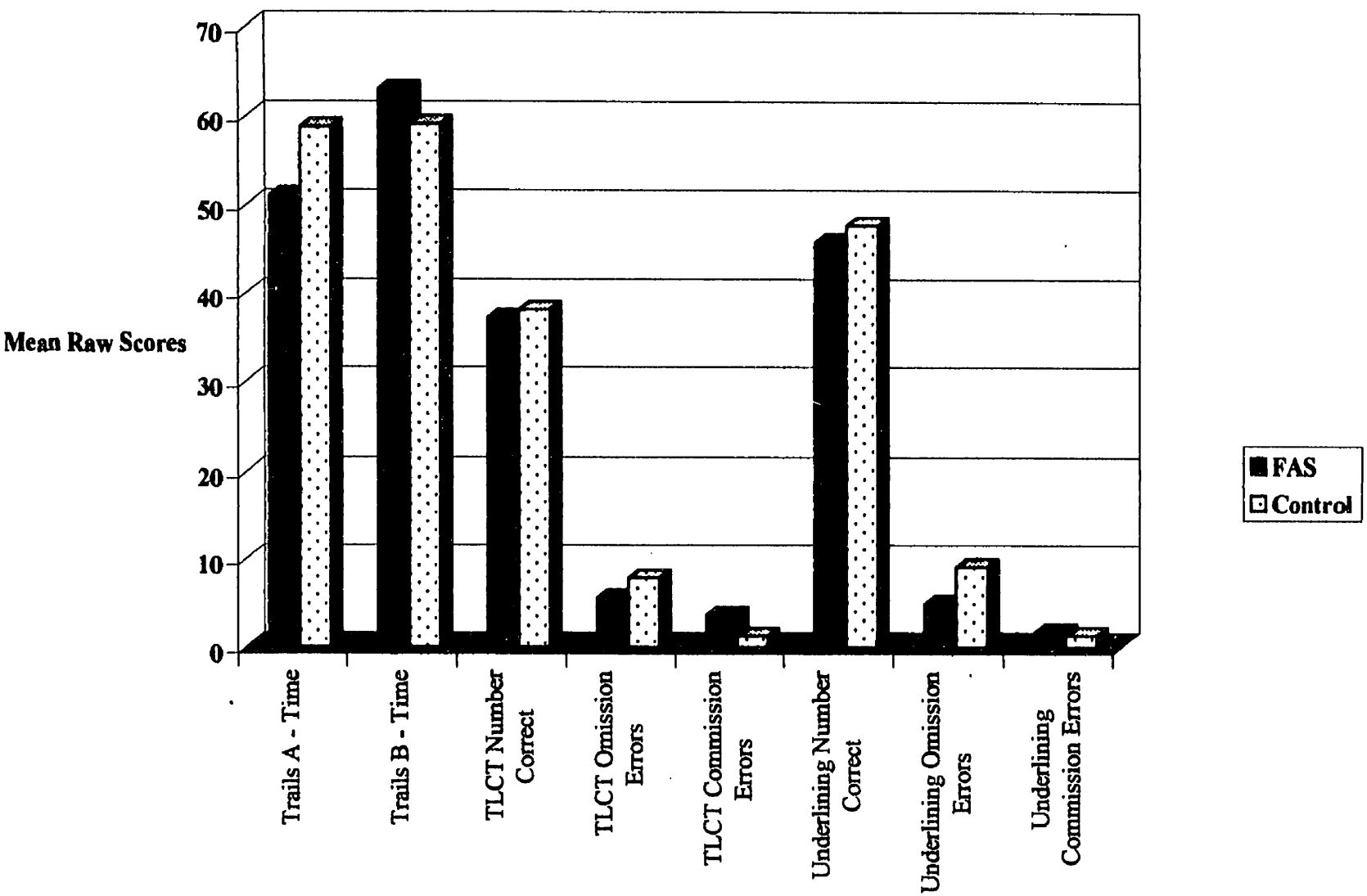
Note. Below each of the group names are the number of observations for each comparison, the mean and standard deviations in parentheses for each dependent variable, the t value with two-tailed significance level in parentheses, and the z value (using Wilcoxin's Signed Rank test) with two-tailed significance in parentheses.

10.5.1 FAS Group and CA and IQ Matched Control Group

'Focus' Attention: On the TLCT, the CA and IQ matched Control group demonstrated more omission errors than the FAS group; 7.87 omissions in the CA and IQ matched Control group versus 5.56 for the FAS group. The parametric test of Mean Number of Omissions was not significant, $t(15) = -1.143$, $p = .270$, whereas the nonparametric test approached significance, $z = -1.862$, $p = .063$. The FAS group demonstrated more commission errors than the CA and IQ matched Control group on the TLCT. The mean score for the FAS group was 3.63 and for the CA and IQ matched Control group was 1.28. The parametric test approached significance, $t(16) = 1.933$, $p = .072$ and the nonparametric test was significant, $z = -2.386$, $p = .017$. Figure 10.5 displays the pattern of results between the two groups across the variables used to assess Mirsky's 'focus' component of attention.

'Sustain' Attention: On the X task of the CPT, the FAS group made more commission errors than the CA and IQ matched Control group. The mean score for the FAS group was 4.83 percent commission errors, whereas it was .60 percent for the CA and IQ matched Controls. Both the parametric and nonparametric statistics were significant, $t(15) = 2.089$, $p = .055$ and $z = -2.589$, $p = .010$. The parametric test of the X task discriminability variable (d') was significant, $t(15) = -2.212$, $p = .043$, whereas the nonparametric test was not, $z = -1.541$, $p = .123$ and therefore will not be interpreted. On the CPT X task β (error response bias), both groups demonstrated more omission errors (as indicated by a negative number); however, individuals with FAS

FIGURE 10.5 FAS PAIRED ANALYSES FOR MIRSKY'S 'FOCUS' COMPONENT OF ATTENTION



had significantly less omission errors relative to total errors (mean score = -.04) than the CA and IQ matched Control group (mean score = -.40), $t(15) = 2.309$, $p = .036$ ($z = -2.244$, $p = .025$).

On the CPT AX task, which requires inhibition of response to the X stimuli unless preceded by an A, the FAS group had an average of 5.56 percent commission errors, whereas the CA and IQ matched Control group had 3.35 percent commission errors. The parametric statistic was not significant, $t(16) = .977$, $p = .343$, whereas the nonparametric statistic approached significance, $z = -1.178$, $p = .074$. On the measure of error response bias (β) for the AX task, both groups demonstrated more omission errors (as indicated by a negative number); however, individuals with FAS had significantly less omission errors relative to total errors (mean score = -.19) than the CA and IQ matched Control group (mean score -.21), $t(16) = 2.759$, $p = .014$ ($z = -2.249$, $p = .025$).

On the CPT Tones task, the FAS group had a higher percentage of commission errors (mean score = 7.65) than the CA and IQ matched Control group (mean score = 4.77). The parametric statistic for percent commission errors was not significant, $t(16) = .986$, $p = .341$, whereas the nonparametric statistic approached significance, $z = -1.791$, $p = .073$. Figure 10.6a through 10.6c displays the pattern of results between the two groups across the CPT X, AX, DX, and Tones tasks used to assess Mirsky's 'sustain' component of attention.

'Shift' Attention: The FAS group achieved an average of 3.47 categories (sets) on the WCST, whereas the CA and IQ matched Control group achieved an average of 2.05 categories and both the parametric and the nonparametric tests approached

FIGURE 10.6a FAS PAIRED ANALYSES FOR MIRSKY'S ' SUSTAIN' COMPONENT OF ATTENTION

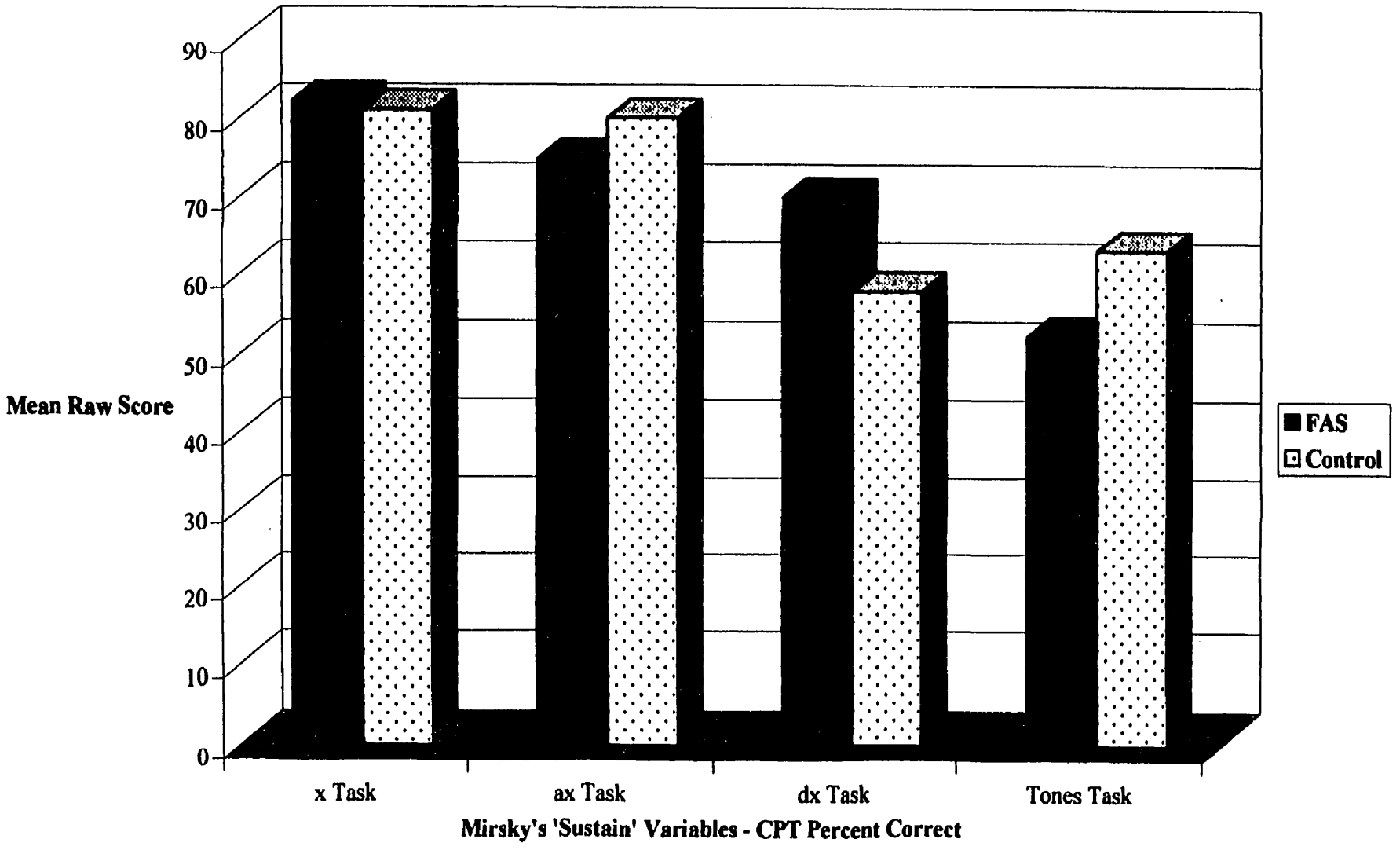


FIGURE 10.6b FAS PAIRED ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION

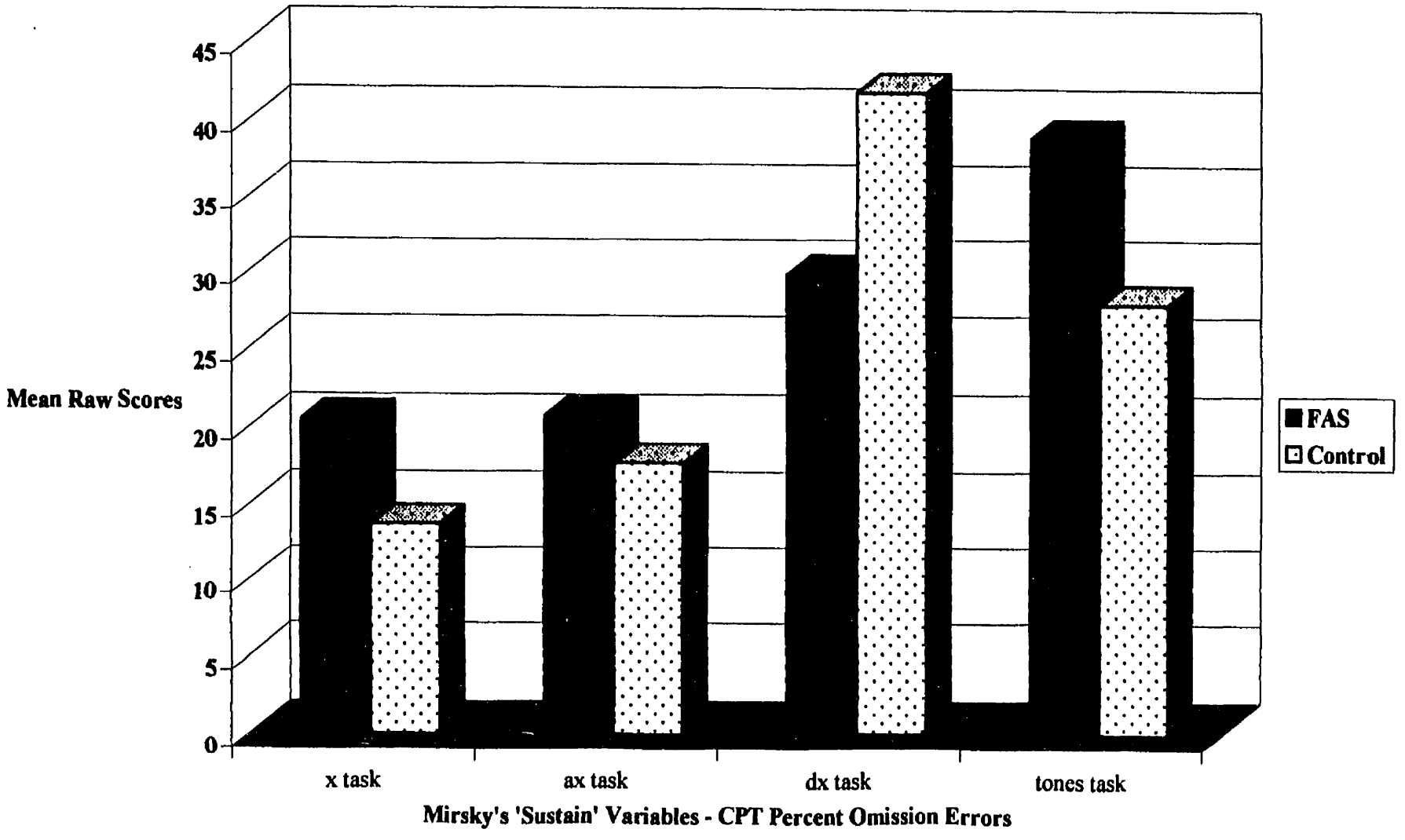
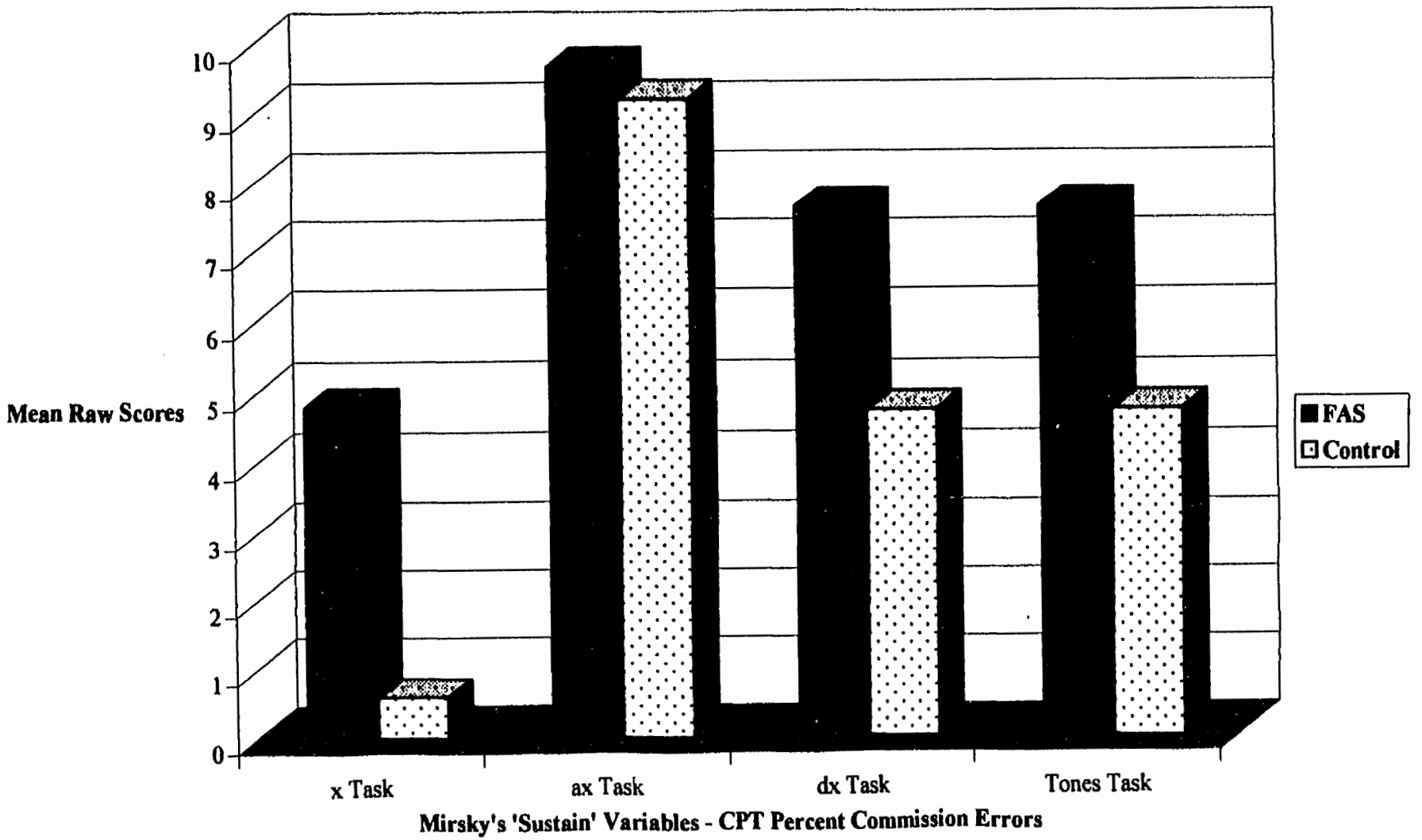


FIGURE 10.6c FAS PAIRED ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION



significance, $t(16) = 1.888$, $p = .077$ ($z = -1.740$, $p = .082$). The FAS gave a higher percentage of correct responses (mean score = 59.14) than the CA and IQ matched Control group (mean score = 46.68), $t(16) = 2.710$, $p = .015$ ($z = -2.533$, $p = .011$). The FAS group also had significantly less perseverative errors (mean score = 22.00) than the CA and IQ matched Control group (mean score = 31.35), $t(16) = -2.839$, $p = .012$ ($z = -2.438$, $p = .015$). Figure 10.7 displays the pattern of results between the two groups across the variables used to assess the 'shift' component of attention.

'Encode' Attention: On the WAIS-R Arithmetic subscale, the CA and IQ matched Control group outperformed the FAS group. The mean score for the CA and IQ matched Control group was 4.88 and for the FAS group was 4.00, $t(16) = -2.252$, $p = .039$ ($z = -2.025$, $p = .043$). On the WAIS-R Digit Span variable, the CA and IQ matched Control group scored higher than the FAS group (mean score = 8.35 versus 6.64); however, the parametric statistic was not significant and the nonparametric statistic only approached significance, $z = -1.666$, $p = .096$. Similarly, on WRAT-3 Arithmetic the CA and IQ matched Control group outperformed the FAS group, with a mean score of 25.70 versus 21.11. Both the parametric and nonparametric statistics approached significance, $t(16) = -1.908$, $p = .075$ ($z = -1.682$), $p = .093$). Figure 10.8 depicts the pattern of scores for the two groups across the 'encode' variables of attention.

Ability to Learn (Memory): On the RAVLT Learning Index the FAS group demonstrated a flatter learning curve across the five trials than did the CA and IQ matched Control group. The mean score for the FAS group was 4.41 and for the CA and IQ matched Control group was 6.00. The difference between groups approached

FIGURE 10.7 FAS PAIRED ANALYSES FOR MIRSKY'S 'SHIFT' COMPONENT OF ATTENTION

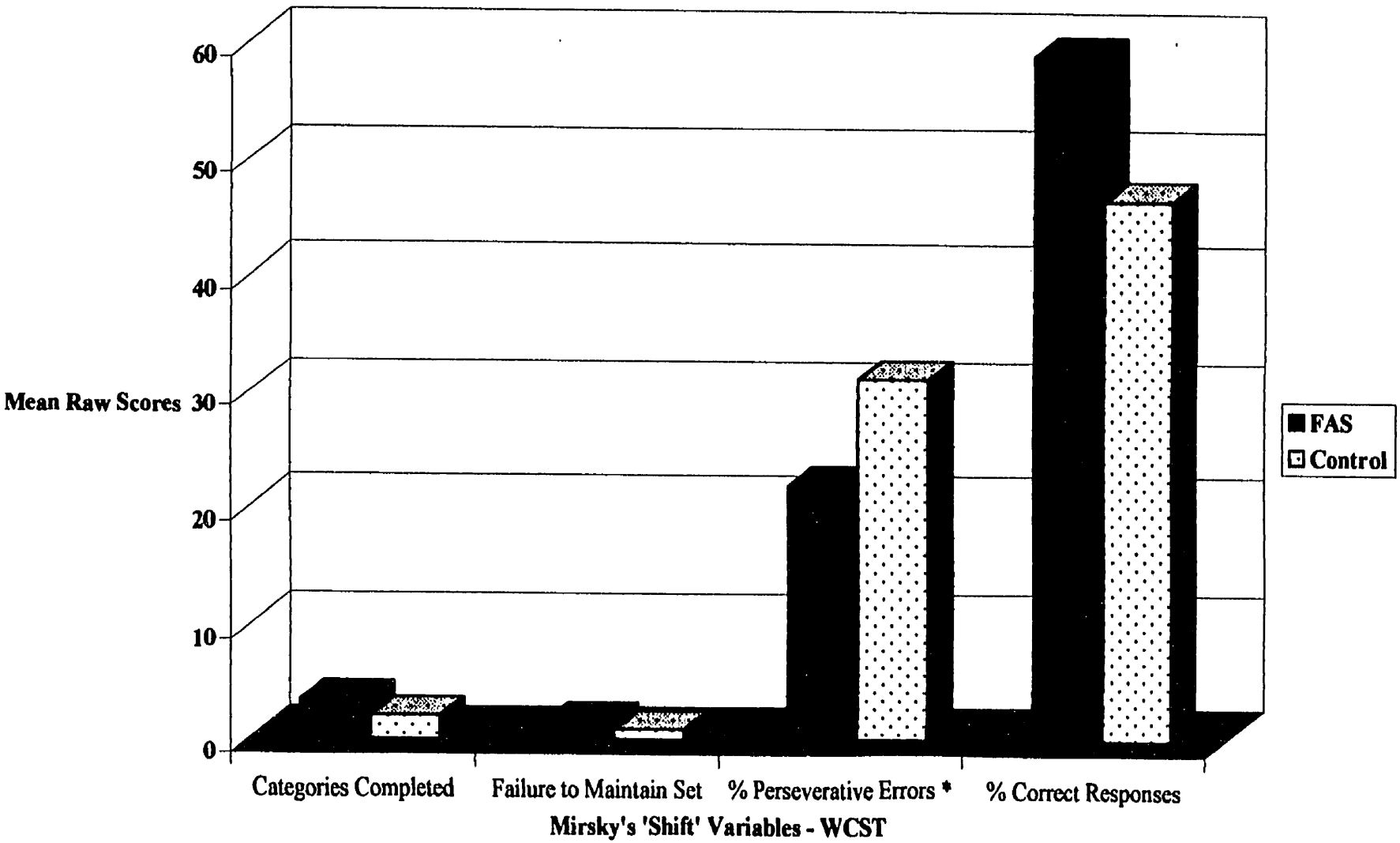
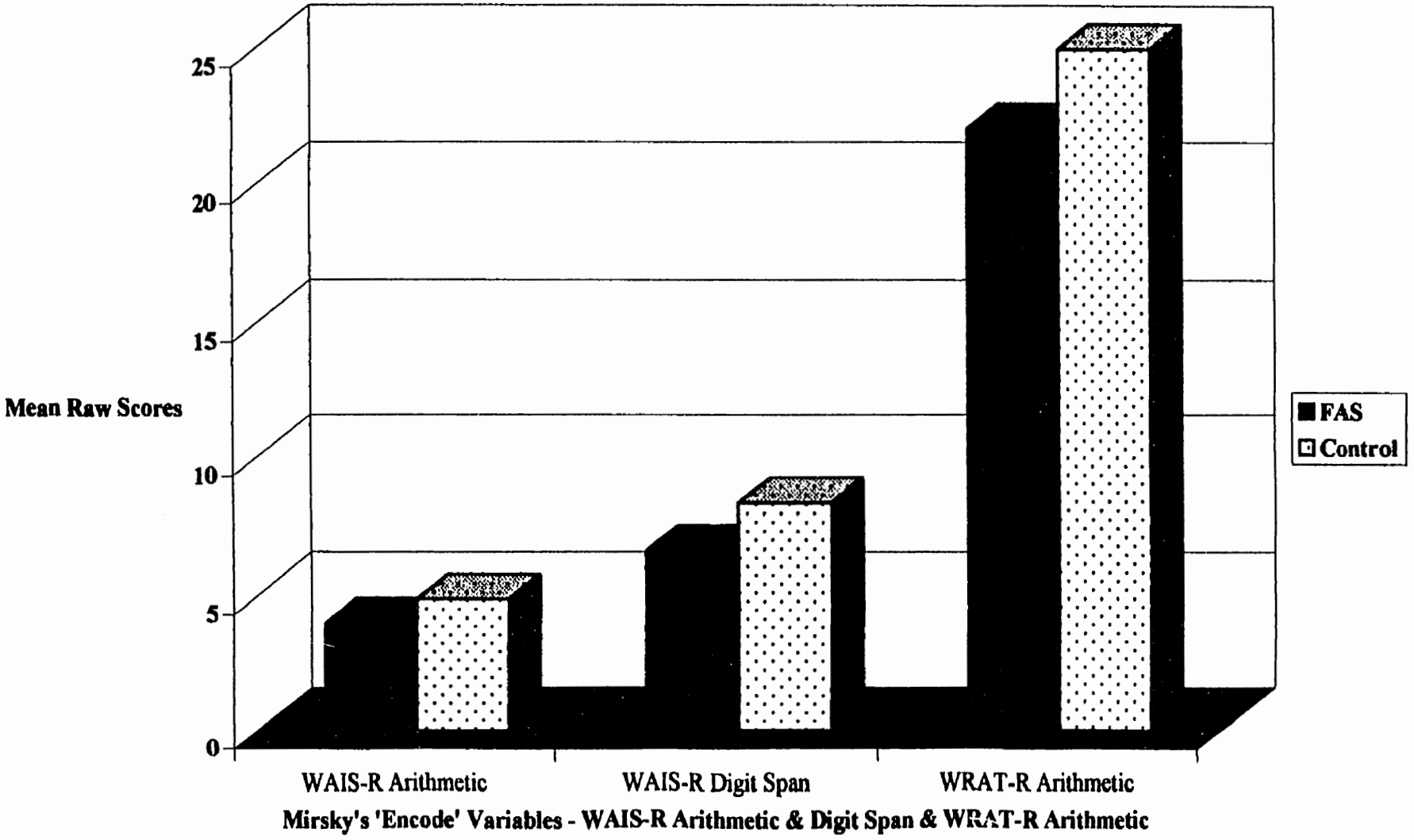


FIGURE 10.8 FAS PAIRED ANALYSES FOR MIRSKY'S 'ENCODE' COMPONENT OF ATTENTION



significance, $t(16) = -2.057$, $p = .056$ ($z = -1.909$, $p = .056$). The FAS group also demonstrated significantly more intrusion errors across all trials than the CA and IQ matched Control group. On average the FAS group made 14.52 intrusion errors, whereas the CA and IQ matched Control group made 5.05, $t(16) = 2.590$, $p = .020$ ($z = -2.528$, $p = .011$). Both the parametric and the nonparametric tests of Proactive Interference approached significance with the FAS group demonstrating more proactive interference than the CA and IQ matched Control group, $t(16) = -1.707$, $p = .10$ ($z = -1.664$, $p = .096$).

Verbal Memory (immediate): On trial six of the RAVLT (immediate recall) the FAS group recalled significantly fewer words than the CA and IQ matched Control group. The FAS group recalled an average of 6.70 words, whereas the CA and IQ matched Control group recalled 9.41 words, $t(16) = -2.718$, $p = .015$ ($z = -2.287$, $p = .022$).

Delayed Recall Memory (verbal): On the WMS-R Logical Memory II the groups differed significantly with the FAS group recalling less material following a period of delay than the CA and IQ matched Control group. The mean score for the FAS group was 9.58 and for the CA and IQ matched Control group was 14.70, $t(16) = -2.466$, $p = .025$ ($z = -2.199$, $p = .028$). On trial seven of the RAVLT (Delayed Recall), the CA and IQ matched Control group again outperformed the FAS group, recalling significantly more words after a period of delay. The mean score for the CA and IQ matched Control group was 8.94 and for the FAS group was 5.82, $t(16) = -3.253$, $p = .005$ ($z = -2.629$, $p = .009$). On the WMS-R Verbal Paired Associates II the FAS group recalled significantly less word pairs than their CA and IQ matched Control

group. The mean score for the FAS group was 5.95 and for the CA and IQ matched Control group was 7.00, $t(16) = -3.816$, $p = .002$ ($z = -2.835$, $p = .005$).

Recognition (Memory): There were no significant differences between the groups on the RAVLT recognition variables.

To get a more accurate picture of both immediate and delayed recall performance on the RAVLT, loss of information was considered by comparing the groups on the proportion of information recalled relative to the amount learned by the end of trial 5 (see Figure 10.9). When asked to recall the list of words they had learned over five trials, immediately following the presentation of a distractor trial (Percent Recall (A6/A5)), individuals with FAS lost significantly more information than the CA and IQ matched Control group. Whereas the CA and IQ matched Control group recalled 96.73 percent of the words they had learned by trial 5, the FAS group only recalled 74.40 percent of what they had learned, $t(16) = -2.376$, $p=.030$ ($z = -2.215$, $p = .027$) indicating that the individuals in the FAS group were more subject to retroactive interference. There were no significant differences between groups on the Forgetting Index (A7/A6), indicating that the FAS group did not differ from the CA and IQ matched Control group in their ability to retain what they recalled on the immediate recall trial following a period of delay. Figure 10.10 graphically displays the pattern of responding by the two groups across the RAVLT. The FAS group learned less words between list 1 and list 5 (depicted by the Learning Index variable), recalled less on both immediate and delayed trials than the CA and IQ matched Control group, and had significantly more intrusions; however, their recognition scores did not differ.

FIGURE 10.9 RECALL PERFORMANCE

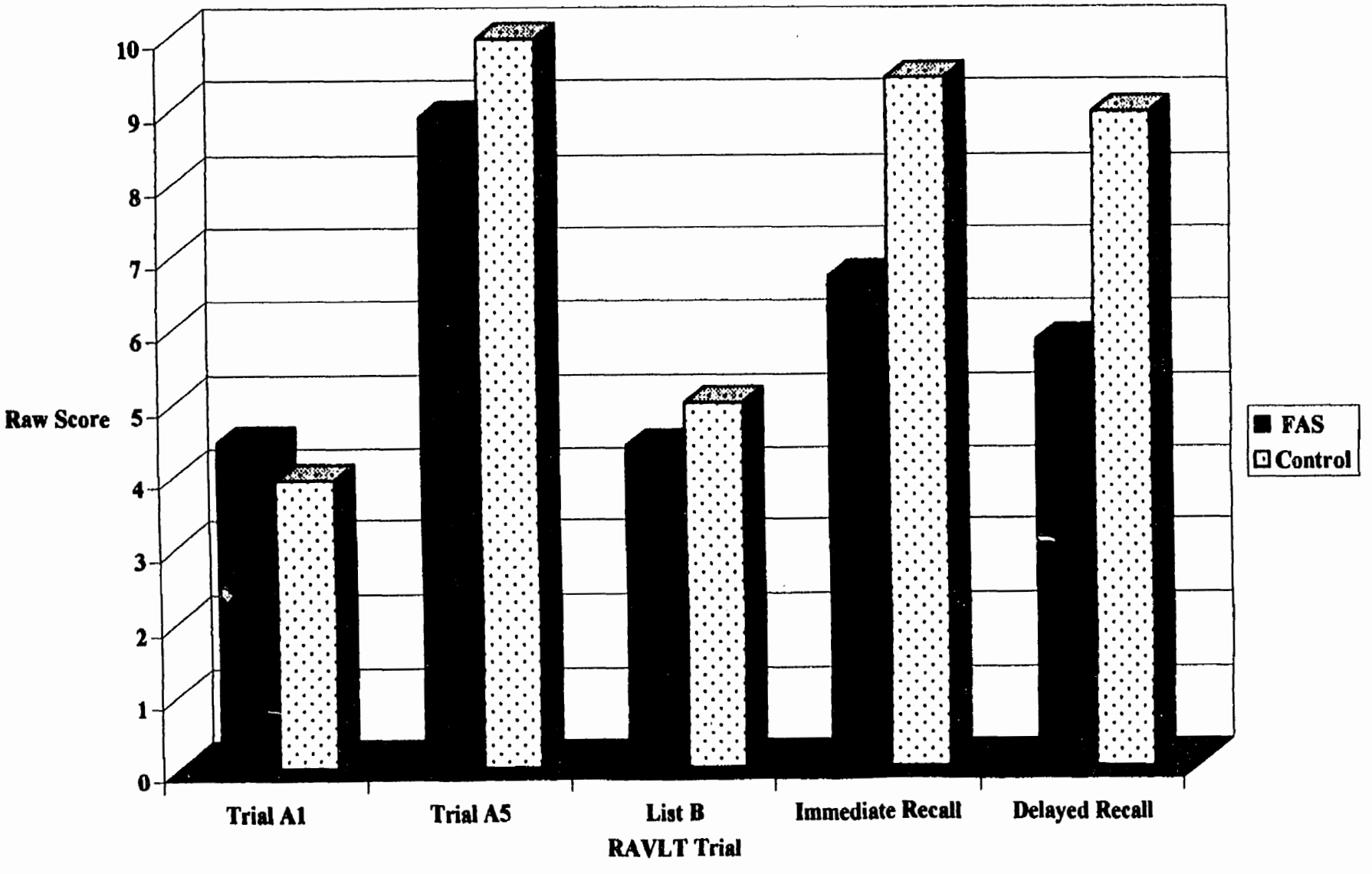
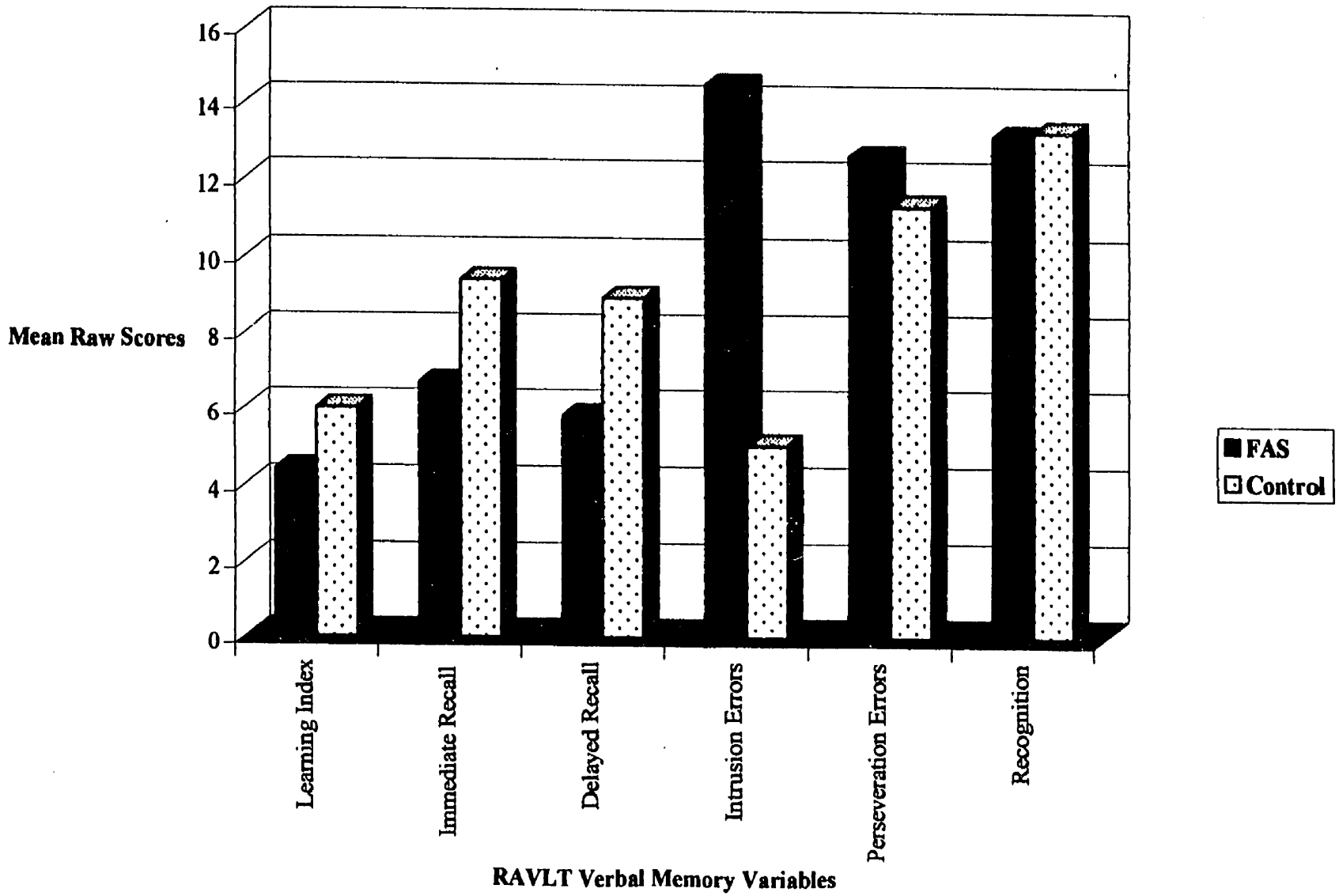


FIGURE 10.10 FAS PAIRED ANALYSES FOR RAVLT VERBAL MEMORY VARIABLES



Similarly, an examination of both the WMS-R Logical memory and Verbal Paired Associates variables revealed a pattern of decreased immediate and delayed recall for the FAS group compared to the CA and IQ matched Control group; however, only the delayed memory scores were significantly different between the two groups (see Figure 10.11). The mean score for Logical Memory II (delayed recall) was 9.58 for the FAS group and 14.70 for the CA and IQ matched Controls, $\underline{t}(16) = -2.466$, $p = .025$ ($\underline{z} = -2.199$, $p = .028$). The mean score for Verbal Paired Associates (delayed recall) was 5.95 for the FAS group and 7.00 for the CA and IQ matched Control group, $\underline{t}(16) = -3.816$, $p = .002$ ($\underline{z} = -2.835$, $p = .005$).

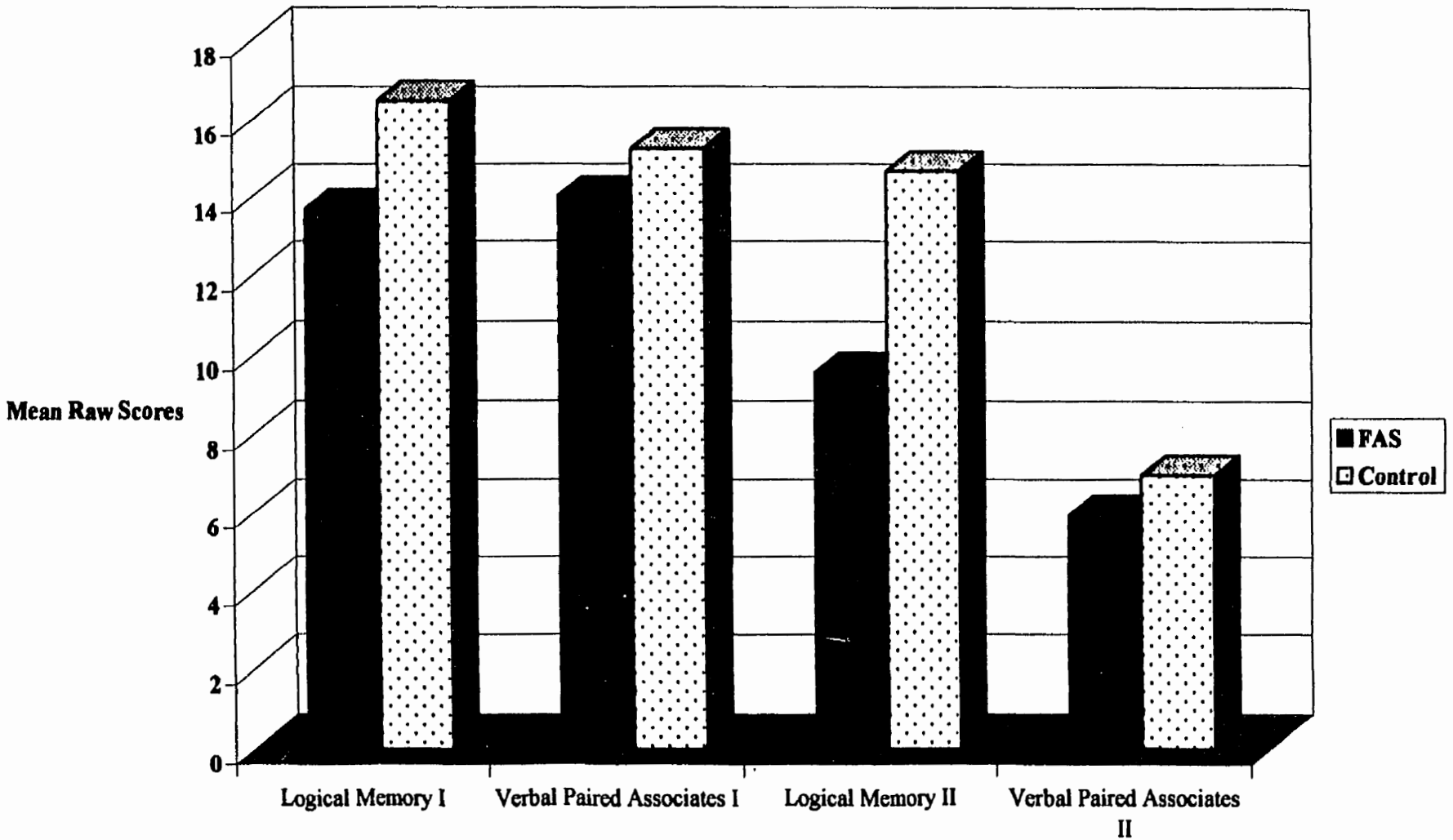
Visual Memory (immediate and delayed): There were no differences between the FAS group and the CA and IQ matched Control group on any of the variables taken from the WMS-R and the Rey Complex Figure to assess visual memory (see Figure 10.12).

10.5.2 MPKUS Group and CA and IQ matched Control Group

'Focus' Attention: There were no significant differences between the MPKUS group and the CA and IQ matched Control group on any of the variables assessing the 'focus' components of attention.

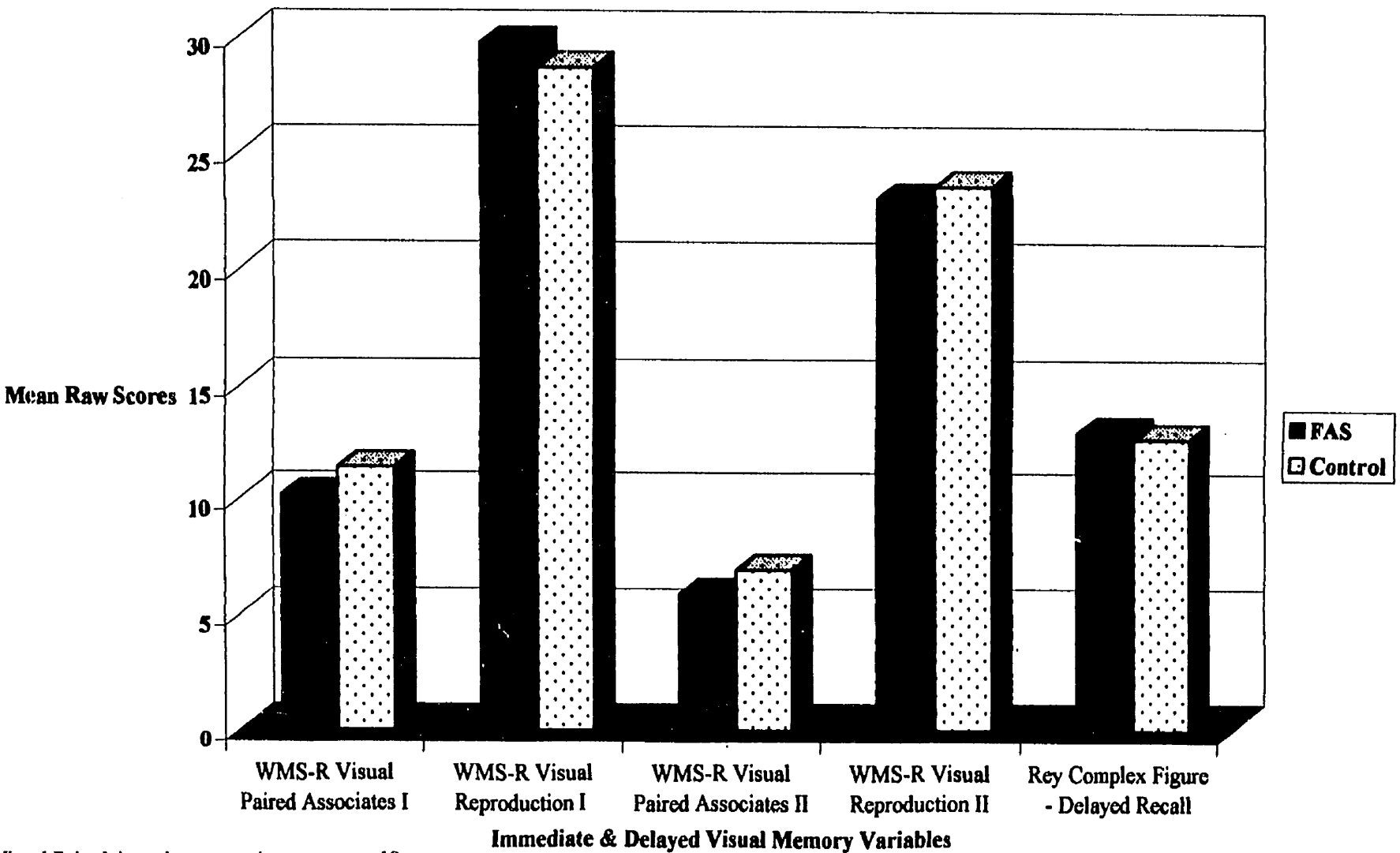
'Sustain' Attention: On the Percent Correct Responses on the CPT Tones task the Control group outperformed the MPKUS group with a mean score of 54.29 versus 36.11. The parametric statistic was not significant, $\underline{t}(10) = -1.484$, $p = .169$, whereas the nonparametric statistic was significant, $\underline{z} = -1.956$, $p = .050$. On the Tones task Percent Omission Errors the MPKUS group demonstrated more omission errors (mean

FIGURE 10.11 FAS PAIRED ANALYSES FOR WMS-R VERBAL MEMORY VARIABLES



Logical Memory - maximum score = 50
Verbal Paired Associates - maximum score = 24

FIGURE 10.12 FAS PAIRED ANALYSES FOR VISUAL MEMORY VARIABLES



Visual Paired Associates - maximum score = 18
Visual Reproduction - maximum score = 41
Rey Complex Figure - maximum score = 36

score = 60.19) than the CA and IQ matched Controls (35.74). The parametric statistic approached significance, t(10) = 1.834, p = .097, and the nonparametric statistic was significant, z = -2.045, p = .041. On the CPT Tones Discriminability task (d'), the MPKUS group had significantly more difficulty discriminating between critical and non-critical stimuli relative to the total number of critical stimuli (mean score = 136.73) than the CA and IQ matched Control group (mean score = 109.45), t(10)= 2.974, p =.014 (z = -2.223, p = .026).

'Shift' Attention: The groups differed significantly on the WCST Failure to Maintain Set score with the CA and IQ matched Control group failing to maintain set more frequently than the MPKUS group. The mean score for the CA and IQ matched Control group

was 2.20 and for the MPKUS group was .50, t(9) = -3.042, p = .014 (z = -2.384, p = .017.

'Encode' Attention: There were no significant differences between the MPKUS and their matched IQ Controls on any of the variables assessing the 'encode' components of attention.

Figures 10.13 to 10.16 depict the pattern of scores across the two groups for the variables used to assess the Mirsky's four components of attention.

Ability to Learn: No differences were found in terms of the groups' ability to learn new material as assessed by the RAVLT.

Verbal Memory (immediate and delayed): There were no significant differences between the MPKUS group and the CA and IQ matched Control group on the variables

score = 60.19) than the CA and IQ matched Controls (35.74). The parametric statistic approached significance, t(10) = 1.834, p = .097, and the nonparametric statistic was significant, z = -2.045, p = .041. On the CPT Tones Discriminability task (d'), the MPKUS group had significantly more difficulty discriminating between critical and non-critical stimuli relative to the total number of critical stimuli (mean score = 136.73) than the CA and IQ matched Control group (mean score = 109.45), t(10)= 2.974, p =.014 (z = -2.223, p = .026).

'Shift' Attention: The groups differed significantly on the WCST Failure to Maintain Set score with the CA and IQ matched Control group failing to maintain set more frequently than the MPKUS group. The mean score for the CA and IQ matched Control group

was 2.20 and for the MPKUS group was .50, t(9) = -3.042, p = .014 (z = -2.384, p = .017.

'Encode' Attention: There were no significant differences between the MPKUS and their matched IQ Controls on any of the variables assessing the 'encode' components of attention.

Figures 10.13 to 10.16 depict the pattern of scores across the two groups for the variables used to assess the Mirsky's four components of attention.

Ability to Learn: No differences were found in terms of the groups' ability to learn new material as assessed by the RAVLT.

Verbal Memory (immediate and delayed): There were no significant differences between the MPKUS group and the CA and IQ matched Control group on the variables

FIGURE 10.13 MPKUS PAIRED ANALYSES FOR MIRSKY'S 'FOCUS' COMPONENT OF ATTENTION

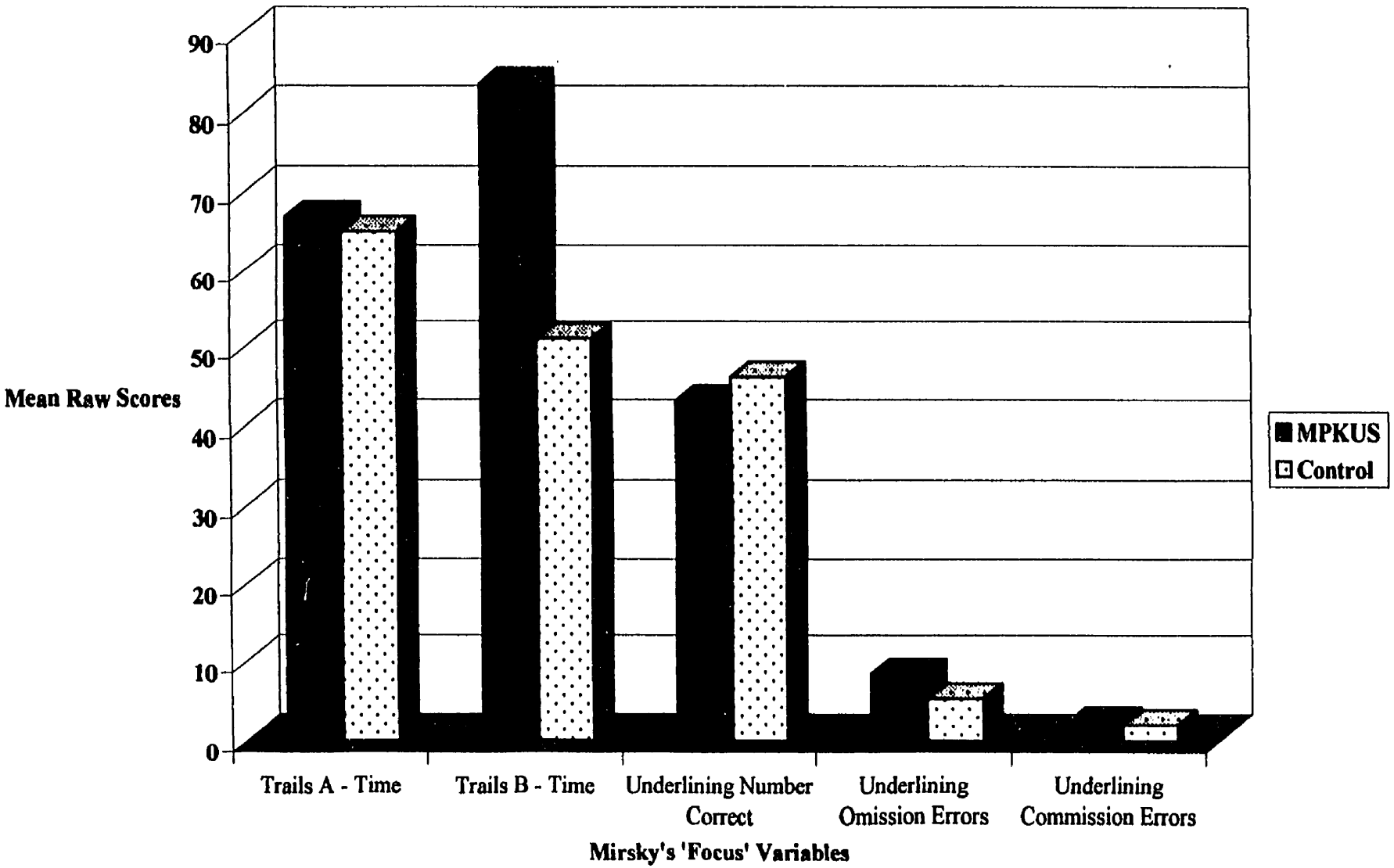


FIGURE 10.14a MPKUS PAIRED ANALYSES FOR MIRSKY'S ' SUSTAIN' COMPONENT OF ATTENTION

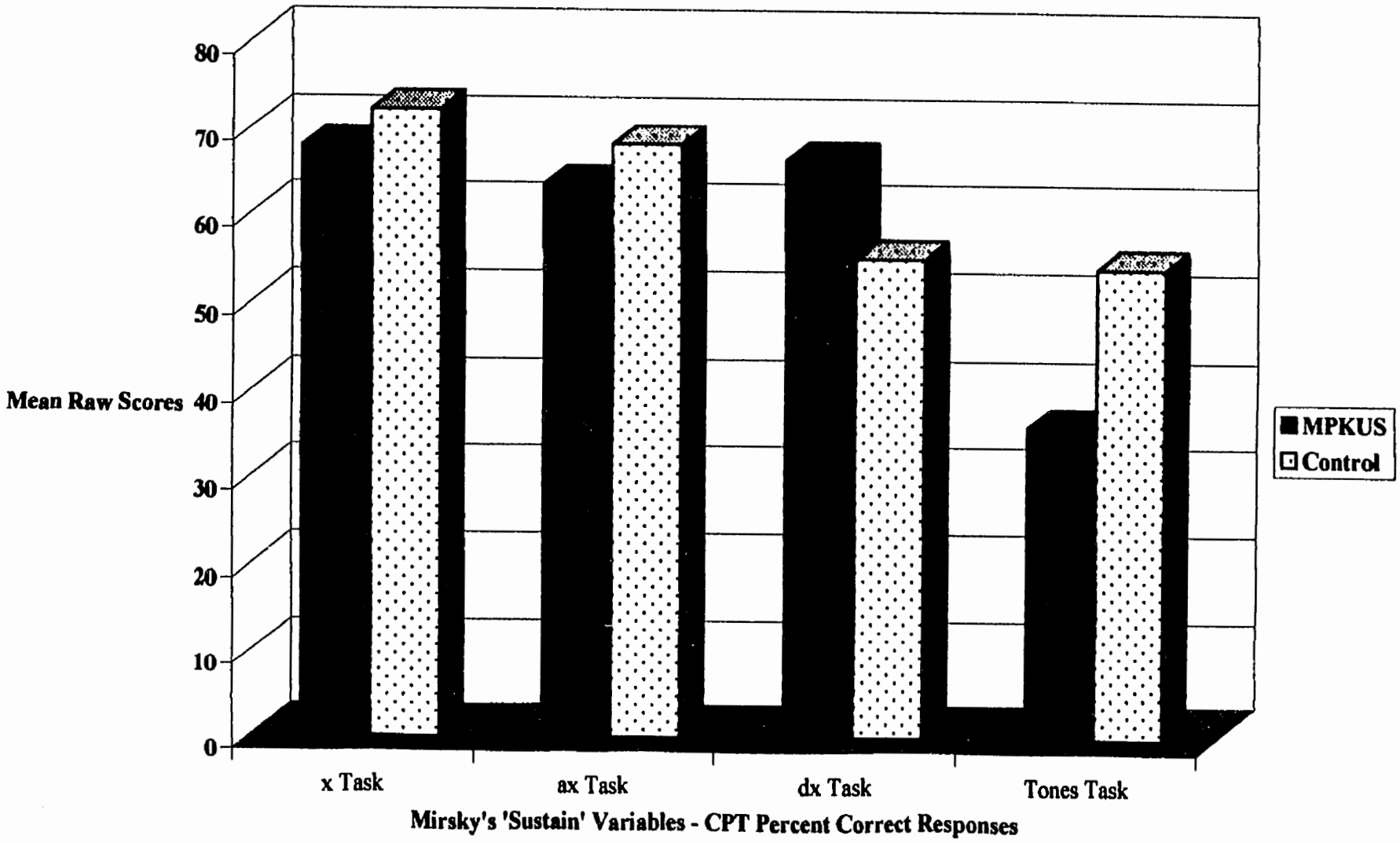


FIGURE 10.14b MPKUS PAIRED ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION

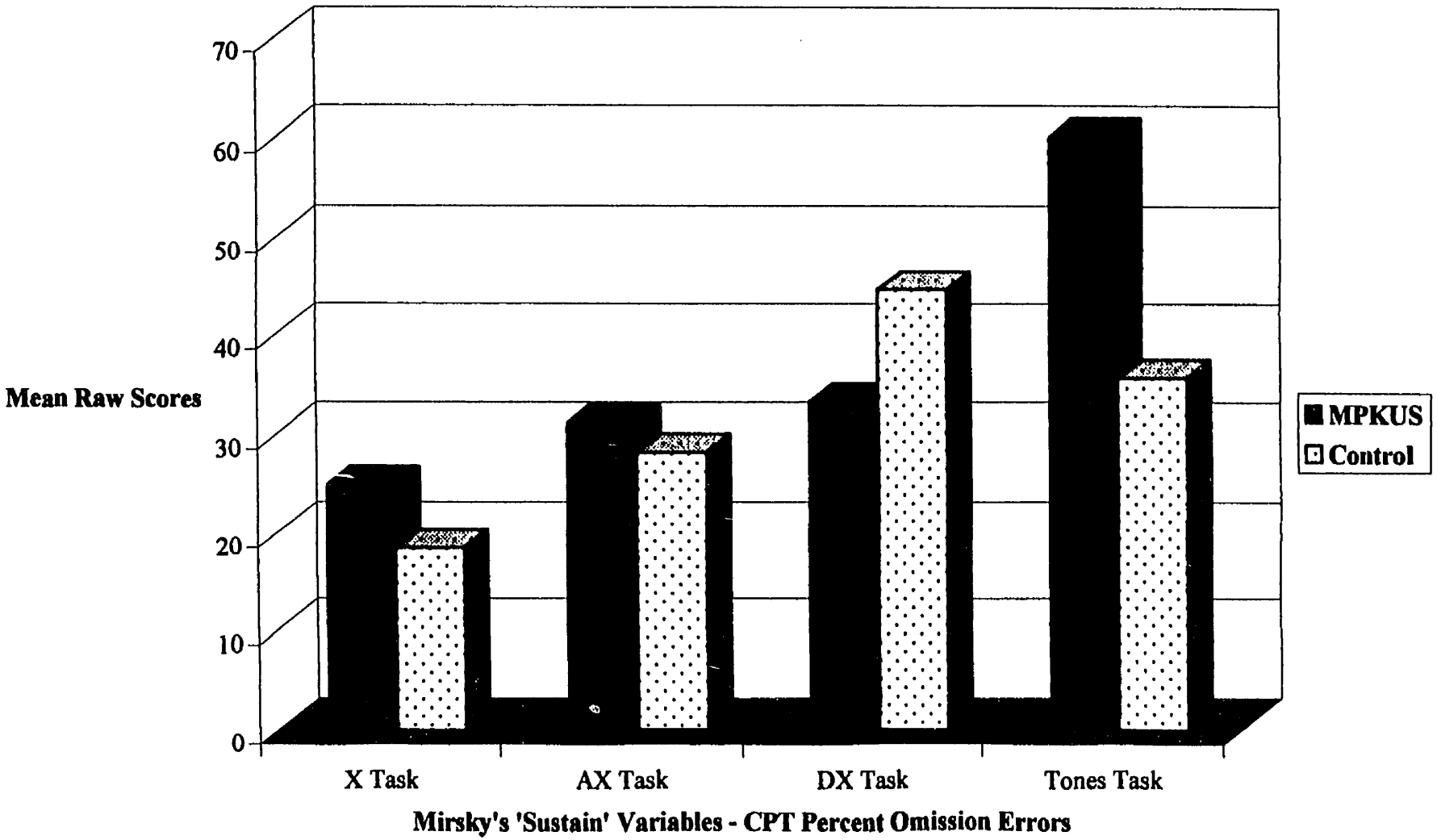


FIGURE 10.14c MPKUS PAIRED ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION

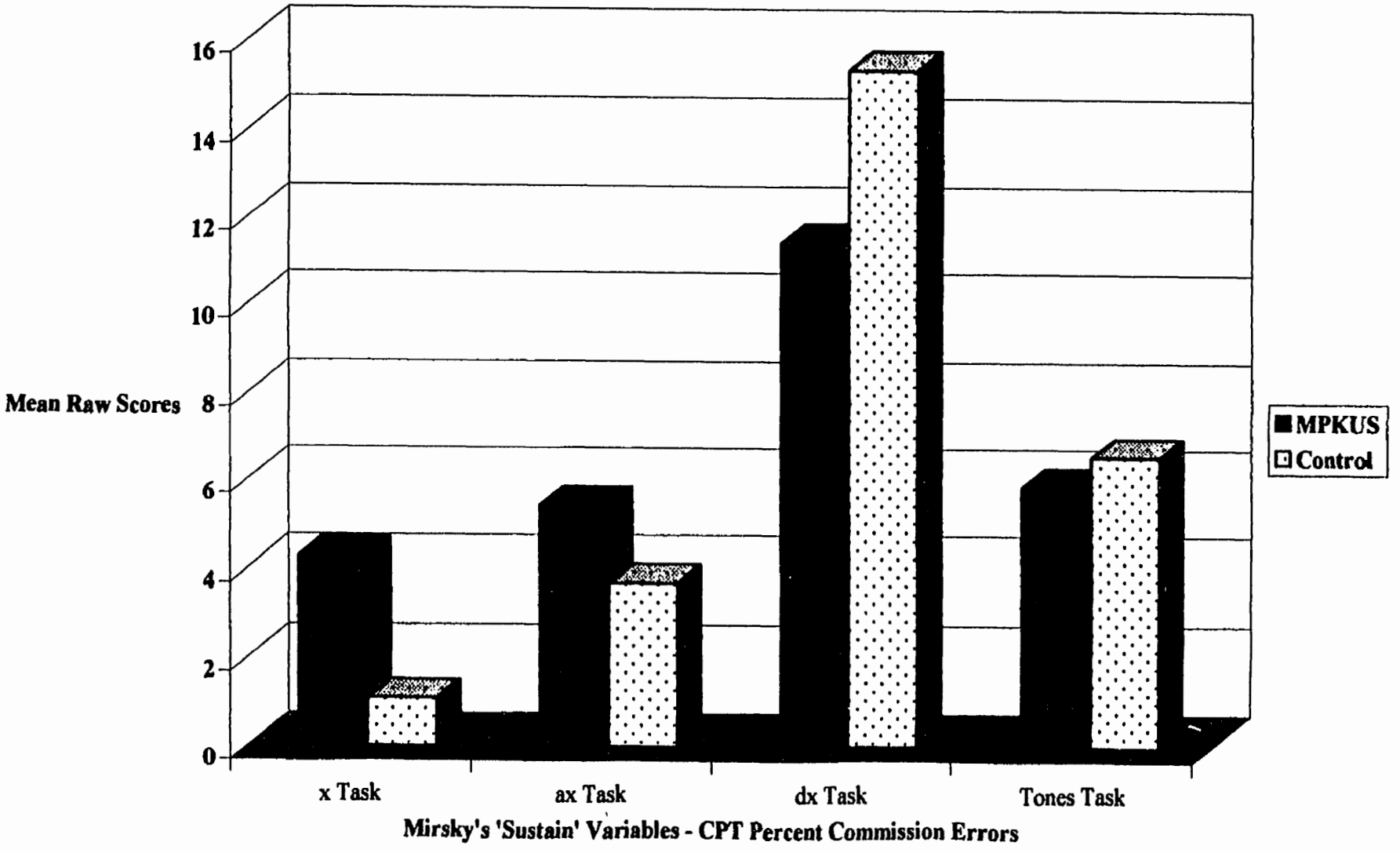


FIGURE 10.15 MPKUS PAIRED ANALYSES FOR MIRSKY'S 'SHIFT' COMPONENT OF ATTENTION

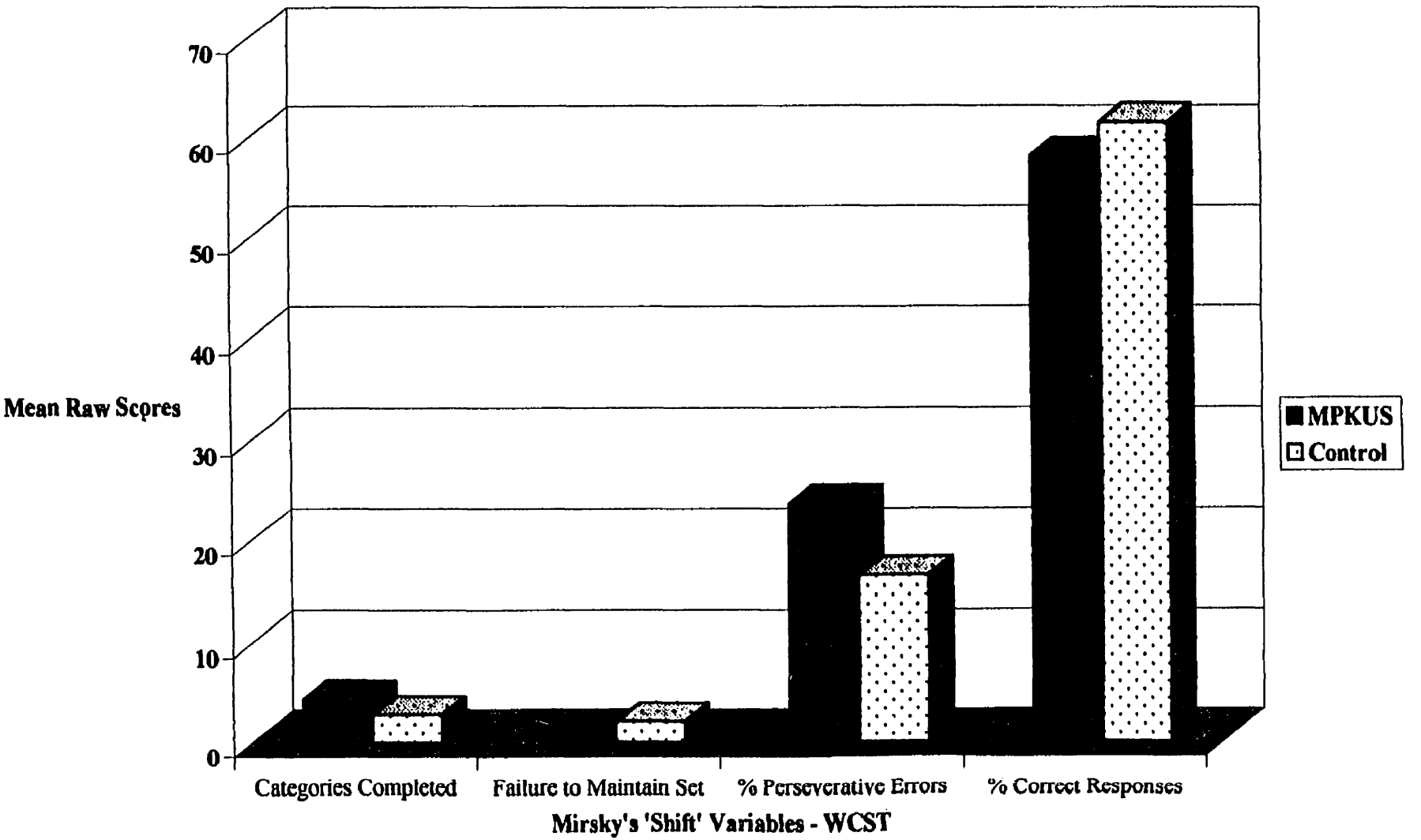
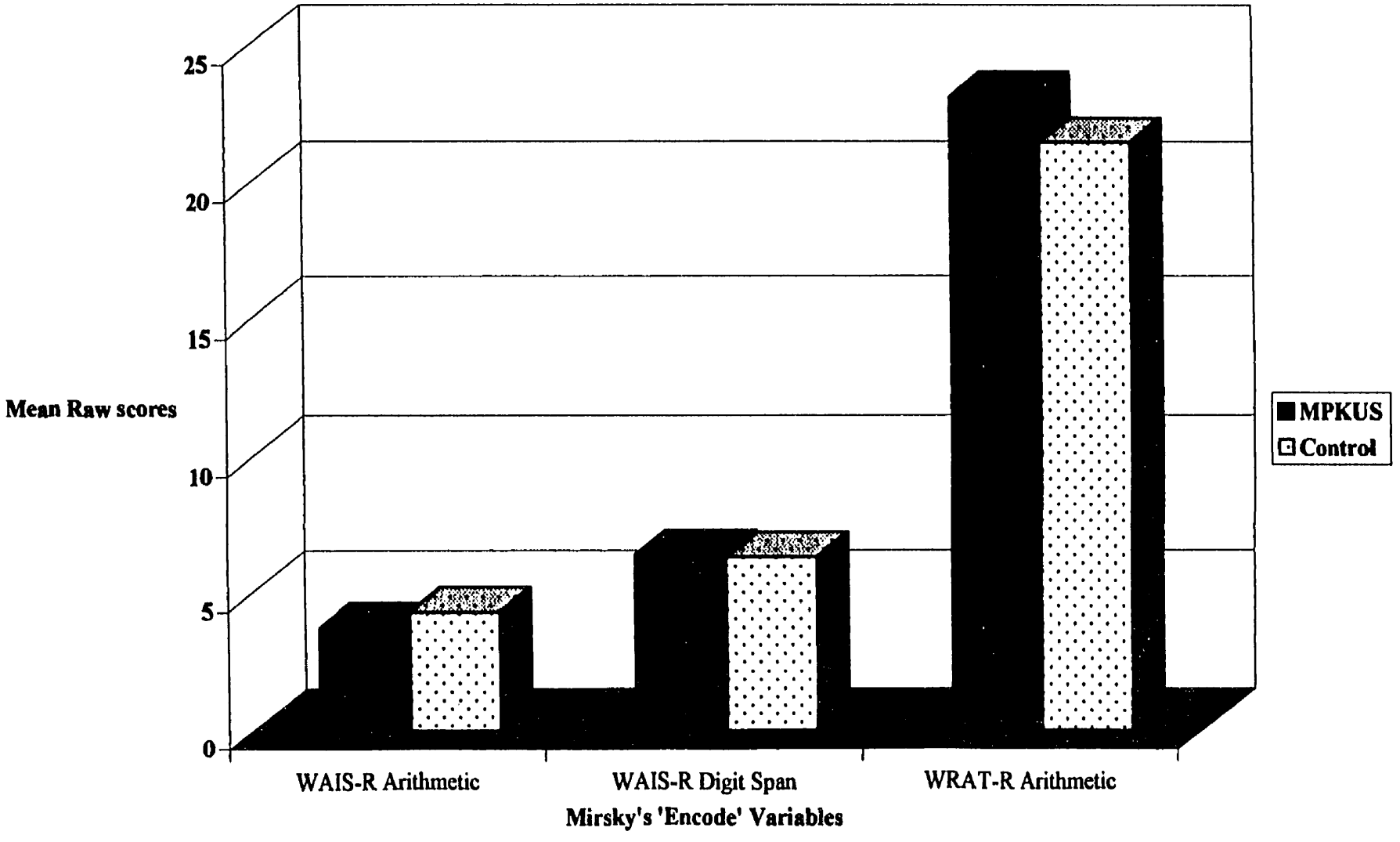


FIGURE 10.16 MPKUS PAIRED ANALYSES FOR MIRSKY'S 'ENCODE' COMPONENT OF ATTENTION



taken from the WMS-R and the RAVLT to assess verbal memory and delayed recall (see Figures 10.17 and 10.18).

Recognition Memory: On the RAVLT Recognition task, the MPKUS group scored significantly lower than the CA and IQ matched Control Group. The mean score for the MPKUS group was 12.27 and for the CA and IQ matched Control group was 14.27. Both the parametric and the nonparametric tests were significant, $t(10) = -2.507$, $p = .031$ ($z = -2.084$, $p = .037$).

Visual Memory (immediate and delayed): There were no differences between the MPKUS group and the CA and IQ matched Control group on the variables taken from the WMS-R and the Rey Complex Figure to assess visual memory (see Figure 10.19).

10.6 Randomized Block Results

The significant results from the randomized block analyses are presented in Tables 10.15 and 10.16. A complete listing of the significant and non-significant results are tabled in Appendix M. Table 10.15 shows both the parametric (F) and nonparametric group (χ^2) comparisons. When both F and χ^2 statistics were significant, the F value was interpreted because it is the stronger test. If only the F statistic was significant and the derivational assumptions were violated, then it was not interpreted. When only χ^2 was significant, it was interpreted. Because the groups were intentionally matched within blocks on IQ, it was expected that the F statistic for blocks would be significant and thus was not interpreted.

As outlined previously, the groups were compared on a number of variables designed to assess various components of attention and memory (see Table 10.8). The randomized block design results are discussed within the framework of these

FIGURE 10.17 MPKUS PAIRED ANALYSES FOR RAVLT VERBAL MEMORY VARIABLES

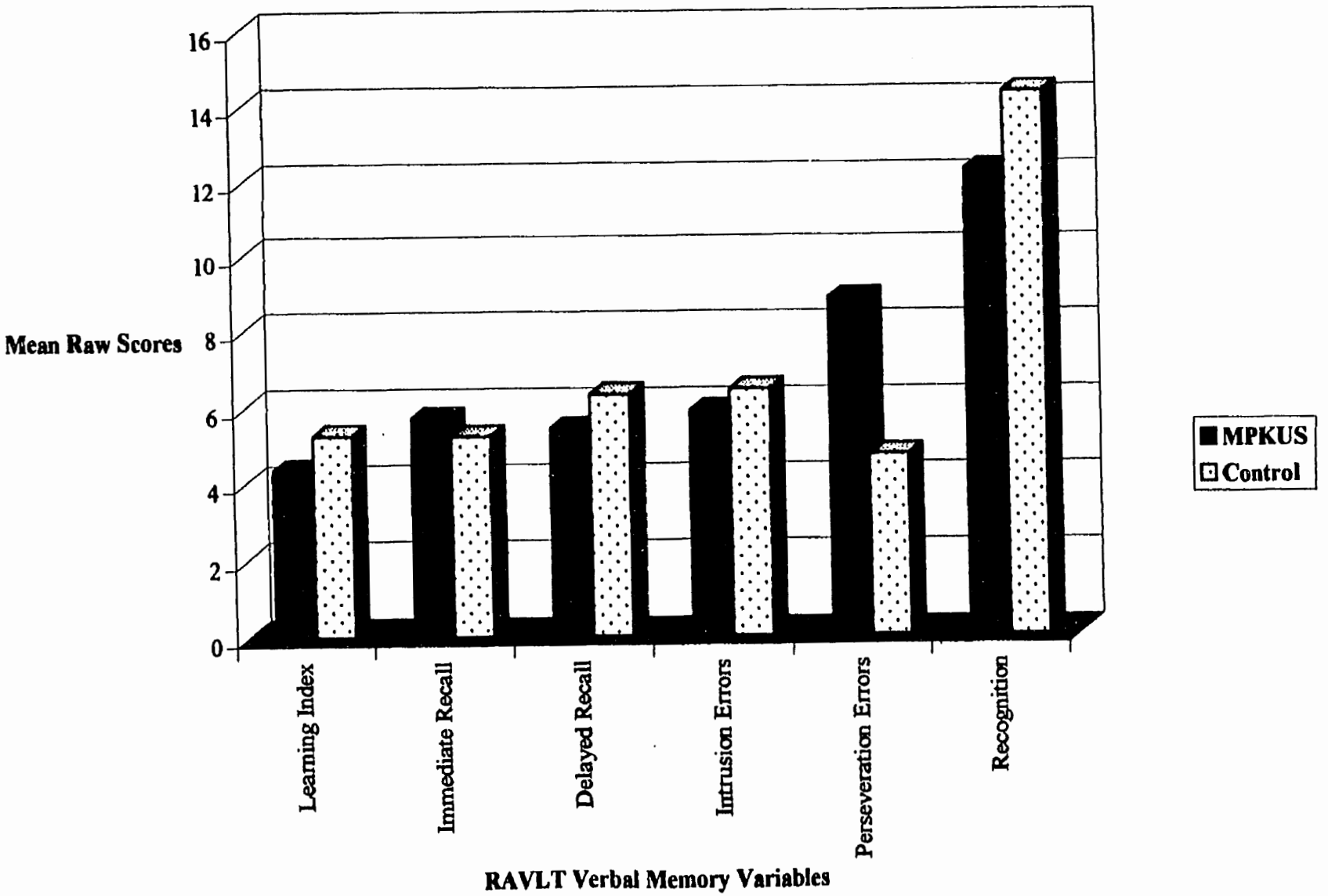
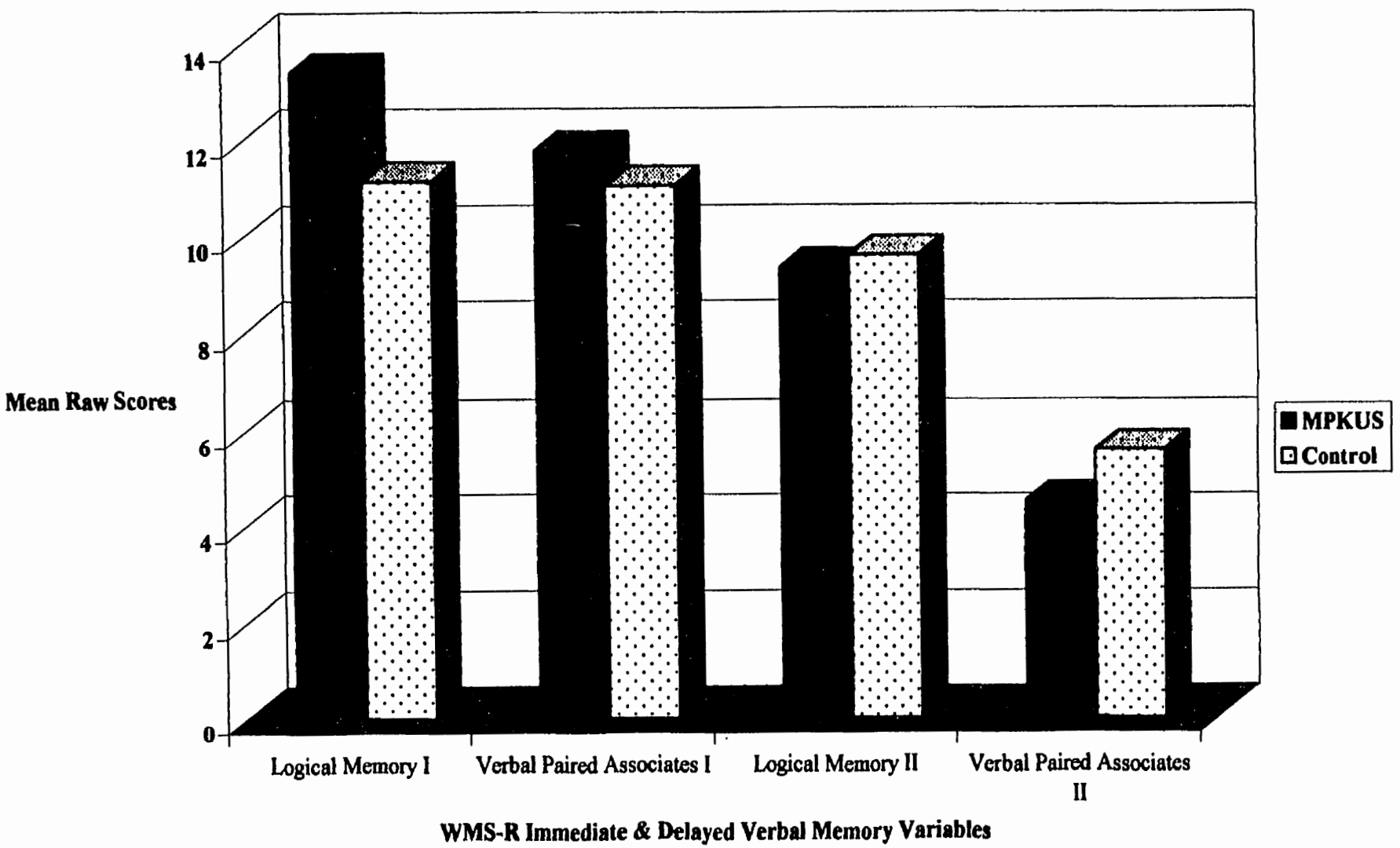
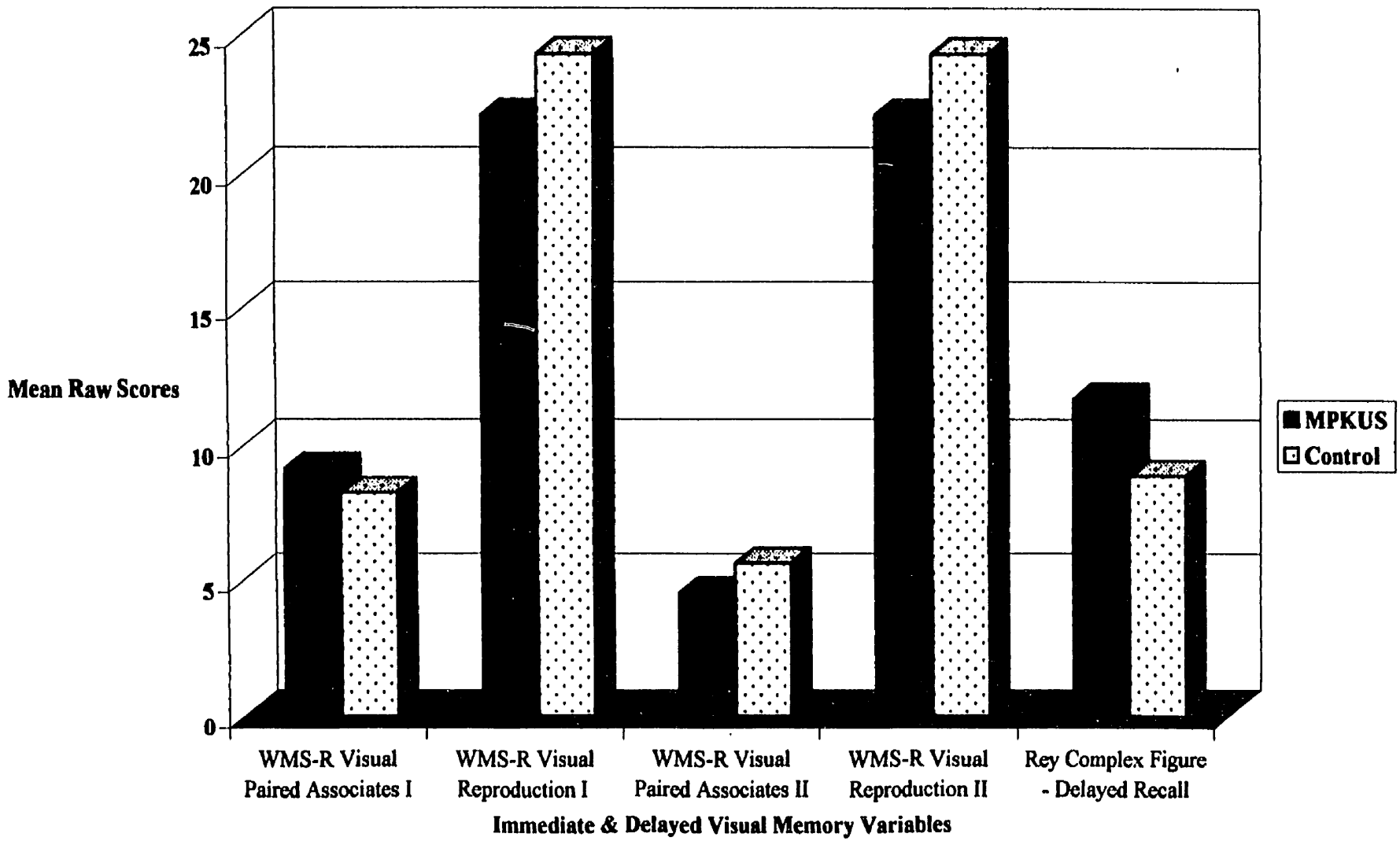


FIGURE 10.18 MPKUS PAIRED ANALYSES FOR WMS-R VERBAL MEMORY VARIABLES



Logical Memory - maximum score = 50
Verbal Paired Associates - maximum score = 24

FIGURE 10.19 MPKUS PAIRED ANALYSES FOR VISUAL MEMORY VARIABLES



Visual Paired Associates - maximum score = 18
Visual Reproduction - maximum score = 41
Rey Complex Figure - maximum score = 36

Table 10.15 Parametric and Nonparametric Comparisons between Groups on Attention Tasks.

Test & Subscale	FAS	MPKUS	Control	F	χ^2	SNK
Underlining Test 10 & 8 Blocks						
Mean # Hits	43.25 (8.59)	41.46 (10.63)	46.13 (4.77)	1.876 (.182)	4.051 (.132)	
	40.58 (5.44)	46.18 (5.62)	50.18 (.89)	8.072 (.005)	10.750 (.005)	1=2≠3
Mean # Omissions	5.93 (7.31)	5.68 (5.01)	4.28 (3.17)	1.044 (.375)	6.889 (.032)	
	11.08 (5.44)	3.66 (4.04)	1.52 (.88)	11.062 (.001)	10.516 (.005)	1≠2≠3
Mean # Commissions	1.48 (1.91)	3.73 (4.34)	1.91 (2.91)	1.693 (.212)	2.811 (.245)	
	3.16 (2.48)	1.18 (.83)	.62 (.72)	5.668 (.016)	4.710 (.095)	
Trails B Time 10 Blocks	65.10 (45.66)	93.10 (50.17)	63.38 (42.01)	1.945 (.192)	6.821 (.033)	
Trails B Time 7 Blocks	49.14 (35.02)	76.28 (44.34)	45.68 (26.95)	1.881 (.195)	4.963 (.084)	
CPT - 7 Blocks						
X Task Percent Commission Errors	5.28 (10.29)	3.50 (6.94)	.714 (.90)	1.371 (.291)	6.083 (.048)	1=2≠3
AX Task β	.007 (.32)	.197 (.43)	-.385 (.55)	4.538 (.034)	4.571 (.102)	

Note. Below each of the group names is the number of observations for each comparison and the mean and standard deviations in parentheses for each dependent variable. Means with different superscripts are significantly different by SNK procedures.

Table 10.16 Parametric and Nonparametric Comparisons between Groups on Memory Tasks.

Test & Subscale	FAS_1	$MPKUS_2$	$Control_3$	F	χ^2	SNK
RAVLT						
Total # of Intrusions 10 Blocks	17.30 (18.13)	3.70 (2.98)	3.80 (3.45)	5.638 (.013)	6.000 (.050)	1≠2=3
9 Blocks	15.55 (18.32)	4.11 (2.84)	4.22 (3.38)	3.720 (.047)	4.545 (.103)	
Immediate Recall A6 10 Blocks	6.90 (3.07)	5.50 (4.28)	8.00 (4.37)	3.857 (.040)	7.538 (.023)	1=2≠3
9 Blocks	7.11 (3.17)	6.11 (3.78)	8.88 (3.29)	5.443 (.016)	8.667 (.013)	1=2≠3
Percent Recall A6/A5 – 10 Blocks	79.01 (23.74)	59.03 (28.01)	80.69 (42.50)	1.956 (.170)	4.769 (.092)	
9 Blocks	76.68 (23.94)	65.58 (19.97)	89.66 (33.58)	2.989 (.079)	4.667 (.097)	
Delayed Recall A7 10 Blocks	5.50 (3.27)	5.50 (4.53)	8.00 (3.77)	2.586 (.103)	4.514 (.105)	
9 Blocks	5.78 (3.35)	6.11 (4.34)	8.89 (2.67)	3.279 (.064)	5.688 (.058)	
Recognition 10 Blocks	13.20 (2.53)	10.90 (4.28)	13.80 (2.49)	3.200 (.065)	8.647 (.013)	1=3≠2
9 Blocks	13.56 (2.40)	12.11 (2.03)	13.67 (2.60)	2.239 (.139)	7.267 (.026)	1=3≠2
WMS-R						
Visual Reproduction I – 10 Blocks	28.50 (10.20)	24.00 (12.73)	26.80 (10.84)	3.342 (.058)	7.579 (.023)	1≠2=3
9 Blocks	30.11 (9.37)	26.00 (11.72)	28.66 (9.64)	2.311 (.131)	5.882 (.053)	1≠2=3

Note. Below each of the group names is the number of observations for each comparison and the mean and standard deviations in parentheses for each dependent variable. SNK results are presented in the far right column.

components. Significant differences between the randomized block analyses with a calculated score for missing data (to adjust for floor effects) are presented first, followed by randomized block analyses where blocks with empty cells were discarded. When both the analysis corrected for missing data and the non-corrected analysis (blocks with empty cells discarded) are significant, SNK comparisons will be made on the non-corrected analysis results.

10.6.1 Attention

'Focus' Attention: There were significant differences between groups on the variables from the Underlining Test and the Trail Making Test used to assess the 'focus' component of attention. Both the parametric and the nonparametric statistics for the Underlining Test Mean Number of Hits variable approached significance in the 10 block analysis (with corrected data for two empty cells), $\underline{F}(2,18) = 1.876$, $p = .182$ (χ^2 (2) = 4.051, p = .132), and were significant for the eight block analysis (blocks with empty cells discarded), $\underline{F}(2,16) = 8.072$, $p = .005$ (χ^2 (2) = 10.750, p = .005. SNK comparisons for the eight-block analysis indicated that the IQ matched Control group differed significantly from the two-teratogen groups making significantly more correct responses. The mean score was 50.18 for the IQ matched Control group, 40.58 for the FAS group, and 46.18 for the MPKUS group.

The parametric statistic for the 10 block analysis for the Underlining Test Mean Number of Omissions variable (corrected for two empty cells) was not significant $\underline{F}(2,18) = 1.044$, $p = .375$, whereas the nonparametric statistic was significant, χ^2 (2) = 6.889, p = .032. Both the parametric and nonparametric analyses for the eight-block analysis (blocks with empty cells discarded) were significant, $\underline{F}(2,16) = 11.062$, p =

.001 (χ^2 (2) = 10.516, p = .005. SNK comparisons for the eight-block analysis indicated that the IQ matched Control group (mean score = 1.52) differed significantly from the two-teratogen groups (mean score for FAS = 11.80 and MPKUS = 3.66) making significantly less omission errors and the MPKUS group differed significantly from the FAS group making less omission errors.

The 10-block analysis for the Underlining Test Mean Number of Commission Errors variable was not significant. The parametric statistic for the eight-block analysis (blocks with empty cells discarded) was significant, F(2,16) = 5.668, p = .016, whereas the nonparametric statistic only approached significance, χ^2(2) = 4.710, p = .095. An examination of the means revealed that the FAS group made the most commission errors (mean score = 3.16), followed by the MPKUS group (1.18), with the IQ matched Control group making the least (.62).

The nonparametric 10 block analysis (corrected for three empty cells) for the Trail Making Test Trails B Time variable was significant, χ^2 (2) = 6.821, p = .033, whereas the parametric statistic for the 10-block analysis was not, F(2,18) = 1.945, p = .192. Neither the parametric nor the nonparametric statistic for the seven block analysis (blocks with empty cells discarded) were significant (F(2,12) = 1.881, p = .195 and χ^2(2) = 4.963, p = .084), although the nonparametric statistic approached significance. An examination of the means for the seven block analysis revealed a significant difference between the MPKUS group and both the FAS and IQ matched Control groups, with the MPKUS group being slower (mean score = 76.28) in completing the task than either the FAS group (mean score = 49.14) or the IQ matched Control group (mean score = 45.68).

'Sustain' Attention: Due to computer error, there was missing data for one FAS participant on the CPT X task and for another FAS participant on the Tones task. There was also missing data for one MPKUS participant who did not complete the practice trials for any of the CPT tasks. Data points were not calculated for the missing data resulting from computer error, and due to the numerous computed variables across the CPT tasks, the decision was made to not calculate data for the MPKUS individual who was unable to complete the tasks. Thus, only a seven-block analysis was run. The nonparametric statistic for percent commission errors on the CPT X task was significant, χ^2 (2) = 6.083, p = .048, whereas the parametric statistic was not $\underline{F}(2, 14) = 1.371$, p = .291). SNK comparisons indicated that the three groups differed significantly from each other with the FAS group making the most commission errors (mean score = 5.28) followed by the MPKUS group (mean score = 3.50), with the IQ matched Control group making the least commission errors (.714).

The parametric statistic for the CPT AX β (response bias) task was significant, $\underline{F}(2,14) = 4.538$, p = .034, whereas the nonparametric only approached significance, $\chi^2(2) = 4.571$, p = .102. An examination of the means revealed that the IQ matched Control group made more omission errors relative to total number of errors (-.385), whereas the FAS and MPKUS groups both made more commission errors relative to total number of errors with the MPKUS group making the most commission errors (MPKUS mean score = .197; FAS mean score = .007).

'Shift' Attention: There were no significant differences between groups on the variables taken from the WCST to assess the 'shift' component of attention.

'Encode' Attention: There were no significant differences on any of the variables utilized to assess the 'encode' component of attention (i.e., WAIS-R Arithmetic and Digit Span; WRAT-3 Arithmetic).

10.6.2 Memory

Ability to Learn: The FAS group, MPKUS group, and IQ matched Control group did not differ in terms of their ability to learn new information as measured by the RAVLT.

Verbal Memory (immediate): Floor effects were obtained on the RAVLT for one individual with MPKUS. As discussed previously (see Table 10.10), a score was calculated to account for the missing data. There were differences among the three groups on the RAVLT Total Number of Intrusions variable. Both the parametric and nonparametric test were significant, $\underline{F}(2, 18) = 5.638$, $p = .013$ ($\chi^2(2) = 6.000$, $p = .050$) and SNK comparisons showed that the FAS group demonstrated a greater number of intrusion errors (mean score = 17.30) across all trials than the MPKUS group (mean score = 3.70) and the IQ matched Control group (mean score = 3.80). There were no significant differences between the MPKUS group and the IQ matched Control group.

A second randomized block analysis was run for the RAVLT Total Number of Intrusions variable without correction for missing data leaving nine blocks appropriate for analysis. The parametric statistic was significant, $\underline{F}(2, 16) = 3.720$, $p = .047$, whereas contrary to the previous analysis employing a correction for floor effects, the nonparametric statistic only approached significance, $\chi^2(2) = 4.545$, $p = .103$. This difference may be due to the small sample size and consequent lack of statistical power.

The groups differed significantly on the RAVLT Immediate Recall variable, $\underline{F}(2, 18) = 3.857$, $p = .040$ (χ^2 (2) = 7.538, $p = .023$) and SNK comparisons showed that the IQ matched Control group recalled more words (mean score = 8.00) than the FAS (mean scores = 6.90) or MPKUS (mean score = 5.50) groups, but that the two teratogen groups did not differ. There were nine blocks appropriate for analysis discarding the block with an empty cell. Consistent with the 10 block analysis, both the parametric and nonparametric statistic were significant, $\underline{F}(2, 16) = 5.443$, $p = .016$ (χ^2 (2) = 8.667, $p = .013$).

To more clearly understand the differences between groups, the proportion of words recalled on the immediate recall trial relative to the number of words learned on trial 5 was examined (RAVLT Percent Recall - A6/A5). Both the 10 block analysis and the nine-block analysis (block with empty cell discarded) approached significance, $\underline{F}(2, 18) = 1.956$, $p = .170$ ($\chi^2(2) = 4.769$, $p = .092$) and $\underline{F}(2, 16) = 2.989$, $p = .079$ (χ^2 (2) = 4.667, $p = .097$), and an examination of the means revealed that on immediate recall following a distractor list, the IQ matched Controls retained 80.69 percent of what they had learned by trial five, the FAS group retained 79.01 percent, and the MPKUS retained only 59.03 percent.

Delayed Recall Memory (verbal): On the delayed recall trial of the RAVLT, the IQ matched Control group recalled an average of 8.00 words, whereas both the FAS and MPKUS groups only recalled an average of 5.50 words. Both the 10 block (corrected for one empty cell) analysis and the nine block analysis (block with empty cell discarded) approached significance, $\underline{F}(2,18) = 2.586$, $p = .103$ (χ^2 (2) = 4.514, $p = .105$), $\underline{F}(2,16) = 3.279$, $p = .064$ ($\chi^2(2) = 5.688$, $p = .058$). A comparison of immediate

and delayed recall scores for the three groups revealed that both the MPKUS and the IQ matched Controls retained the number of words they recalled between the immediate and delayed recall trial, whereas the FAS group did not. No differences were identified between the groups on any of the WMS-R Delayed Memory variables.

Recognition Memory: On the RAVLT recognition variable both the 10- and the nine-block nonparametric statistics were significant, $\chi^2 = (2) = 8.647$, $p = .013$ and $\chi^2 (2) = 7.267$, $p = .026$, whereas the parametric statistics were not, $F(2,18) = 3.200$, $p = .065$ and $F(2,16) = 2.239$, $p = .139$. SNK comparisons indicated that the MPKUS group recognized fewer words (10.90) than the FAS group (13.20) or the IQ matched Control group (13.80).

Visual Memory (immediate and delayed): The groups differed on the WMS-R Visual Reproduction I variable (immediate recall). The mean score was 28.50 for the FAS group, 24.00 for the MPKUS group, and 26.80 of the IQ matched Control group. Data was calculated for one missing cell. The nonparametric statistic for the 10 block WMS-R Visual Reproduction I analysis was significant, $\chi^2 (2) = 7.579$, $p = .023$, whereas the parametric statistic only approached significance, $F(2, 18) = 3.342$, $p = .058$. SNK comparisons showed that the FAS group performed significantly better than the MPKUS group. There were no differences between the FAS group and the IQ matched Control group or the MPKUS group and the IQ matched Control group. The parametric statistic for the nine block analysis (block with empty cell discarded) was not significant, $F(2,16) = 2.311$, $p = .131$, whereas the nonparametric approached significance, $\chi^2 (2) = 5.882$, $p = .053$.

There were no differences identified between the three groups on any of the variables assessing visual memory delayed recall (WMS-R Visual Reproduction II and Rey Complex Figure).

Figures 10.20 through 10.26 provide a visual representation of the pattern of differences (both significant and nonsignificant) between the groups on the attention and memory variables. For each variable z scores were calculated by subtracting the grand mean from each group mean and dividing by the MSE. All figures were designed using the analyses in which blocks with empty cells were dropped.

FIGURE 10.20 BLOCK ANALYSES FOR MIRSKY'S 'FOCUS' COMPONENT OF ATTENTION

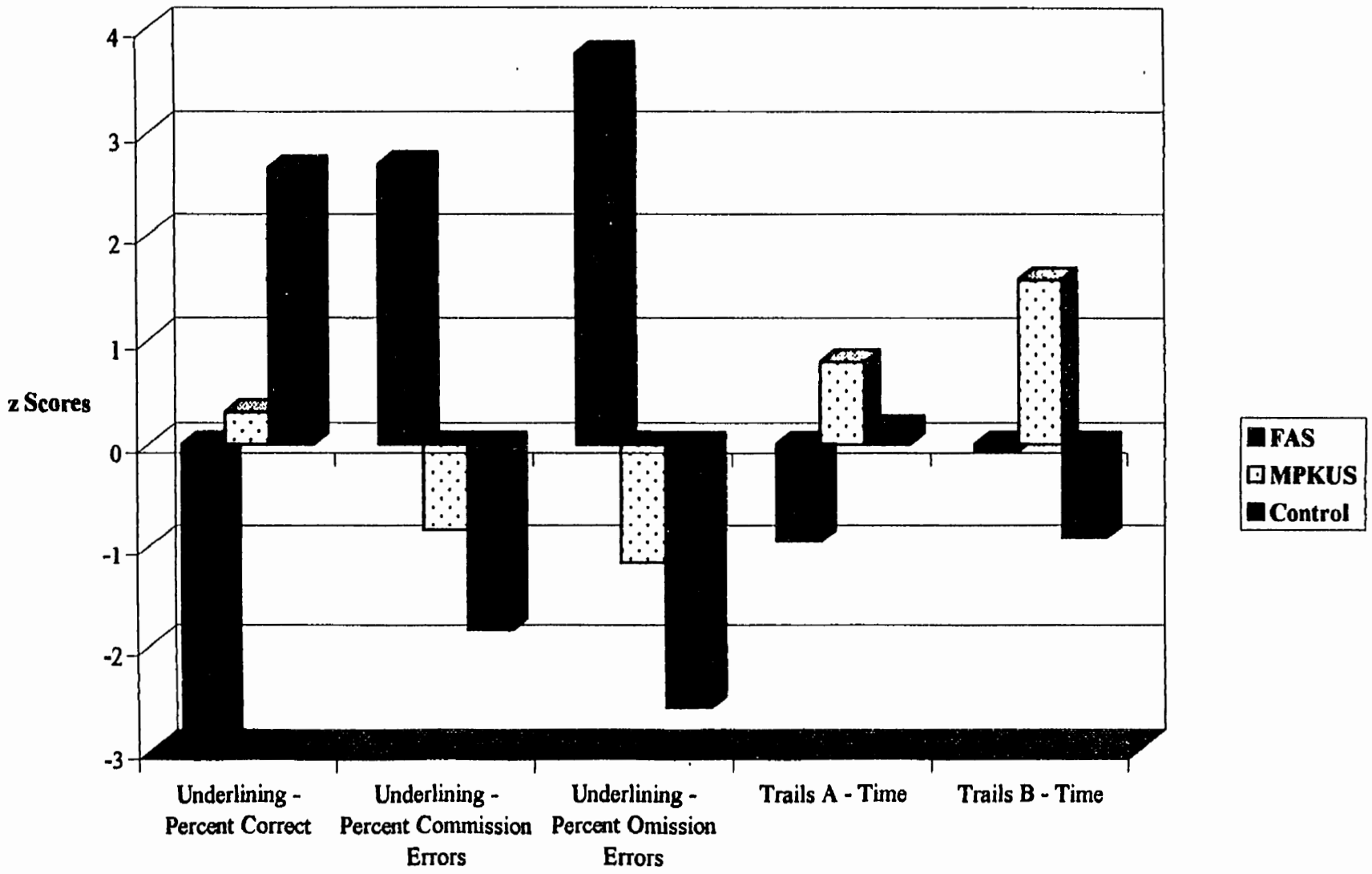


FIGURE 10.21a BLOCK ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION

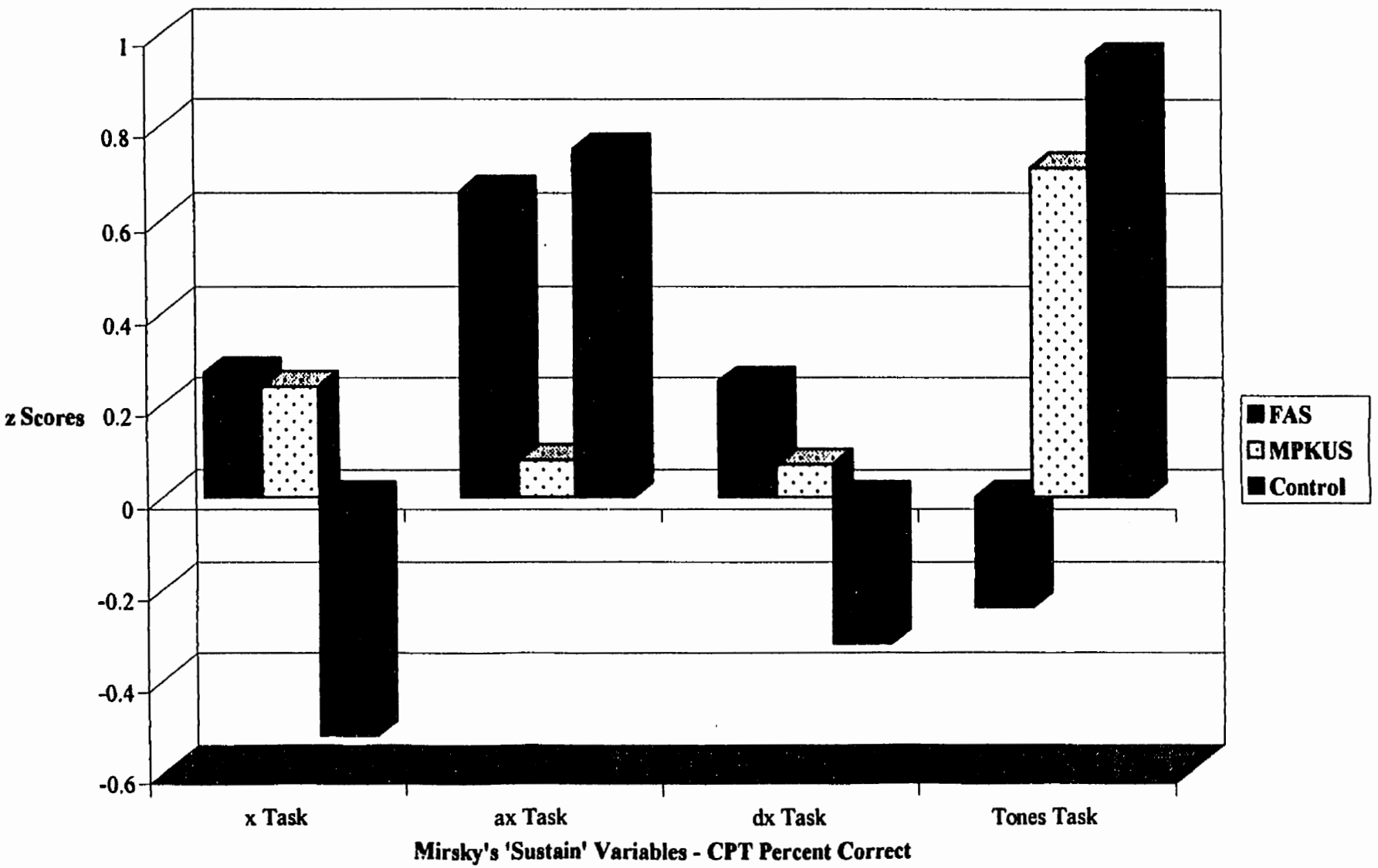


FIGURE 10.21b BLOCK ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION

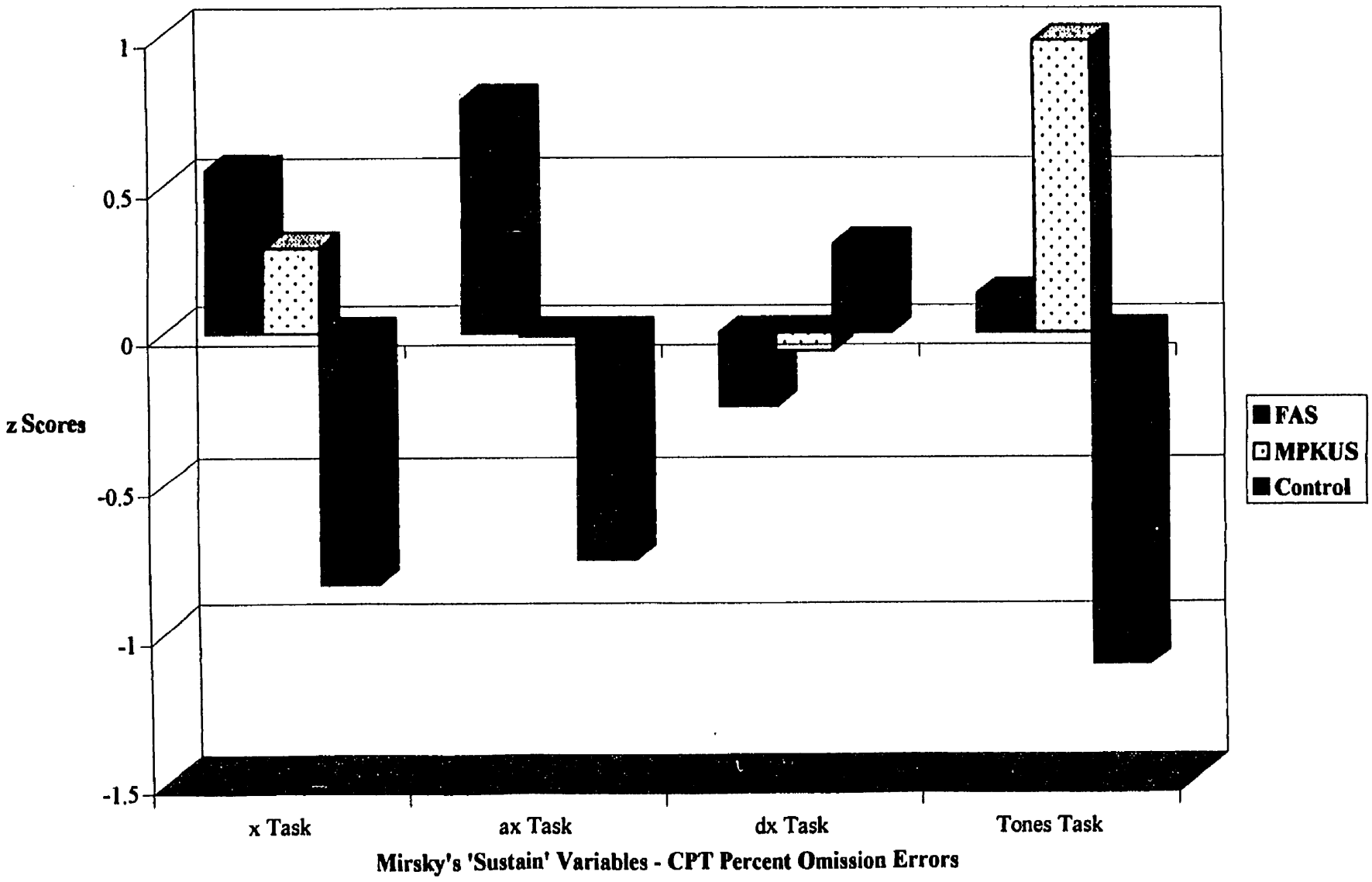


FIGURE 10.21c BLOCK ANALYSES FOR MIRSKY'S 'SUSTAIN' COMPONENT OF ATTENTION

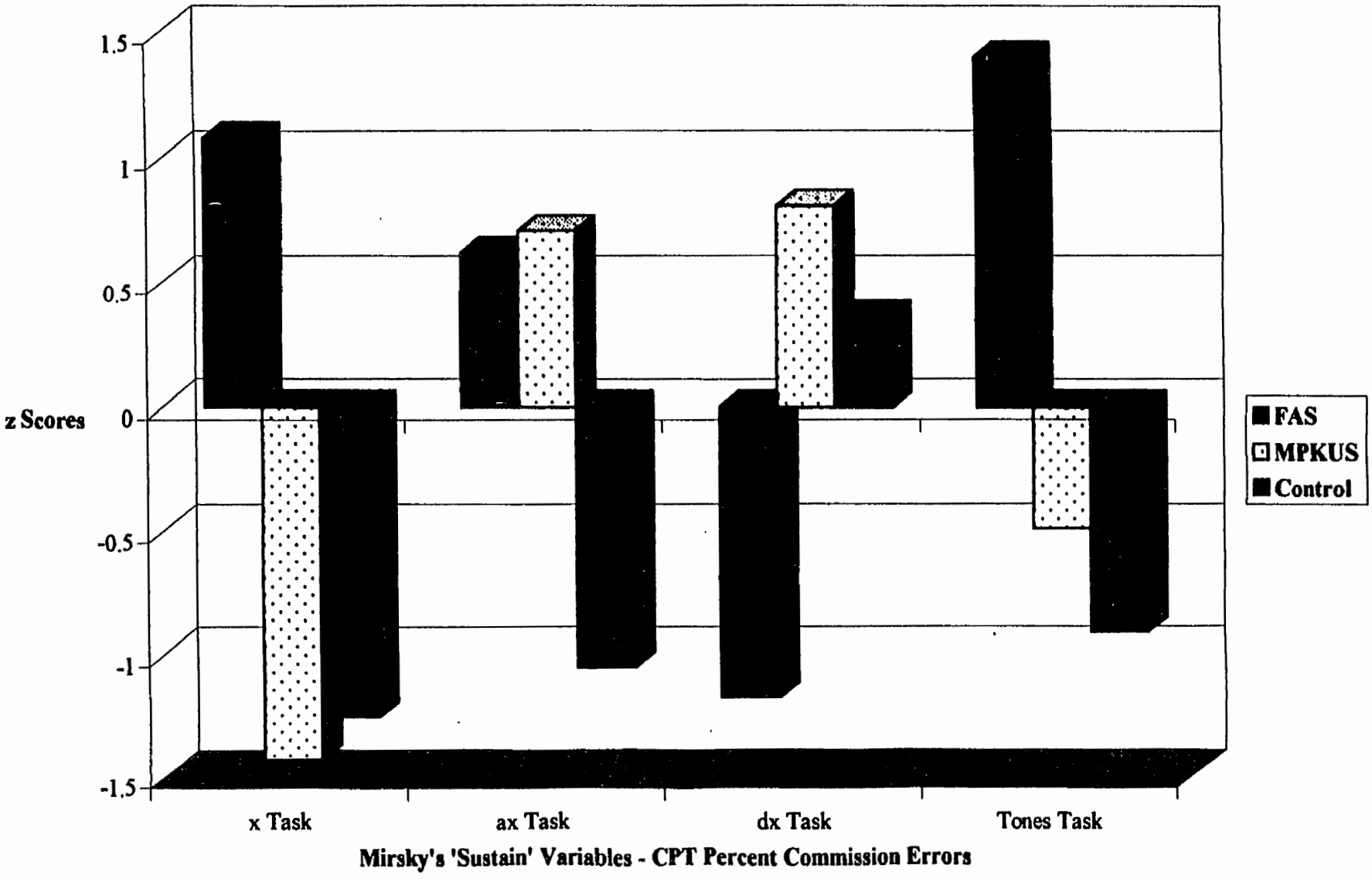


FIGURE 10.22 BLOCK ANALYSES FOR MIRSKY'S 'SHIFT' COMPONENT OF ATTENTION

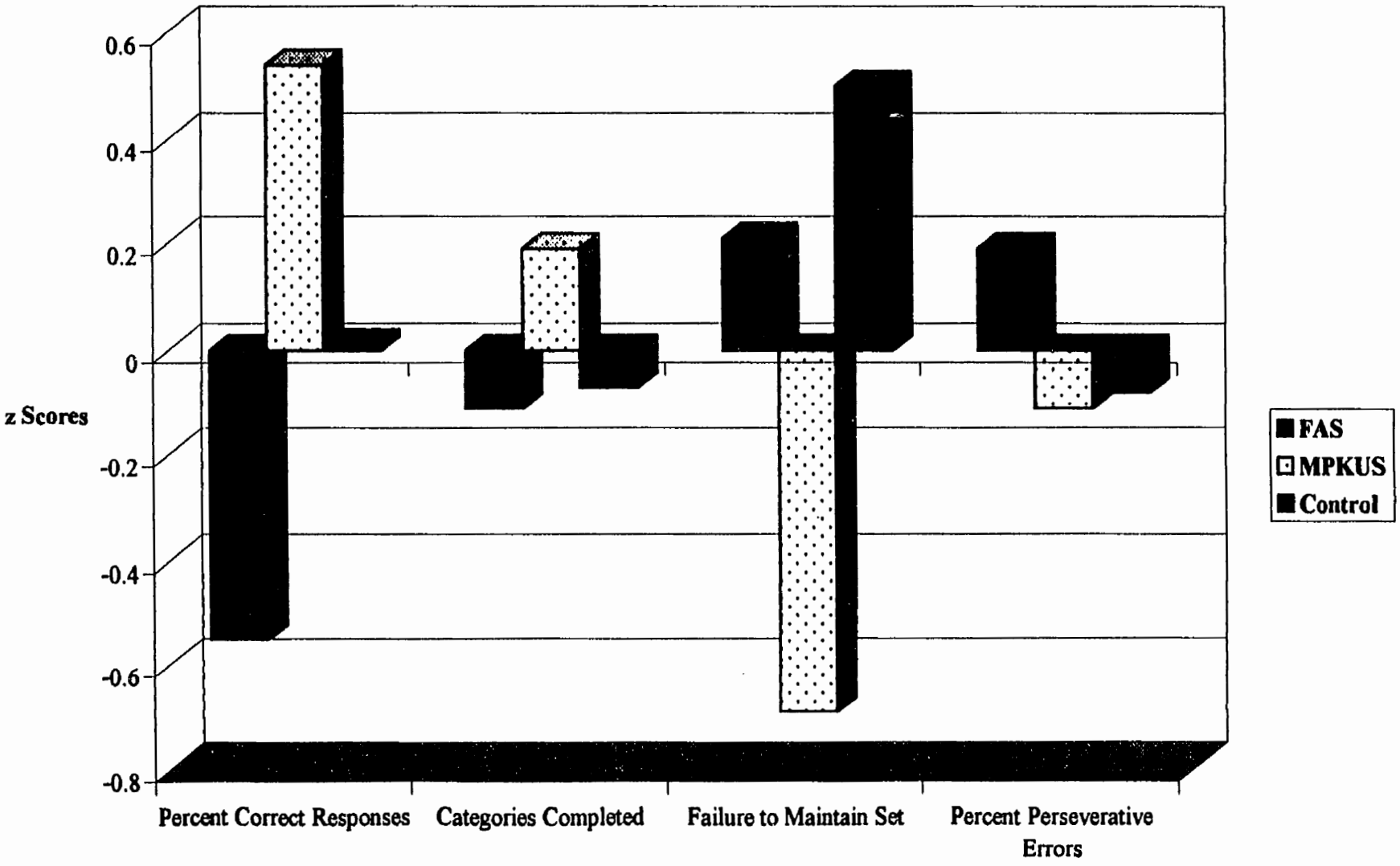


FIGURE 10.23 BLOCK ANALYSES FOR MIRSKY'S 'ENCODE' COMPONENT OF ATTENTION

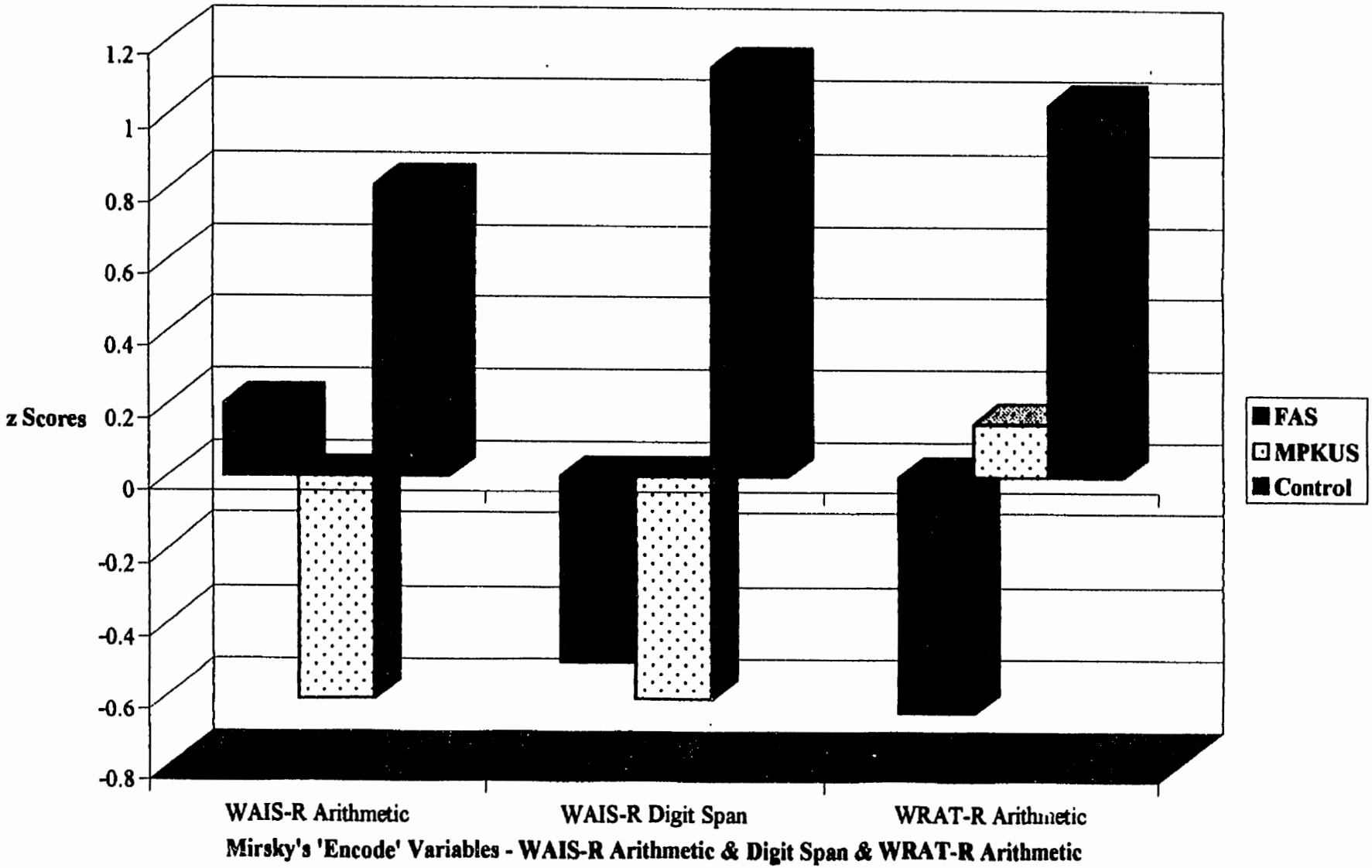


FIGURE 10.24 BLOCK ANALYSES FOR RAVLT VERBAL MEMORY VARIABLES

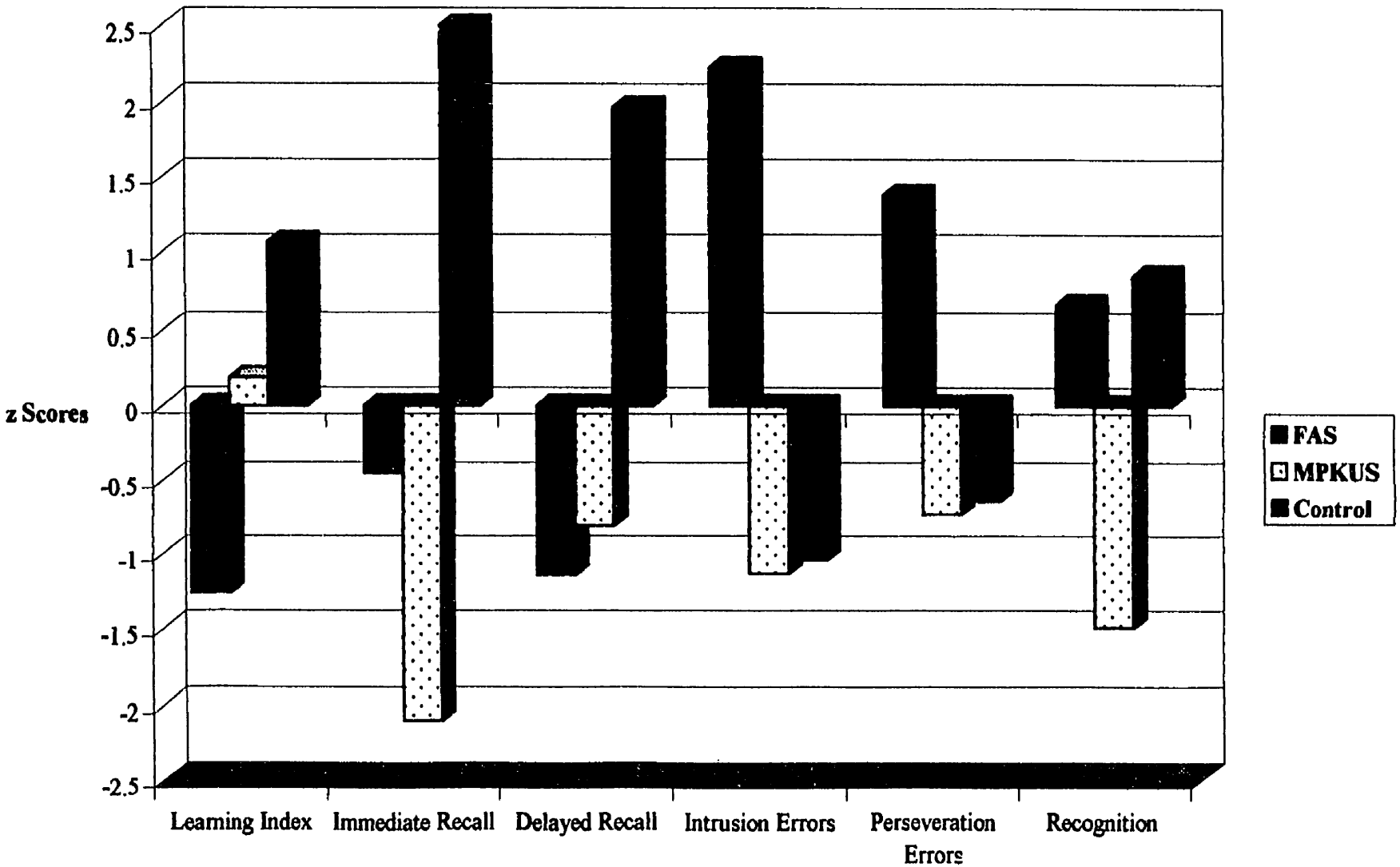


FIGURE 10.25 BLOCK ANALYSES FOR WMS-R VERBAL MEMORY VARIABLES

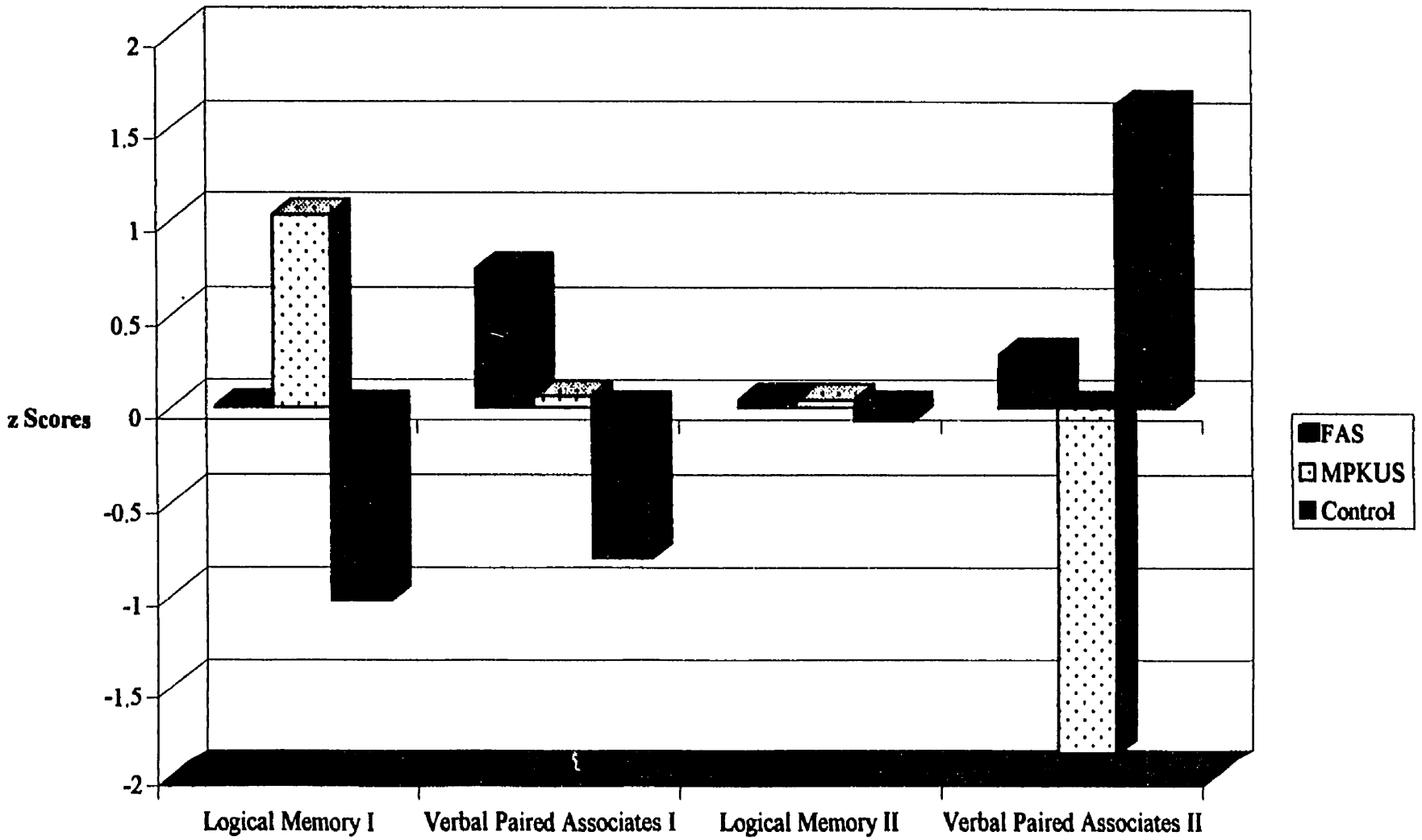
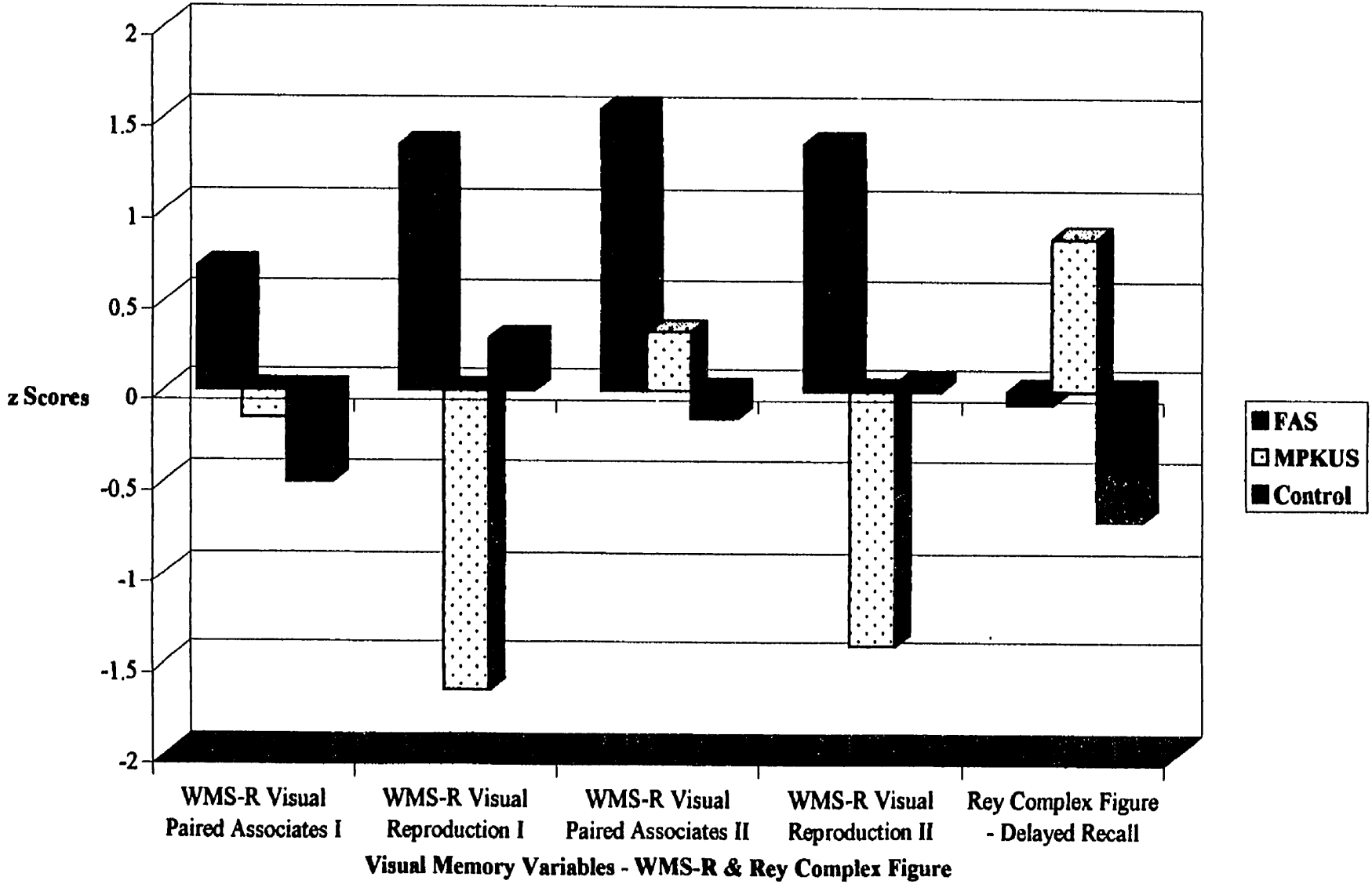


FIGURE 10.26 BLOCK ANALYSES FOR VISUAL MEMORY VARIABLES



11 Discussion

The present study examined the long-term neuropsychological outcome of prenatal teratogenic exposure, specifically in the areas of attention and memory. Attention and memory were broadly assessed with standardized measures commonly used in the area of neuropsychological assessment. The primary thrust of the study was to gather much needed descriptive data on adults with FAS and adults with MPKUS, particularly in terms of how they differ from CA and IQ matched Controls. Additionally, the study examined whether prenatal teratogenic exposure to alcohol or phenylalanine can be differentiated at a behavioural level.

The results will be discussed in terms of the research questions and hypotheses posed and further reviewed with respect to existing literature. The characteristics of the participants and the limitations of the present study will then be presented followed by a summary of the findings.

11.1 Research Questions and Hypotheses

Two major questions of the current research were whether there was a specific pattern of attention and memory deficits associated with prenatal teratogenic exposure and whether the relative effects of alcohol and phenylalanine could be meaningfully differentiated at the behavioural level. The results of the planned comparisons between the FAS and CA and IQ matched Control groups and the MPKUS and CA and IQ matched Control groups will be discussed followed by the results of randomized block analyses.

11.2.1 FAS and IQ Matched Controls

Planned comparisons between the FAS group and the CA and IQ matched Control group revealed several differences. Individuals in the FAS group displayed deficits on three of Mirsky's four-factor model of attention, the 'focus', 'sustain', and 'encode' components of attention.

In terms of the 'focus' component, the FAS group had more commission errors than the CA & IQ matched Control group, whereas the Control group demonstrated more omission errors than the FAS group. The groups did not differ in the percentage of correct responses they had on either the TLCT or the Underlining Test, nor did they differ on the Trail Making Test. The lack of differences on the Trail Making Test was unexpected, particularly Trails B, which requires alternating between numbers and letters in an ordered sequence. An assumption of the Trail Making Test is that letter recognition and sequencing are automatized, which in the present sample may not hold in the lower tail of the IQ distribution. There was also a large within-group variance for time and number of errors on Trails B for both groups. Both the FAS group and the CA and IQ matched Control group were able to accomplish letter recognition for the TLCT and the CPT; thus, the difficulty they had with the Trail Making Test may lie in their sequencing ability.

As expected, the groups differed in their ability to 'sustain' their attention as measured by the CPT. On the X task the groups differed in terms of commission errors, with the FAS group making significantly more commission errors than the CA and IQ matched Control group. The groups did not differ significantly in terms of the percentage of correct responses achieved or in terms of the percentage of omission

errors made. On the AX task, the pattern was similar except the differences between the groups on the percentage of commission errors made only approached significance. With the DX task both the Percent Correct and the Percent Omission Errors scores approached significance, with the FAS group achieving a higher percentage of correct responses and a lower percentage of omission errors than the CA and IQ matched Control group. There were no differences between the FAS and CA and IQ matched Control groups on Percent Commission Errors for the DX task; however, relative to the X, AX, and Tones tasks, both groups made more commission errors. On the Tones task there was a trend towards the Control group performing significantly better than the FAS group. The FAS group made less correct responses, more omission errors, and more commission errors. Relative to their performance on the X, AX task, and DX tasks, the FAS group's scores across the Tones task (Percent Correct, Percent Omissions, and Percent Commission scores) was much poorer, whereas the Control group's worst performance was on the DX task.

Statements made during testing indicated that participants in both groups found the DX task difficult and the least enjoyable. Many participants were restless during this task; they averted their gaze away from the screen, moved in their seat and questioned when they would be finished. Individuals in both groups required encouragement to complete the DX Task. It is possible that the effort required in terms of visual attention was both frustrating and fatiguing resulting in both groups' high percentage of commission errors and their expressed dislike.

The differences between outcome on the Tones Task and the X, AX, and DX tasks for the FAS group could result from the auditory versus the visual nature of the

tasks. It may be that without the attention demanding stimuli of the visual tasks (flashing letters on computer screen), individuals with FAS were unable to maintain their attention, accounting for their high percentage of both omission and commission errors. Kerns et al. (1997) also found significant deficits in sustained attention using an auditory attention task with individuals with FAS.

An examination of the pattern of error response bias scores indicated that for all tasks, with the exception of the Tones task, the FAS group made more commission errors (responding to non-target stimuli) than omission errors (non-response to target stimuli), whereas their CA and IQ matched Control group made more omission errors (see Figures 10.6b and 10.6c).

The groups differed in their ability to 'shift' attention as measured by the WCST. The CA and IQ matched Control group demonstrated significantly more perseverative errors and a lower percentage of correct responses than the FAS group. The number of categories completed approached significance with FAS achieving more categories than Controls. These results are contrary to what was expected. Previous studies have found that adolescents and adults with FAS achieved fewer categories and made more perseverative responses on the WCST (Carmichael Olson et al., 1992; Kodituwakku, Handmaker, Cutler, Weathersby, & Handmaker, 1995; Streissguth et al., 1994). However, these studies used normative data for comparison. Thus, it may be that the performance of individuals with prenatal teratogenic exposure on the WCST is worse than normal Controls, but superior to CA and IQ matched Controls.

As expected, the groups differed on the 'encode' factor of attention with the FAS group demonstrating a poorer performance than the CA and IQ matched Control

Group. The groups' performance on the WAIS-R Arithmetic subtest was significantly different and both the WAIS-R Digit Span subtest and the WRAT-R Arithmetic subtest approached significance.

The current results are similar to those reported by Streissguth (1994) who used Mirsky's attention battery to compare alcohol exposed children to normal Controls. On both the TLCT and the visual tasks of the CPT, she found that commission errors were more prominent for alcohol exposed children than omission errors and that both the WCST Total Number of Categories score and WAIS-R Digit Span score were moderately salient for alcohol exposure. Several other studies have also shown deficits on the WCST although it is unclear how these deficits relate to overall cognitive ability (Kodituwakku et al., 1995; Carmichael Olson et al., 1992).

Although previous studies examining individuals with FAS have reported finding a significantly high perseveration ratio on both attention and verbal memory tasks (Kerns et al. 1997; Carmichael Olson et al. 1992; Mattson et al. 1996), the present study did not. Previous studies reporting this finding have relied on age-matched controls, mental age-matched controls, or normative data for comparison, whereas the present study employed IQ-matched Controls, which may account for the different findings.

Based on Mirsky's conceptualization of the localization of elements of attention within the brain, the behavioural deficits identified in the FAS group in the areas of focused, sustained, and encoding attention are suggestive of widespread structural anomalies. Animal research, human autopsy studies, and MRI studies of prenatal exposure to alcohol have identified widespread anomalies (Barnes and Walker, 1981;

Clarren et al., 1978; Mattson et al., 1994). Animal studies have also clearly linked structural deficits caused by prenatal alcohol exposure to deficits in response-inhibition mechanisms (Riley et al., 1979). The performance of the FAS group across the tasks used to measure the 'focus', 'sustain', and 'encode' components of Mirsky's attention model could be interpreted as deficits in response-inhibition mechanisms. Although both groups demonstrated a high number of omission errors, compared to the CA and IQ matched Control Group, the FAS group also had a higher percentage of commission errors across attention tasks.

As expected, adults with FAS demonstrated poorer performance on measures of verbal memory. The RAVLT Ability to Learn Index score indicated a flatter learning curve for the FAS group compared to the CA and IQ matched Control group. Whereas the Control group increased an average of six words between trials 1 and 5, the FAS group increased an average of four words. However, the FAS group did not differ significantly from the Control group in number of words learned by trial 5 suggesting that although they were able to retain more words following the initial trial, they did not benefit from repeated trials to the same extent as the Control group. Further, the FAS group demonstrated more proactive interference than the CA and IQ matched Control group indicating a decremental effect of previously learned material on new learning.

As expected, the FAS group demonstrated greater difficulty recalling information immediately following a distractor list and following a period of delay. On the RAVLT, individuals with FAS lost a higher percentage of words from trial 5 to trial 6 (immediate recall following the distractor list) than the Control group indicating a

decremental effect of subsequent learning on their retention of previously learned material.

The FAS group also had significantly more intrusion errors across the RAVLT trials. It appeared that they were aware there should be more words than they could recall following each trial, and so they guessed words. Further, they tended to perseverate with their intrusions across the subsequent learning and recall trials. This pattern of responding is similar to that reported by Delis, Massman, Butters, and Salmon (1991) using the California Verbal Learning Test (CVLT) (Delis, Kramer, Kaplan, & Ober, 1987) to examine memory functioning in individuals suffering from alcoholism. They reported that these individuals confabulated across all trials. Using the CVLT to examine memory functioning Kerns et al. (1997) and Mattson et al. (1994) also reported more intrusion errors in individuals with FAS.

The WMS-R differentiated between the FAS group and the CA and IQ matched Control group with regard to delayed verbal memory, but not with regard to immediate recall memory. The lack of consistent results across the WMS-R and the RAVLT may be due, in part, to the different nature of the tasks involved in the WMS-R. The RAVLT provides five learning trials for a list of 15 words, whereas the WMS-R Logical Memory subtest requires immediate recall of each story paragraph following the initial presentation. Both groups had difficulty with this subtest suggesting that perhaps more repetition was required. Although the WMS-R Verbal Paired Associates I subtest provides five learning trials of easy and hard word pairs, immediate recall score is calculated using only the first three trials and unlike the RAVLT immediate recall trial, there is no intervening distractor list. Overall, participants in all groups

found the WMS-R to be a more difficult test. As noted, verbal memory indices for the WMS-R could not be calculated for either group due to floor effects.

On the delayed recall trial of the RAVLT and on the WMS-R Verbal Paired Associates II, the FAS group recalled significantly fewer words than the CA and IQ matched Control group. The FAS group also recalled significantly less material from the two paragraphs (WMS-R Logical Memory II) following a period of delay. Thus, although both groups performed relatively poorly on immediate recall of the material, the FAS group retained less information following a period of delay than the CA and IQ matched Control group.

There were no differences between the FAS group and CA and IQ matched Control group on recognition memory, suggesting that the deficits observed in terms of verbal memory lie in their ability to freely recall material rather than in their ability to encode.

These results differ somewhat from those found by Mattson et al. (1994) using the CVLT-C with a group of nine FAS adolescents. Her results showed that when compared to standardized scores, children with FAS learned fewer words over all, recall of the distractor list was impaired, and discriminability on a recognition task was severely impaired. Similar to the present study, she found elevated intrusion rates as well as impaired immediate and delayed recall in the FAS group. However, when Mattson compared two FAS adolescents to Controls equated on mental age on the CVLT-C, the learning and recall differences disappeared, although the FAS individuals still demonstrated significant intrusions and poor recognition discrimination. There are two possible reasons for the noted differences between the present study and Mattson et

al. (1994). First, Mattson's initial study examined nine FAS adolescents and used standardized scores for comparison, and the latter study involved only two adolescents and used mental age matched Controls, whereas the current study utilized an CA and IQ matched Control group and employed a larger sample. Second, although both the RAVLT and CVLT-C are auditory verbal learning tasks employing a list of words, there may be differences between the tasks in terms of familiarity of the words.

Other studies in the area of verbal learning and memory in individuals with FAS have demonstrated deficits in learning and recalling a word list, impaired recall on both free and recognition recall trials, and an increased number of intrusion, perseveration, and false positive errors (Streissguth et al. 1994; Carmichael Olson et al., 1992). This same pattern of impaired learning and relatively unimpaired retention was also demonstrated in adolescents and young adults with FAS and thought to be suggestive of pervasive deficits in encoding verbal information (Kerns et al., 1997). It is likely that the somewhat different pattern of results between the present study and previous research is attributable to the current study's use of an CA and IQ matched Control group, the different measures used, and the differences between the FAS cohorts employed.

No differences between the FAS and Controls groups in the area of immediate and delayed visual memory were identified; however, the lack of differences may be the result of the small sample size and subsequent lack of statistical power.

Examination of the verbal memory deficits identified in the current study indicates that individuals with FAS have more difficulty with free recall than the CA and IQ matched Control group, but not with verbal recognition memory or with visual

memory. Based on Petri and Mishkin's 1994 model of memory, these findings would suggest impairment in the left prefrontal cortex (as cited in Kolb & Whishaw, 1996). From a cognitive perspective there appear to be deficits in the storage and consolidation process accounting for the observed retrieval deficits. Perhaps, if as theorized by Hebb (1949), synapses undergo change during learning, then perhaps the efficiency with which these changes occur is impaired when the brain has been exposed to alcohol prenatally, resulting in deficits in the way in which information is stored. Unfortunately, current models of memory are based largely on data from normal and brain damaged adults, and not on data from adults with developmental disorders, whose brain anomalies arise prenatally. There is a need to develop developmental models of memory that account for aberrant developmental processes.

In summary, the present study indicates that the pattern of attention and memory deficits seen in adults with FAS is distinguishable from that associated with general mental retardation. Specifically, adult individuals with FAS appear to have deficits in acquisition of new material, delayed recall of verbal material and deficits in response inhibition. Further, the present study indicates that the pattern of deficits seen in adults with FAS is similar to the pattern seen in children with FAS, suggesting that these deficits are stable and likely to be present across the lifespan of affected individuals.

11.2.2 MPKUS and CA and IQ matched Controls

Planned Comparisons between the MPKUS group and an CA and IQ matched Control group revealed few differences (see Figures 10.13 to 10.19). The MPKUS group appeared more similar than different from the CA and IQ matched Control

Group on Mirsky's four-factor model of attention. As noted earlier, the TLCT was replaced with the Underlining Test as a measure of the 'focus' component of attention because the TLCT was found to be too difficult for individuals functioning in the lower end of the IQ distribution. The Underlining Test indicated a trend toward less correct responses and more omission errors for the MPKUS compared to the CA and IQ matched Control Group, which with a larger sample may have reached significance. On the Trail Making Test, Trails B Time approached significance with the MPKUS group taking significantly longer to complete the task. The difference was likely due to difficulty with sequencing rather than slowed motor speed, as there were no differences in reaction time between the groups on any of the CPT variabies.

On the 'sustain' component of Mirsky's attention battery, the MPKUS group differed from the CA and IQ matched Control Group on the Tones task of the CPT, with the MPKUS individuals making less correct responses and more omission errors than Controls and also demonstrating poorer discriminability skills.

The MPKUS group demonstrated more difficulty discriminating between critical and noncritical stimuli on the Tones Task than the CA and IQ matched Control group. Interestingly, during the training phase of the Tones Task, the MPKUS participants had difficulty learning to identify the high tone on the CPT Tones task out of a series of three tones (low, medium, and high). Three MPKUS participants made statements during the training phase indicating that the low tone sounded the highest and many others appeared to need more time to learn the task. With continued feedback during the practice trial they were eventually able to respond correctly to the

high tone; however, examination of their performance across blocks of trials indicated that they reverted back to responding to the low tone.

On the WCST Failure to Maintain Set subtest of the 'shift' component of attention, the MPKUS group outperformed the CA and IQ matched Control Group with the Control group losing set more often than the MPKUS group. There was a trend toward the MPKUS group having significantly more perseverative errors than the CA and IQ matched Control Group (see Figure 10.15).

The groups' performances on measures of the 'encode' component of attention were comparable. On the WRAT-R Arithmetic, which is often used as a measure of achievement, no appreciable differences were found between the MPKUS and the CA and IQ matched Control Group suggesting that the MPKUS group's achievement level is consistent with their IQ.

In the area of verbal memory, the CA and IQ matched Control group scored significantly higher than the MPKUS group on the RAVLT recognition variable. An examination of the pattern of performance across the RAVLT variables suggests that for both groups recognition skill was more efficient than recall (see Figure 10.17). The MPKUS group had a large number of perseverative errors relative to the CA and IQ matched Control group; however, the differences were not significant. The MPKUS group's within group variance for perseverative errors was extremely large, which may have been a factor in the lack of significant findings for this variable.

Although there were no significant differences on any of the WMS-R memory variables, an analysis of Figure 10.18 would suggest that with more difficult verbal memory tasks (e.g., Logical Memory and Verbal Paired Associates), both groups lost

more information following a period of delay than with simpler word learning lists such as the RAVLT. As noted, the WMS-R was a more difficult test than the RAVLT for all groups.

In summary, the present study indicates that when compared with CA and IQ matched controls, there does not appear to be a pattern of attention and memory deficits that is unique to adults with MPKUS. It may be that the endogenous, and continuous exposure nature of phenylalanine results in a different pattern of deficits that were not identified in the present study. For example, the verbal fluency of individuals with MPKUS was observed to be impaired relative to the FAS and CA and IQ matched Control groups and parents and caretakers identified it as an ongoing concern. As well, the small sample size together with a bimodal distribution in IQ suggests caution in what conclusions are drawn from the present data.

11.2.3 Randomized Block Analyses

The second major question addressed by the present study was whether the relative effects of alcohol and phenylalanine could be meaningfully differentiated at the behavioural level. The randomized block analyses highlighted differences between the groups on two of Mirsky's four-factor model of attention. The deficits were within the 'focus' and 'sustain' components of attention.

On the measures comprising the 'focus' component of attention, the groups differed on all three subtests of the Underlining Test and on the Trails B Time variable of the Trail Making Test. The Control group made more correct responses on the Underlining Test than both the FAS and MPKUS groups. Similar to the findings with the paired analyses, the eight-block analysis revealed that the FAS group made

significantly more omission and commission errors than the MPKUS and Control groups, and the MPKUS made significantly more omission and commission errors than Controls (see Figure 10.20).

Only two of the CPT subtests comprising the 'sustain' component of attention differentiated between the three groups. The CPT X task Percent Commission Errors analysis indicated that the FAS group made significantly more commission errors than both the MPKUS and Control groups, and that the MPKUS group made significantly more commission errors than the Control group. The CPT AX β score (error bias) approached significance with both the FAS and the MPKUS groups demonstrating more commission errors relative to total number of errors compared to Controls. Opposite to that found with the two-teratogen groups, the IQ matched Control group produced more omission errors than commission errors. Although not significantly different, the error bias scores for the Tones test suggest a similar pattern to that seen in the FAS paired analyses with the FAS group making more commission errors, whereas the MPKUS and Control groups made more omission errors.

In terms of memory functioning, a similar pattern to that seen in the paired analyses was identified. The Control group recalled significantly more words on the RAVLT than both teratogen groups on immediate recall following a distactor list. An examination of the proportion of words recalled on the RAVLT Immediate Recall Trial, relative to the number of words learned after five learning trials indicated that the differences were a result of the Control group having improved recall ability compared to the two teratogen groups. Thus, the differences between the three groups are likely

accounted for by their differing skill in recalling verbal material rather than by their ability to learn or encode new material.

The FAS group differed from both the MPKUS and from matched Controls in terms of the number of intrusions they made across all trials of the RAVLT on the 10-block analysis. Although the nine-block analysis only approached significance, this was likely due to the small sample size. The finding that individuals with FAS demonstrated higher numbers of intrusions across trials than the other groups was consistent with the results found in the FAS paired analyses, which employed a larger sample. Figure 10.24 indicates that, although not significant, the mean number of perseveration errors was larger for the FAS group than for the MPKUS or Control groups. However, the within group variance for the FAS group was extremely large, which likely accounted for the lack of significant findings.

On delayed recall of verbal material, as measured by the RAVLT, the nine block analysis approached significance and an examination of the means showed that the Control group recalled 2.5 words more on average compared to the two teratogen groups. Further, examination of the difference between number of words recalled immediately following the distractor list with the 30 minute delayed recall indicated that on average the MPKUS and Control groups maintained the number of words they recalled across the period of delay, whereas the FAS group lost words (see Figure 10.24).

On the recognition task of the RAVLT, similar to the results of the paired analyses, the FAS and Control groups demonstrated a higher number of 'hits' (i.e., correct identification of words from the target list) than the MPKUS group.

An examination of the pattern of scores across the WMS-R verbal and visual memory subtests indicated that similar to the paired analyses, there were few appreciable differences between the groups.

In the FAS paired analyses the Logical Memory II and Verbal Paired Associates II scores (delayed recall) were significant with the FAS group recalling less information than the Control group. The differences on Verbal Paired Associates II in the randomized block analysis were between the Control group and the MPKUS group with the Control group recalling more word pairs; however, the difference between the Control group and the FAS group was not significant in this analysis. No differences were found on Logical Memory II in the randomized block analysis.

In terms of visual memory (Visual Reproduction WMS-R), the FAS group performed better than the MPKUS group on immediate recall for geometric designs. There were no differences found between FAS and Controls or MPKUS and Controls. In the present sample, short-term memory for visual material appears more impaired by prenatal exposure to phenylalanine than to alcohol.

There were no significant differences between groups on delayed memory for visual material or in terms of ability to learn new material.

In summary, the randomized block analyses identified few differences between the two teratogen groups (intrusion errors, recognition, and immediate recall of visual material and commission errors) and failed to reveal a number of the differences found in the paired analyses between the teratogen groups and their IQ matched Control groups. Together with the small sample size, the degree of within group variance may have been too large to measure meaningful differences. Further research employing this

methodological design, a larger sample, and utilizing a battery of tests with broader normative data is needed.

11.2 Participant Characteristics

Although the current study did not randomly sample, selection bias was minimized in that all available individuals with MPKUS were included and all adult individuals with FAS that could be located in Saskatchewan were included. Although there were relatively equal numbers of males and females in the Control group, gender was not used as a matching criterion due to the difficulty in finding CA and IQ matched Controls. Consistent with previous studies on FAS that have employed larger samples (Majewski, 1981), there was an equal male to female ratio in the FAS group. There were also equal male to female ratios in both the MPKUS and the Control groups. Previous research has suggested males with FAS have more deficits than females (Nanson, 1989; Qazi & Masakawa, 1976). Nanson's (1989) study restricted participant selection to individuals scoring 75 and above on Full Scale IQ, which resulted in a bias in favor of females in her FAS groups. In the current study, the number of males and females in the FAS group was relatively equal, as was the number of males and females scoring in the low average and average IQ range. As mentioned earlier, there was a bimodal distribution for IQ in the MPKUS group. Within this distribution, three females and one male scored in the low average to average range. This is consistent with findings from the International MPKUS study, in which almost all high functioning individuals with MPKUS are female (Waisbren, 1998, personal communication). The sample size in the present study limits conclusions drawn from these observations; however, it does support the call for further research into the role

gender may play with regard to the severity of the deficits seen in individuals prenatally exposed to alcohol or phenylalanine.

The mean IQ level of the FAS group was in the borderline range. This is consistent with the mean IQ reported in the literature for children with FAS (Little & Streissguth, 1981; Majewski, 1981). There was a bimodal distribution for IQ within the MPKUS group. As minimal information has been published with regards to this population, it is unclear as to whether this distribution simply reflects sampling error or whether it is a characteristic of the disorder. One MPKUS participant was eliminated from the study because his IQ was below 50, and one available participant could not be tested due to severe communication difficulties. Consequently, the present MPKUS sample may not be representative of the true population range. Interestingly, these two participants had been tested at a younger age and although they scored in the mentally retarded range, they were able to complete testing. It is possible that individuals with MPKUS experience a decline in measured IQ at some point. Such a decline has been noted in children with Down's Syndrome and in children with William's syndrome, beginning in middle childhood. The decline in children with Down's Syndrome is thought to be related to the difficulty these individuals experience with abstract thinking, a skill that undergoes marked development in middle childhood (Tingey, 1987). The present study is not adequate to address the issue of intellectual decline in MPKUS, but the question is worthy of future research.

There was a Verbal/Performance split on IQ for both teratogen groups, with their Performance scores averaging approximately 10 points higher in the FAS group and eight points higher in the MPKUS group than their Verbal scores. Previous

research in FAS has attributed this difference to the native ancestry of its participants rather than as a characteristic associated with prenatal teratogenic exposure. However, in the current study, there were no Native participants in the MPKUS group, and all participants were monolingual English speakers. The fact that both teratogen groups had the same pattern of performance, whereas the Control groups did not, suggests that this difference may be related more to prenatal teratogenic effects than to culture. Preliminary data from the International Collaborative Study in MPKUS suggests a similar pattern in younger children with treated MPKUS. Further support is found in a study of preschoolers with FAS that utilized race-matched controls (Janzen, Nanson, & Block, 1995). The authors reported that the Native children in their control group who resided in an urban area and attended subsidized daycare did not demonstrate a pattern of below average cognitive ability, or a significant difference between verbal and nonverbal skills; however, the Native preschoolers with FAS did demonstrate verbal deficits, again suggesting that the differences are due to teratogenic exposure rather than to race.

Both the MPKUS and Control groups demonstrated consistency between full scale IQ and achievement level, whereas the FAS group demonstrated lower achievement scores on site reading, spelling, and oral and written arithmetic. This finding is consistent with previous research examining children and adolescents with FAS (Streissguth et al., 1990; 1991; 1994).

The structured interview revealed that, with the exception of one MPKUS individual, none of the FAS or MPKUS individuals were living independently. Because of their young age, approximately half of the FAS participants continue to live

with their adoptive parents or foster parents. The remainder of the group and the majority of the MPKUS group live in supervised group homes.

11.3 Limitations

There are several limitations to the data collected in this study. Due to the finite population of individuals with untreated MPKUS, the sample size was small; restricting what conclusions can be drawn from this data. The bimodal nature of the MPKUS IQ distribution further circumscribes the generalizability of the data, as well as the conclusions that can be drawn with regard to the similarities and differences between FAS and MPKUS. Due to the clinical nature of the study, there could be no control for degree or timing of prenatal exposure. Although all participants were diagnosed in infancy or early childhood, there were no data collected concerning the degree or timing of the alcohol or phenylalanine exposure.

A further limitation was the lack of control for post-natal environmental influences. Although attempts were made to control for socioeconomic status and living arrangements, the limited population of individuals with untreated maternal PKU, together with the limited number of CA and IQ matched Controls recruited, rendered this impossible.

Race was also not controlled for in the analyses. Twelve out of the 17 FAS participants were of Native ancestry, compared to four of the 17 CA and IQ matched Controls; however, all were raised in Caucasian, English speaking foster or adoptive homes since infancy or early childhood. Thus, any differences between the Native and non-Native participants in this study are likely to be genetic, rather than environmental. There were no Native participants in the MPKUS group. A review of the findings on

racial differences in attention found little evidence for racial effects when intelligence and language were controlled for in the analyses (Birch and Kantor, 1984).

Another limitation was the disproportionate number of young adults (< 20 years old) in the FAS group compared with the MPKUS group. However, the difference in age distribution likely reflects the actual population distribution for age for both FAS and MPKUS. Inclusion criteria for this study required a formal diagnosis of FAS or MPKUS in infancy or early childhood. For participants in the FAS group this meant a diagnosis based on the clinical characteristics delineated by Clarren and Smith in 1978, accounting for the larger number of late adolescent, early adult aged participants. For participants in the MPKUS group, this meant having a diagnosis of MPKUS in infancy resulting from the mother's PKU being untreated PKU during pregnancy. Increased awareness of the effects of uncontrolled phenylalanine on the fetus has greatly reduced the number of untreated pregnancies over the past two decades. Thus, the population of individuals with MPKUS was weighted toward the older end of the age distribution.

Further, a number of the measures proved to be too difficult for the present sample. All of the measures were piloted on individuals with IQs in the borderline and mentally retarded range, and with the exception of the TLCT, all were completed. However, individuals in the present study had difficulty with the WMS-R subtests, and with the Trail Making Test. Further, the within group variance was large across the majority of the tests, which combined with the small sample size, and a heterogeneous sample, lowered the statistical power in the analyses.

Moreover, a number of the measures used were highly correlated. The intercorrelation together with the large number of analyses run significantly increased

the possibility of Type I errors. However, due to the exploratory nature of the study and the small population of participants available, the likelihood of making Type II errors was deemed to be more critical. Thus, a less stringent criterion for significance was employed throughout this study. As a result of these limitations, it is important that the findings be replicated, as there is the possibility that the pattern of results identified is specific to this sample.

11.4 Summary

The present study was designed to provide data to delineate the pattern of strengths and weaknesses in the areas of attention and memory in individuals prenatally exposed to alcohol or phenylalanine and how they compare with the attention and memory abilities of individuals matched on CA and IQ.

The strength of the current data is largely due to the use of IQ-matched Controls to examine the pattern of attention and memory functioning specific to prenatal teratogenic exposure. The majority of previous studies have used normative data for comparisons; thereby leaving unanswered the question as to whether the pattern of attention and memory deficits associated with prenatal alcohol exposure is distinct. The few studies that have used matched controls equated for mental age rather than IQ. Further, only individuals with an early childhood diagnosis of FAS were selected for the present study, whereas previous research has often utilized both FAS and FAE participants thereby limiting conclusions regarding the specific effects of FAS.

Many of the documented deficits from the present study have been reported by previous studies that have examined the role of prenatal alcohol exposure in the development of neurobehavioural abilities. Although there is some inconsistency

across the results of the present study and previous studies with regard to the pattern of deficits associated with FAS, they are likely due to the more rigorous design of the present study (i.e., CA and IQ matched Controls). Some differences may also be attributable to the differing ages of the participants. Perhaps, the earlier findings with regards to decreased learning ability, poor recognition skills, and perseveration have been modified with education. The current sample consisted of individuals who were either still enrolled in school or some type of training program and those involved in some form of sheltered workshop or modified work environment.

The current data suggest that adult individuals with FAS demonstrate similar attention and memory deficits as documented in research with children with FAS. Compared to CA and IQ matched Controls, adults with FAS appeared to have difficulty recalling even well rehearsed information when there was not a period of consolidation without distraction. They also demonstrated difficulty inhibiting their response as evidenced by the high number of intrusions across verbal learning tasks and the high number of commission errors on attention tasks. These data suggests that individuals with FAS have permanent attention and memory deficits and that even in those individuals with a normal IQ, these deficits would limit their ability to function as independent adults. Their ability to learn from mistakes, to think before acting, and to understand cause and consequence would compromise their ability to live and work independently.

FAS is a devastating developmental disorder associated with a wide variety of neurobehavioural deficits. The present study has further elucidated the specific pattern of deficits associated with prenatal alcohol exposure in the areas of attention and

memory. These results will inform ongoing research aimed towards understanding the pattern of psychosocial deficits associated with FAS as well as assist in the development of programs designed around the limitations imposed by these deficits (e.g., independent living and employment).

MPKUS is also a devastating developmental disorder associated with a wide variety of neurobehavioural deficits. The present data indicate that it is difficult to distinguish individuals with MPKUS from CA and IQ matched Controls in terms of attention and memory functioning; however, the small sample size and bimodal IQ distribution within this sample may have severely limited what differences could be identified.

Prior to the present research, there was little information available regarding the pattern of deficits associated with this disorder. The current study highlights the lifelong pattern of attention and memory deficits associated with prenatal exposure to uncontrolled levels of phenylalanine and provides preliminary comparison data for the International Collaborative Study on MPKU to examine the impact of prenatal dietary treatment.

Comparisons between the FAS, MPKUS, and IQ matched Control groups revealed more similarities than differences between the two teratogen groups. However, the current results do not allow for firm conclusions regarding the distinct versus general nature of the two prenatal teratogens due to the small sample size, bimodal distribution in IQ in the MPKUS sample, and large within group variance.

Future research utilizing a broader array of nonverbal tasks and adding cued recall, cued recognition, and multiple choice recognition tasks to the verbal and visual

memory tasks would likely limit floor effects, reduce variability within groups, and more clearly highlight any differences between groups. Future research should also examine how teaching effective use of rehearsal strategies and cueing may be useful in facilitating learning and recall. In addition, research into the development of programs designed to improve self-monitoring of concentration and attention skills may assist in improved learning.

Further, future research should address the psychosocial functioning of individuals with prenatal teratogenic exposure since many of the caregivers interviewed highlighted behaviour as their primary concern with regards to the FAS and MPKUS individuals under their care.

The present study provided data regarding the long-term neuropsychological functioning in the areas of attention and memory in individuals with FAS and in individuals with MPKUS and how they differed from CA and IQ matched Control participants. The results from the present study also contribute to the existing literature that is being used to provide educational and training programs specific to the needs of individuals with FAS and MPKUS. Finally, this study provided initial data towards the question of whether or not the pattern of deficits associated with prenatal exposure to alcohol or phenylalanine can be meaningfully differentiated at a behavioural level.

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APPENDIX A Structured Community Assessment Interview

Structured Community Assessment Interview (Crossley et al., 1992).

STRUCTURED COMMUNITY ASSESSMENT INTERVIEW
(Adapted from McKerracher Follow-Up Project Community Assessment Interview)

Interviewer Initials: _____

CODE

1. Subject #:_____

2. Gender: 1. Male 2. Female ___ ___

3. Date of Birth: _____ Current Age: ___ ___

A. Demographics

4. What is his/her country of birth? _____ ___ ___
   1.Canada 2.Other

5. Race: 1 Caucasian 2.Black 3.Asian 4.Native/Metis 5.Other ___ ___

6. What is his/her first language? 1. English 2. Other ___ ___

7. How many years of formal education does he/she have?
   Total elementary + high school + university = ___ ___

8. What is the highest level of schooling he/she has reached?
   1. Some primary school
   2. Completed primary school
   3. Some high school
   4. Completed high school
   5. Technical training beyond high school
   6. College or some university
   7. University undergraduate degree
   8. University graduate degree

   ___ ___

9. What is his/her current marital status?
   1. single (never married)
   2. married
   3. separated/divorced
   4. widowed
   5. living common-law

   ___ ___

10. How long has this been his/her marital status? (closet # of Yrs) ___ ___

B. Housing/Home Environment

General description of residential situation

11. What type of housing does he/she currently live in?
    1. own house (or family-owned)
    2. rented house
    3. apartment
    4. room/board
    5. special care home
    6. group home
    7. supervised apartment
    8. other type of housing: _____

12. How many people live with him/her? ___ ___

13. Who does he/she live with?
    1. alone
    2. parents &/or siblings
    3. spouse &/or children
    4. other relative
    5. friend(s)
    6. roommates/boarders, with landlady/landlord/operator
    7. roommates/boarders, without landlady/landlord/operator
    8. other: _____ ___ ___

14. Is his/her bedroom private or shared?
    1. private (or shared with partner)
    2. shared with family member
    3. shared with non-family member ___ ___

15. How long has he/she lived in his/her current residence? months: _____years ___ ___

Meals/Domestic Management

16. Does he/she regularly shop for food and personal items?
    1. does not shop at all
    2. needs to be accompanied on any shopping trip
    3. shops independently for small purchases
    4. takes care of all shopping needs independently ___ ___

17. Does he/she do his/her own laundry?
    1. all laundry done by other
    2. does laundry with assistance or assists other with laundry
    3. does small amounts of personal laundry
    4. does own laundry (or household laundry) independently ___ ___

18. Does he/she look after any of the housekeeping in the home?

1. all housekeeping done by other
2. performs day-to-day tasks under supervision or cannot maintain acceptable levels of cleanliness
3. performs day-to-day tasks with acceptable level of cleanliness without supervision
4. maintains home alone or with occasional assistance ___ ___

19. Does he/she receive any assistance with personal care?
    1. requires supervision in all aspects of personal care
    2. receives assistance in selecting clothing, planning bath, etc.
    3. bathes, changes clothes regularly without prompting or assistance; dresses appropriately for weather
    4. all requirements met and pays attention to grooming details ___ ___

Transportation

Categories: 1. walks 2. bus 3. bicycle 4. drives self
5. driven by other 6. taxi 7. other

20. How does he/she usually travel?
    to buy groceries and other essentials? ___
    to medical services? ___
    to work/school? to recreational outings? ___
    to visit friends or family? ___

21. Does he/she have a valid driver's license? 0.No 1. Yes ___ ___

22. City bus travel:
    1. does not use the bus
    2. travels only with assistance or accompanied by another
    3. independent with familiar routes, needs assistance with unfamiliar routes
    4. knowledgeable and uses bus independently ___ ___

C. Employment/Meaningful Activity

Current employment/financial situation

23. What is his/her current employment status?
    1. full-time regular employment
    2. part-time regular employment
    3. casual or contract employment
    4. sheltered employment
    5. pre-employment assessment/training (SAC, Manpower, TOJ, etc.)
    6. sick leave
    7. unemployed
    8. retired
    9. homemaker ___ ___

24. What is his/her current occupation? (if working)

_____ category code: ___ ___

25. How long has he/she had this position? (# of months) ___ ___

26. How many hours per week does he/she work? ___ ___

27. What is his/her primary source of income?
    1. employment
    2. social assistance
    3. unemployment insurance
    4. disability
    5. workers compensation
    6. family
    7. other: _____ ___ ___

28. Does he/she have any other main source of income?

_____ code from above: ___ ___

29. What is his/her average annual personal income?

1. up to $1000	5. up to $20 000
2. up to $5000	6. up to $25 000
3. up to $10 000	7. up to $30 000
4. up to $15 000	8. over $30 000

___ ___

30. How does he/she manage money?
    1. all personal financial matters handled by other
    2. handles small amounts of money, does not bank or lends/borrows inappropriately
    3. manages day-to-day purchases but needs help with banking, major purchases, etc.
    4 manages finances independently: budgets, pays bills, goes to bank, keeps track of income, etc.

___ ___

<u>Unpaid meaningful activities</u>

Key: 0.No 1 Yes (part-time) 2.Yes (full-time)

31. Is he/she currently going to school? ___ ___

32. How much do you (participant) like your current work situation? (paid or unpaid work activities) ___ ___

What would you like to do if you could get a job?

_____

Social/recreational activities

33. What kinds of social/recreational activities/groups has he/she been involved in?
    __church services or groups
    __ self-help groups
    __member of Sask. Mental Health Association
    __ volunteer organizations; political/professional associations; local boards/executives
    __ special interest groups (e.g., chess, drama, choir)
    __ sports activities or recreational groups (e.g., curling, biking)
    __ socializing with friends or relatives
    __ solitary activities (e.g., hobbies, crafts, reading)
    __ Other: _____

34. How satisfied are you (subject) with your current involvement in social and recreational activities?

    _____

35. Leisure time management/planning:
    1. all time management done by others or not at all
    2. plans very little, would spend majority of time in room, etc.
    3. plans activities with assistance, keeps to a schedule
    4. independently plans and schedules leisure activities

    ___ ___

D. Mental Health Services

Medication management

36. What medications is he/she currently taking? _____
_____

37. Who usually keeps track of or administers oral medications?
    1. self-administered
    2. family member
    3. landlady
    4. home care nurse
    5. physician
    6. other: _____ ___ ___

E. General Health and Lifestyle

38. Smoking status: 0.Never smoked 1 Ex-smoker 2.Current smoke ___ ___

39. How many cigarettes does he/she smoke per day? ___ ___

40. How many times per week does he/she exercise? ___ ___

41. How many alcoholic drinks does he/she have in a day/week/month? (1 drink = 1 beer, 4oz glass of wine, 1 oz liquor) ___ ___

Alcohol problems:

Has he/she had job or school troubles because of drinking or drugs? _____

42. Has he/she ever been charged with a criminal offence? 0. No 1. Yes ___ ___

43. When was the last time he/she saw a family doctor for physical concerns (or a physical check-up)?
    1. within the past year
    2. 1-2 years ago
    3. 2-5 years ago
    4. more than 5 years ago

    ___ ___

44. When was the last time he/she saw an optometrist or opthamologist? (use codes from above) ___ ___

45. Has he/she ever had a serious accident or assault resulting in head injury with a loss of consciousness? 0.No 1 Yes ___ ___
    If yes, at what age? _____

46. Does he/she have any of the following conditions or disorders? (check)

__ Arthritis/Rheumatism/Bursitis
__ Cancer
__ Epilepsy/Convulsions/Seizure
__ Headaches (severe)
__ Heart disease/attack/angina
__ High Blood Pressure
__ Diabetes
__ Kidney/Liver trouble
__ Hearing loss
__ Strokes
__ Stomach Trouble/Ulcer/ Gallbladder
__ Surgery in last 6 months
__ Thyroid disease
__ Respiratory problems (Emphysema, Asthma, Bronchitis, persistent cough, shortness of breath)
__ Other:_____
__ Other:_____

# of health complaints ___ ___

47. Is he/she experiencing any difficulties with sleep?
    __ insomnia _____
    __ excessive daytime sleeping _____
    __day/night reversals _____
    __ other

Rating of sleep difficulties:
1. not at all 2. a little 3. moderately 4. quite a bit 5. extremely ___ ___

48. Physical health management (neglect):
    1. neglects genuine physical health problems
    2. inadequate approach to health management
    3. complies when directed by other or when seriously ill; physically well but does not make preventative appointments
    4. looks after legitimate physical concerns promptly; has regular preventative appointments

___ ___

APPENDIX B Talland Letter Cancellation Test

Talland Letter Cancellation Test (Talland, 1965).

Letter Cancellation Test

6 pages of letters
Stopwatch
Pen (nonerasable)

Instructions

CAPS First sheet (starts with ur) "In this test, you are to look for the capital letters and mark each one with a slash. Go across the lines, from left to right, one after the other, marking the capital letters as quickly as you can. Try not to miss any." Show, on the last line, how to mark it, and also, if an error has been made, how to indicate it by making another slash so the mark becomes a cross. "Go ahead." Stop after 60 seconds and indicate the subject's place.

Second sheet (starts with wb) "You are going to do the same thing on this sheet as you did on the last one; mark all capital letters." "Go ahead." Stop after 60 seconds; mark where the subject ended.

SPACES Third sheet (starts with Oa) "This time, you are to look for the double spaces (show them on the last line), and mark the letter that precedes and the one that follows the double space" (show them on the last line). "Go as quickly as you can without missing any. Go ahead." Stop after 60 seconds; mark where the subject ended.

Fourth sheet (starts with t o) "This is another sheet on which to look for the double spaces. Mark the letters before and after the double space, just the way you did on the last page. Go ahead." Stop after 60 seconds; mark where the subject ended.

BOTH Fifth sheet (starts with uS) "Now you have to do both tasks at once; mark the capital letters as well as the letters before and after double spaces. Go ahead." Stop after 60 seconds; mark where the subject ended.

Sixth sheet (starts with u d) "This is a last sheet, just like the one before. Mark the capital letters and the letters before and after the double spaces. Go ahead." Stop after 60 seconds; mark where the subject ended.

Scoring

There are 36 letters per line, 10 of which are capital letters; there are four double spaces per line. The number correct is the number of letters correctly marked. (Scoring templates are helpful, especially for the third task. One can use transparency sheets and a special marking pen to indicate correct answers.)

w b i L m p p h c g m r A f v I Z a d f j r y c Z M e F I w k s w X i D
c n p d t U v l h z h r t b v S m x B G s F y z k b I v E E Q c u N i k
o x k G e X t c o j W i l r r s r O k L z i f t x c i n S h Z V Z y f W
t v X L x u a l Y u n q s s x n o r h j s G H B z d t D T a b d f d B H

c B y v x a v a q m v Z L w z F g x l l A R r j W p H v R r y B v y e u
u j T b q A f w r l i n b n a A J c Q W p X g i W B a g G y h e l w g i
y b s q T o z g s v o N x g r E P U m q q z Z D a R f r d o h g t M z M
w t y d d o H n W v X i z v D l Q n B q h e y T k m o i f a v K h W z S

i d C f j n u R f d A i M f j j m L f r b D p t T B m V v d s y z c X m
w j Y y F b d f V l p l U b O p w o u m Q l i E H k i F y u l b f F v g
t z t v s n M i d S l M p p D R j c u v g A j i r E n q m Y k v A l z G
S x h m w W x o a r z y p v y G q e i v r O j C c J B H m r y G o j n U

b h b K t W Z o j a m q m j Q X v c h N c c i l D z a V r C L i y w u c
f P E j k N R n l i W c h g o j Z M l H p n D j v r t e z t J z d t z a
g C c g a k J P b b y f f V X g z j s o e v a d V u Z n n j V d J h N z
J C l f p i B Y a J z j c S p d n d m m f K c Q m F i o l g c p a L u m

wbiLmpp h cgmrAfvIZadfj ryczMeFI wkswXiD
cnpdt Uvlh zhrtbvSm xBGsFyzkbIvEE QcuNik
oxkGeXtcojWil rrs rOkLziftxcin ShZVZy fW
tvXLxualYu nqssxnorhjsGH Bzdt DT abdfdBH

c Byvxavaqmvz LwzFgxllA Rr jWpHvR ryBvyeu
ujTbqAfwrlinb naA JcQWpXgiWBagGy helw gi
y bs qT ozgsvoNxgrEPUmqqzZDaRfrdoh gtMzM
wty dd oHnW vX izvDlQnBqheyTkmoifavKhWzS

idC fjnuRf dAiMfjjmLfr bDptTBmV vdsyzcXm
wjYyF bdfVlplUb OpwoumQliEHk iFyulb fFvg
tztvsnM idSlMppDRjc uvgAjirEn qmY kvAlzG
SxhmwWxoar zypvy GqeivrOjCcJBH mryG ojnU

b hb KtWZojamqmjQXv chNc cilDzaVrCLiywuc
fPEjkNR nliWchgojZ MlH pnDjvrtezt Jzdtz a
gCcga kJPbbyf f VXgzjsoev adVuZnnjVdJhNz
JClfpiBYaJzjc Spdndmm fKcQmFio lgcp aLum

O a j l P A y x x N f j V d q w z l r f S W o o F y v r s Y G n e z b y
w u Y S U d c a x q T j c g q g o z x g e M t W z g V e v N d X r u z B
Z c n s h e K r y W O c r Y l Z Q j m x s g i v V f o C x f f z z R w c
q X c f a v j h Y h a E m D d f O c j j m R z m b R a g s c S y m z G U

y c k b C l y y k y f m b i u q n t i n v v y x T L L S m M Z N Q t h W
j V C a v z w k t q o E i f d d l w t c y B a M L d e c M M l K R g b w
d y b r v d X g s S i g X f Y W h e r T W c p U n T X u j b w z b z d j
V w j t g r u g r k U x f Y m m g l M H I C x g N u u u y Z y f e Q z l

o U s d g v o k t N Y p K c O y L h a c n h r m m K Y x P h r z Y k b c
E h g v y u q C t w s u d j z Y k g q b A Z c V a Y w e j Z r X I x y k
w g i w d o D Q J e o h m x n k o b M r V r m E f z U u k y k m V b L S
d b v z l d q e r i d g u K w L G K j y r c r e A k L i V S p v T t k Z

K L q t X u k G f z r k o h j w w z g y v a h a b f B E p v N I b Y a P
R s l r f v l r d m e z Q p n i a P i m N j g I A E w G o r w B j T x
k g a D p d v S N q z t q J U t a e w a b c r n i v x f e N L C u K U f
L s g a n s E I Q f s h T e I b s c k j d m l c z k H s t q r i S R C e

t o J x M z m K y R z l a w r d v H t a u m E k s m e w E z M V r b P p
x a X g p n a E Q l b z I o m X g u x b l q o d i j K S x l l k T D Q r
r v Z t y j s n i o r c y H q j y E M Y n S q v g A v R i x m M x p U e
o t r p n m l l g y l a v e E N B Q w F M k u s y n I a Z y v n z U Y p

l K b r t A m t L A G a o c z h p S D b t V y v E j h g i J h j n n d o
b O v f D t y h v P p v o d N p e K M t n e Z b A y T w r S o v d l q r
M f r j Y n S u l a z k m V A c G N w y A p f x q a y o u y a F N s s h
l e q b w x s M z h l f X G h B n o j y g L Z V a w u C f f j h S e I o

K t l r k i Z u Z q l w w a L k w i J m j l v q E k r O u s V g H j T q
e k Y i N x I s m k p E t Y K d g t e x e f h N S q m q q G e u w V u v
j c R r i a x h g R D b E j w j z P B v a X j t X f s h o Z e m v m Q h
c e r E o c x d M k c L c x o v B F A R g n G g g v r D f r n l y A b t

b x x R y r b V G b f r y m c c p c L W k S b J Q S o a z M q y p l y e
h u z h v j w u g o P x u W X n l r i B q l U U p N x P v a z F N n d e
R v c e d R r q d x t N j O V C u i i t L d R e L u m s c l c j U y r o
e e U Q f b E M a O t v v b M E F g h O e e s b Z c h p o b k d y n c p

u d q C g b P X F n M U i w T e j b m l t c q z Y n v e n g B s x R z t
u o r w P g j Z e L l f l T q a j x R V n t l w g S a h G q f c r G A m
s u o h w n p k F x m k y r F x N Q A v i E F m l U d r t i D w h f A s
J G f o r z m y D t r M i y X y w y t f p b J E r J c F o e D t d j g c

s F g d x r c H o m b u z G x k I W s s s g R j n t B h q Q r y w N Z j
e s w q Z w I x B w h u t m M r o v m j n q w X h X y h a O g m U z M O
b G p Z q b L p k J j x n o v f s X z v w J u A e q b p A X l f H f a t
Z j I i U b k a u r t b g t l Z p q D H i u d E I Y n a i i r n n k R q

c L z y v k G i u c o d b v N C m z y s s t O y a I d t X o H u G n C m
r i k o Q j m G z u D V M k d p x o w P s g U l g w M s l Y s T m a n t
r A e x j j y q s h i C w s F P e h c Q d X x r b B Y o T u E q j h z l
l W Q E p s A V w W I c r g x m u f e a f t r x p Z m u m n R d z e o G

t h p n h c K F f o z L T Q D t m O v k e r o n w u F k J s m d i F i w
i j J u d A l h t p B a U w H r M s g o p v W d q U i t Q e m j h s f K
u i j a P t L e o l y x R r P n z P r i q w K o z h c x k t l o K J C Y
L n Q m c J k v d w m h i v z I f j w n t p L W h p a z N h u e O u Z T

APPENDIX C Underlining Test

Underlining Test (1983).

Subtest 1: Underline the 4.

Example: 1 8 9 4 2 7 6 4 3 5

Practice:

9 8 2 5 4 7 3 1 2 6 5 8 3 7 4 1 9 2 6 3

2 1 4 3 2 7 1 3 8 5 1 1 6 1 9 6 7 4 2 7

Hits ☐ (No norms available)

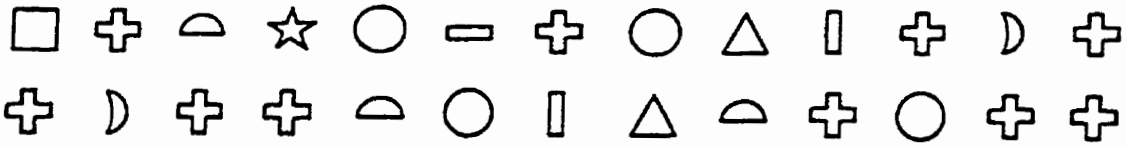
	Time	Errors of Commission	Net Correct	Rate
S				
T	30		Net Correct = Hits − Errors of Commission	Rate = Time ÷ Net Correct

Errors of Omission ☐ (No norms avail.)

Subtest 2: Underline the 

Example: 

Practice:



Hits ☐ (No norms available)

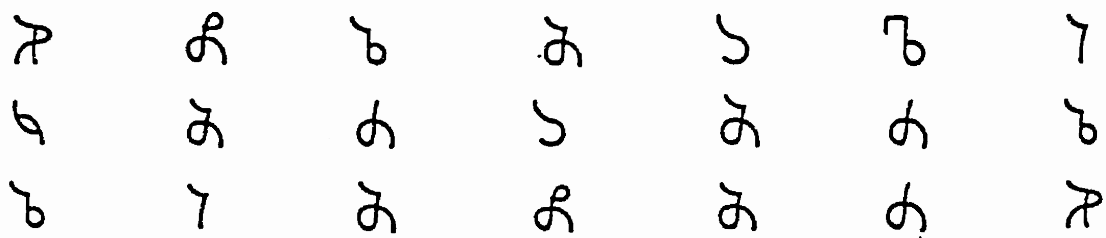
	Time Completed	Errors of Commission	Net Correct	Rate
S				
T	30		Net Correct = Hits - Errors of Commission	Rate = Time + Net Correct

Errors of Omission ☐ (No norms avail.)

Subtest 3: Underline the 

Example: 

Practice:



Hits ☐ (No norms available)

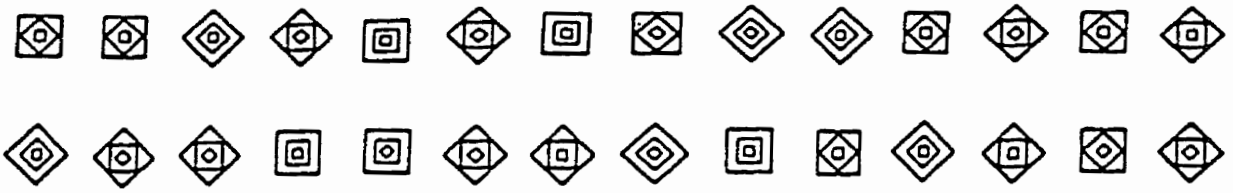
	Time Completed	Errors of Commission	Net Correct	Rate
S				
T	30		Net Correct = Hits − Errors of Commission	Rate = Time ÷ Net Correct

Errors of Omission ☐ (No norms avail.)

Subtest 4: Underline the 

Example: 

Practice:



Hits ____ (No norms available)

	Time Completed	Errors of Commission	Net Correct	Rate
S				
T	60		Net Correct = Hits - Errors of Commission	Rate = Time ÷ Net Correct

Errors of Omission ____ (No norms avail.)

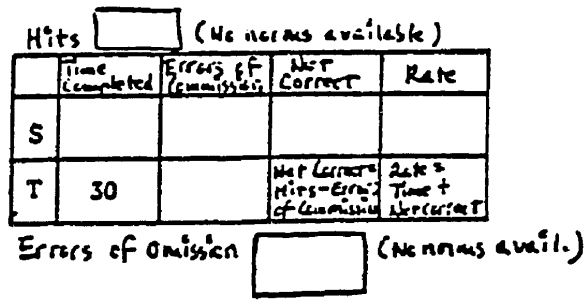
Subtest 5: Underline the s.

Example: v u s p f t s e s u c d

Practice:

s u c d j y c s s e h q g s k a s x u j

f g f s h r z y o h o s j s x n y h w m



Subtest 13: Underline the S

Example: 1 8 0 S 2 7 6 S 3 4

Practice:

9 8 2 4 5 7 3 1 2 6 4 8 3 7 5 1 9 2 6 3

2 1 4 3 2 7 1 3 8 5 1 1 6 1 9 6 7 5 2 7

Hits ☐ (No norms available)

	Time Completed	Errors of Omission	Net Correct	Rate
S				
T	30		Total Hits - Errors of Omission	Rate = Time ÷ Net Correct

Errors of Omission ☐ (No norms avail.)

APPENDIX D Continuous Processing Test

Sample Output from the Continuous Processing Test (CPT; Rosevald, Mirsky, Bransome, & Beck, 1956).

```
*SUNRISE SYSTEMS, INC. CPT VERSION 2.23 OUTPUT FILE: dx51.CPT
#MINISI=800
#MAXISI=800
#STDUR =200
#ART  =950
#CSPROB=20
#CSLIM =76
#ETLIM =240
#REINF =OFF
#TASKMD=X-RTS
#TRMAUD=YES
#TODISK=LOG+SC
#VISSET=STANDARD-XAX
#MSKSET=random30.VMF
#VSDGRD=FGND/BKGND SPINS
#AUDSET=SILENT
#SUBJCT=subject name/0000
#ADMIN =your name
#STIMSQ=PSEUDORANDOM/00-15
#NOTES =Degraded X task
#DATE  =08-12-97
#TIME  =23:09:39

>START 23:09:39
 M  /M10
 F  /M9
 B  /M5  @0.09IT
 F  /M6
 A  /M14 @0.67I
 E  /M13
+X  /M7  @0.53RC
+X  /M7  @0.47RC
 E  /M14
 A  /M12
+X  /M15 @0.49RC
 A  /M1
 N  /M7
 N  /M5
 L  /M4
 N  /M7
 A  /M1
+X  /M11 @0.54RC
 A  /M12
 F  /M10
 C  /M1
 E  /M14
 N  /M14
 E  /M10
+X  /M12 @0.51RC
 A  /M10
 C  /M6
+X  /M4  @0.46RC
 P  /M14
 F  /M13 @0.63I
```

```
F /M0
+X /M1 @0.70RC
A /M0
E /M11
N /M14
C /M0
A /M5
L /M13
B /M0
+X /M15 @0.38RC
N /M7
L /M14
L /M5
P /M0
C /M5
P /M15
+X /M15 @0.43RC
+X /M15 @0.57RC
F /M6
C /M3
L /M10
M /M3
M /M14
N /M3
M /M12
B /M2
N /M13 @0.501
N /M5
+X /M5 @0.56RC
+X /M11 @0.59RC
+X /M4 @0.65RC
C /M14
C /M2
B /M15
E /M11
M /M4
M /M5
N /M4
N /M1
+X /M6 @0.51RC
E /M14
B /M15
L /M2
A /M4
B /M2
+X /M13 @0.68RC
N /M14
A /M0
+X /M6  O
N /M14
+X /M9 @0.70RC
P /M5
B /M9
M /M2
N /M8
```

```
 F /M1
 F /M10
 L /M12
+X /M2 @0.50RC
 C /M7
 N /M0
 M /M14
 L /M2
 L /M15
+X /M4 @0.47RC
+X /M12 @0.60RC
 C /M2
 E /M6
 L /M12
 C /M10
 M /M0
 E /M8
 N /M12
 A /M0
 N /M13
 E /M10
 N /M14
+X /M8 @0.51RC
 E /M4
+X /M11 @0.57RC
 E /M3
 N /M8
 L /M3
 L /M3
+X /M4   O
 E /M8
+X /M0   O
 F /M10
 P /M15
 P /M4
 E /M4
 A /M2
+X /M14 @0.50RC
+X /M5   O
 B /M8
 P /M3
 M /M10
 P /M0
 C /M10
 M /M10
 B /M9
 B /M10
 B /M2
 M /M15
 C /M3
 A /M3
+X /M13 @0.55RC
 N /M12
+X /M2 @0.75RC
 M /M3
```

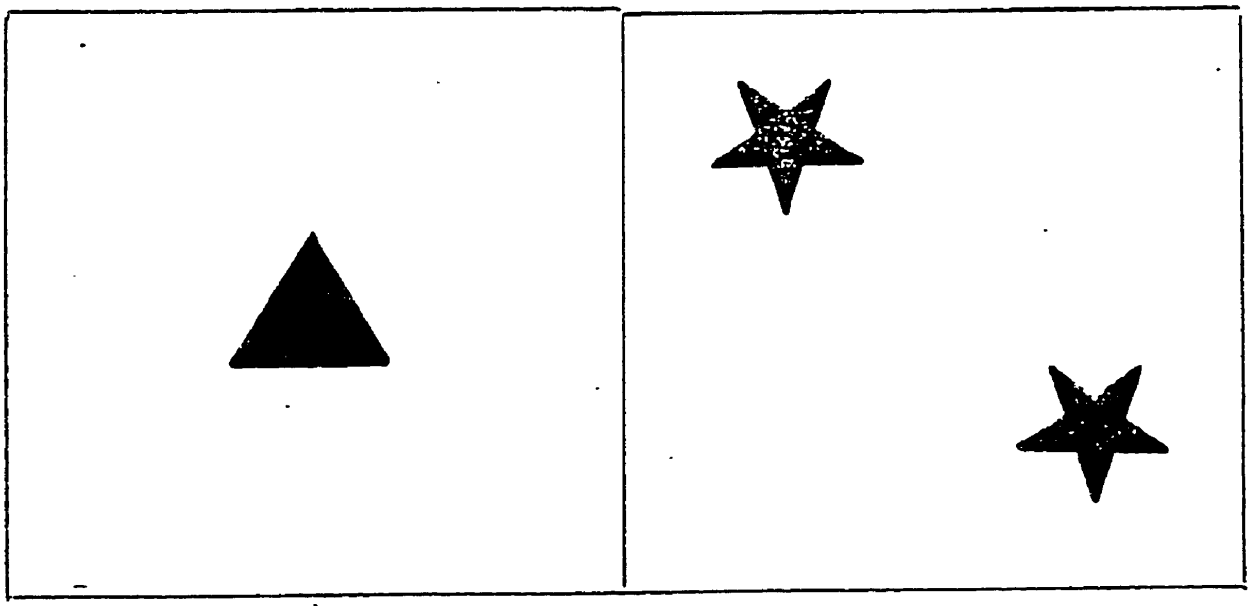
```
 L /M11
+X /M6   O
 C /M0
 C /M4
 E /M2
 A /M14
+X /M7 @0.64RC
 F /M12
 E /M3
 B /M10
 M /M3
 F /M7
+X /M12 @0.64RC
 C /M12
 M /M12
 P /M11
+X /M11 @0.51RC
 P /M15
 L /M0
 C /M7
 F /M5
+X /M4 @0.39RC
 L /M2
 F /M3
 M /M9
+X /M14   O
 C /M13
 A /M11
 A /M8
 N /M1
 P /M13
 C /M12
+X /M11 @0.52RC
 N /M4
+X /M4   O
 P /M13
 C /M10
 E /M10
 M /M11
 L /M3
+X /M12   O
 P /M7
 E /M14
 F /M11
 N /M5
 N /M5
+X /M8   O
 E /M15
 F /M11
 B /M5
 C /M10
 N /M2
 L /M8
 B /M15
 M /M12
```

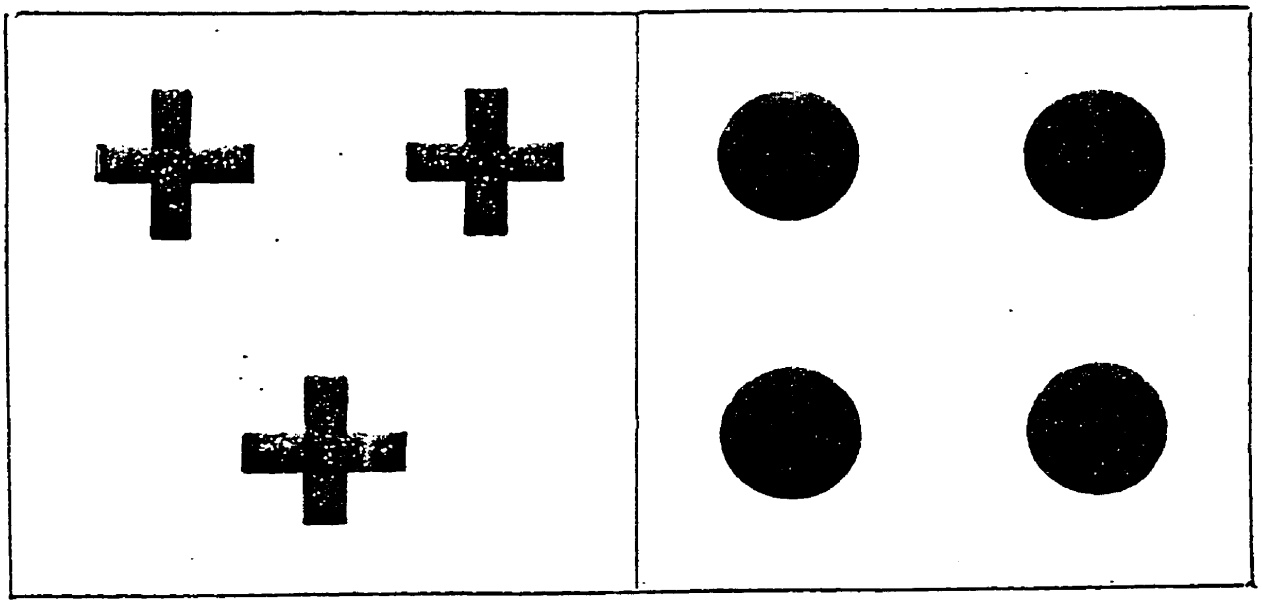
```
+X /M0    O
+X /M5  @0.49RC
 L /M9
 P /M13
 P /M2
 E /M14
 P /M13
+X /M4    O
 L /M15
 C /M0
 L /M13
 P /M13
+X /M15 @0.59RC
 N /M2
 C /M6
 M /M14
 P /M9
+X /M3  @0.55RC
 L /M15
 L /M0
+X /M12 @0.47RC
 P /M10
 F /M6
 C /M3
 L /M15
+X /M3  @0.77RC
 L /M12
 E /M7
 E /M6
+X /M14 @0.60RC
 P /M15
 E /M1
 E /M14
 A /M6
 L /M13
+X /M0  @0.45RC
 L /M11
 L /M10
 E /M4
 E /M3
 F /M15
+X /M1    O
 E /M12
 L /M0
 A /M8
 N /M10
 M /M3
 P /M6
 N /M6
 C /M10
 B /M8
 F /M5
 C /M3
+X /M9    O
+X /M13 @0.49RC
```

```
>STOP 23:13:47

$ETIME   =247
$STIMS   =250
$CRITS   =50
$CORRS  C=37
$LATES  L=0
$INCORS I=4
$VLCORS V=0
$INCA   A=0
$INCANX N=0
$VFRTOT T=1
$VFRPBA P=0
$VFRCOR K=0
$OMISSN O=13
$MTTR    =54
$VTTR    =87
$MTTRC   =54
$VTTRC   =87
$NMVRC  R=37

[END OF FILE]
□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
□□□□□□□□□□□
```





APPENDIX F Ethics Approval Letters

University of Saskatchewan
Advisory Committee on Ethics in Human Experimentation

January 5, 1996

Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	EC #
J.Nanson	Psychology	95-183

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT

CO-INVESTIGATORS

SPONSORING AGENCIES

Roeher Institute

TITLE:

AR Investigation of the Long-term Neuropsychological and Psychosocial Outcome of Prenatal Teratogenic Exposure: Fetal Alcohol Syndrome and Maternal PKU Syndrome

APPROVAL DATE MODIFICATION OF:	TERM (YEARS)	AMENDED:
January 5, 1996	3	

CERTIFICATION:

The protocol and consent form for the above-named project have been reviewed by the Committee and the experimental procedures were found to be acceptable on ethical grounds for research involving human subjects.

APPROVED.

E.A. McKenna, Chair
University Advisory Committee on
Ethics in Human Experimentation

This Certificate of Approval is valid for the above term provided there is no change in the experimental procedures

Please send all correspondence to: Office of Research Services, Room 210 Kirk Hall, University of Saskatchewan, 117 Science Place, Saskatoon, 8K 57N 5C8

Saskatoon District Health
Research Development
Information Systems and Research Division
Site: Royal University Hospital, 103 Hospital Drive, Saskatoon, Sask. S7N 0W8
Ian D.Sutherland, Director Ph: 655-1023 Fax: 665-1037

February 22, 1996

Dr. Jo Nanson, Psychology
Kinsmen Children's Centre
1319 Colony Street
Saskatoon, Saskatchewan
S7N2Z1

RE: **Research Project #95115 (UofS 95-183) (J. Nanson):** An investigation of the long-term neuropsychological and psychosocial outcome of Prenatal Teratogenic Exposure: FAS and MPKUS.

The above mentioned research project is now approved for implementation.

Please advise me when the data collection phase of the research project is completed. Also, I would appreciate receiving a copy of the final report of this research project.

I would like to wish you every success with your project an encourage you to contact me if I can assist you with it.

Ian D. Sutherland
Director of Research Development

IS/dw/aprovsdh.doc
cc. Dr J Cheesman, Head, Dept. of Psychology, 9 Campus Drive, S7N 5A5
dd. Ms. McCulloch, Health Records (RUH)

Committee On Clinical Investigation
Children's Hospital
Boston, MA

To: Susan Waisbren, PhD

From: Susan Kornetsky, Manager
Committee On Clinical Investigation

Date: April 24,1997

Notice of Final Approval-- April 24,1997

Protocol 97-02-028

AN INVESTIGATION OF THE LONG TERM NEUROPSYCHOLOGICAL AND PSYCHOLOGICAL OUTCOME OF MATERNAL PKU SYNDROME

Thank you for responding to the Committee's questions and concerns regarding the above referenced protocol. Final approval has been granted. Risks were determined to be minimal with little potential for direct benefit therefore assent of all adolescents capable of understanding the research and its ramifications should be obtained in addition to parental consent. The informed consent was approved.

The Committee does ask that the recruitment letter be revised to include that statement that if subjects are on medications. they may be asked to discontinue them for 12 hours prior to testing. Please revise the letter and send us a final copy for our files.

The consent form has been placed in our central computer system. I am returning your disk with the final, approved copy included. Please be sure to use the final IRB approved consent. Expiration dates are now included in the consent. Enclosed is a copy of the approved informed consent. Please make duplicate copies as required.

The occurrence of any adverse or unanticipated events should be reported to this office. This includes subject complaints. Any revisions or amendments must also be submitted for review before they are initiated. The Committee has asked me to notify all investigators that protocol and research files are subject to audit at any time.

Enclosures: consent & disk

cc: Dr. Wolff
Dr. Beardslee

APPENDIX G Letters To Participants And Caregivers

Parent/Guardian Request for Participation Letter and Consent Form.

Dear Parent/Guardian

My name is Susan Brock and I am a Ph.D. student in the department of psychology at the University of Saskatchewan. Along with two colleagues and my supervisor I am planning to carry out a large research study which will examine the memory, attention, language, and psychosocial functioning of adults with Fetal Alcohol Syndrome (FAS) or Maternal PKU Syndrome (MPKUS).

Enclosed you will find a description of the study and a copy of the consent form that I will be asking each participant and their parent and/or guardian to sign prior to taking part in this project. I will contact you by telephone within the next two weeks to request participation. For individuals living outside the general area of Saskatoon, I will provide funding for transportation and accommodation. Each participant will receive a small honorarium for their participation in the study.

Sincerely,

Susan R. Brock, M.A.

Consent Form.

Request for Participation and Consent Form for Individuals with FAS or MPKUS and their CA plus IQ-matched Controls.

Dear

I am interested in learning more about people with Fetal Alcohol Syndrome (FAS) and Maternal Phenylketonuria Syndrome (MPKUS).

I would like to invite you to take part in my project, which will take place at the Kinsmen Children's Centre in Saskatoon. The purpose of the project is to learn more about the memory, attention, language, and psychosocial functioning of adults with FAS and MPKUS. Individuals with FAS or MPKUS will be compared to persons of the same age with similar cognitive abilities.

If you agree to take part in my study, we would meet for a few hours on two different days. We will take several breaks while we are working and I will provide drinks and snacks. Lunch will also be provided in the cafeteria on both days. Taking part in this study is voluntary, which means that you may stop at any time. I hope that you will agree to be part of my study. I look forward to meeting you.

I_____, agree to take part in the study on FAS/MPKUS. It has been explained to me that I can quit any time.

Signed: _____

Date: _____

Children's Hospital
IC Smith - Room 106
300 Longwood Avenue
Boston, MA 02115
617-355-6346 (tel)
617-730-04~ (fax)

Children's Hospital

Northeastern Contributing Centre

INTRODUCTORY LETTER TO MPKU PARTICIPANTS

Maternal PKU
Collaborative Study

Harvey L. Levy, M. D.
Principal Investigator

Susan E. Waisbren, Ph.D.
Co-Investigator

Deborah Lobbregt, B.S.
Coordinator

Dear:

In the past we conducted a study on children born to mothers with PKU or hyperphenylalaninemia (maternal PKU). We are now conducting a follow-up study to see how things are going for adults whose mothers had PKU or some degree of hyperphenylalaninemia. As you may remember, you and your mother were involved in the previous study. We would like to invite you to participate once again. This time we are interested in learning more about your attention span and memory skills, your ability to manage day-to-day responsibilities and what you do or fun.

If you decide to participate in the study, you will be asked to complete a variety of tasks. These you can fill out to tell us about yourself, some memory tests, some tasks to measure your fine motor and visual motor skills, and a reading and arithmetic test. Some tests require verbal answers and some involve putting together puzzles, copying geometric designs from pictures or pushing a button in response to a specific letter being presented on a computer screen. There are also questionnaires focused on social and emotional well being. Some of the individual questions may be viewed as sensitive and you do not need to answer any questions that make you uncomfortable.

The research project will take between 3 1/2 and 6 hours of your time, depending on how many breaks you would like to have. You will be provided with a lunch break and several other breaks. If

you agree to take part in this study, we would arrange to meet you either at your home or some place else convenient to you. We will reimburse you for any travel costs.

The person who will administer the various tests is Ms. Brock, who is a graduate student from the University of Saskatchewan in Canada and is spending a year in Boston for further training. She has conducted this study in Canada and would like to continue to study the long-term effects of maternal PKU.

Enclosed you will find a copy of the consent form that we will be asking each subject to sign prior to taking part in this project. We will contact you by telephone within the next two weeks to request participation and to answer any questions you might have about the study. We can arrange to meet you either in your home or we will cover transportation costs for you to come to Boston or another location convenient to you. If you do not wish to be contacted, simply return the enclosed self-addressed, stamped envelope to us.

The benefits to you in participating in this study are to learn more about yourself, what tasks you do well and what tasks are difficult for you. Further, many individuals have found the tasks to be interesting and fun. Taking part in this study is voluntary, which means that you may stop at any time. We hope that you will agree to be part of the study. We look forward to hearing from you.

Sincerely,

Susan Waisbren, Ph.D. Harvey L. Levy, M.D.

Susan R. Brock, M.A.
Psychology Intern

Children's Hospital
IC Smith - Room 106
300 Longwood Avenue
Boston, MA 02115
617-355-6346 (tel)
617-730-0461 (fax)

Children's Hospital

Northeastern Contributing Center

Maternal PKU
Collaborative Study

Harvey L. Levy, M.D.
Principal Investigator

Susan E. Waisbren, Ph.D.
Co-Investigator

Deborah Lobbregt, B.S.
Coordinator

LETTER TO CONTROL PARTICIPANTS

Dear:

We are conducting a study to evaluate the functioning of adults whose mothers had a rare metabolic disorder, called phenylketonuria or PKU. Some of these individuals have had difficulties in school and adjusting to work. In order to see if there is a particular pattern to the types of difficulties they are having, we would like to evaluate a group of other individuals whose mothers did not have PKU, but who may have some other types of difficulties or learning disabilities. That is why we are contacting you.

We would like to invite you to participate in this study. We are interested in learning more about your attention span and memory skills, your ability to manage day-to-day responsibilities, and what you do for fun. If you decide to participate in the study, you will be asked to complete a variety of tasks. These include a test of intelligence, several checklists that you can fill out to tell us about yourself, some memory tests, some tasks to measure your fine motor and visual motor skills, and a reading and arithmetic test. Some tests require verbal answers and some involve putting together puzzles, copying geometric designs from pictures or pushing a button in response to a specific letter being presented on a computer screen. There are also questionnaires focused on social and

emotional well being. Some of the individual questions may be viewed as sensitive and you do not need to answer any questions that make you uncomfortable.

The research project will take between 3 1/2 and 6 hours of your time, depending on how many breaks you would like to have. You will be provided with a lunch break and several other breaks. If you agree to take part in this study, we would arrange to meet you either at your home or some place else convenient to you. We will reimburse you for any travel costs.

The person who will administer the various tests is Ms. Brock, who is a graduate student from the University of Saskatchewan in Canada and is spending a year in Boston for further training. She has conducted this study in Canada and would like to continue to study the long-term effects of maternal PKU.

Enclosed you will find a copy of the consent form that we will be asking each subject to sign prior to taking part in this project. We will contact you by telephone within the next two weeks to request participation and to answer any questions you might have about the study. We can arrange to meet you either in your home or we will cover transportation costs for you to come to Boston or another location convenient to you. If you do not wish to be contacted, simply return the enclosed self-addressed, stamped envelope to us.

The benefits to you in participating in this study are to learn more about yourself, what tasks you do well and what tasks are difficult for you. Further, many individuals have found the tasks to be interesting and fun. Taking part in this study is voluntary, which means that you may stop at any time. We hope that you will agree to be part of the study. We look forward to hearing from you.

Sincerely,

Susan Waisbren, Ph.D.

Harvey L. Levy, M.D.

Susan R. Brock, M.A.
Psychology Intern

APPENDIX H Consent Form

Parent/ Guardian Consent Form

Researchers: Susan Brock, M.A.
Ph. D. student, Department of Psychology
University of Saskatchewan
Phone: (306) 652-8252

Laura Carney, S-LP, Reg.
Speech and Language Rehabilitation Department
Saskatoon City Hospital

Myrna Willick, B.A.
Master's Student, Department of Psychology
University of Saskatchewan

Supervisor: Jo Nanson, Ph. D.
Registered Psychologist
Kinsmen Children's Centre

Title of Project: The Long-term Neuropsychological and Psychosocial Outcome of Prenatal Teratogenic Exposure: Fetal Syndrome and maternal PKU Syndrome.

Description of the Study: The purpose of the present study is to increase our understanding of the memory, attention, language, and psychosocial functioning o adults with either Fetal Alcohol Syndrome (FAS) or Maternal Phenylketonuria Syndrome (MKUS). Individuals with FAS or MPKUS will be compared to a group of individuals matched for age and cognitive ability. This will allow for a clearer understanding of the pattern of strengths and weaknesses associated specifically with FAS and MPKUS. Although we have some knowledge regarding the pattern of deficits seen in children diagnosed with FAS or MPKUS, there is little information available on how these individuals function as adults. In order to develop interventions and support services for these adult individuals, we must first identify how their pattern of strengths and deficits may differ from individuals with other developmental disabilities. For example, it is well documented that there are some individuals with FAS who have an IQ score that falls within the average or low average range who still have significant difficulties in their day-to-day functioning. However, because an IQ level below 70 is typically the cutoff for special assistance/programming, these individuals may not qualify for the help that they need. Data concerning

the adult functioning of individuals with FAS and MPKUS will provide impetus for community assistance/programs designed to meet their ongoing needs as adults

The study will involve a large battery of tests that will be administered to all participants. The entire study will be conducted at Kinsmen Children's Centre and will take approximately eight hours. Testing will be carried out over a two day period with several scheduled breaks throughout the testing periods.

Benefits to the Participants: Current assessment of their individual pattern of strengths and weaknesses across several cognitive areas as well as an assessment of social and emotional functioning.

Possible Risks: The participant may become tired.

Anonymity: Although we may publish the results of the data from this study, we will maintain the anonymity and confidentiality of the participants. Names of the participants and other identifying information will not be released without written permission, unless required by law.

Participation: Participation is strictly voluntary. You may withdraw from the study at any time during testing.

Feedback: Following participation, I will provide participants with information concerning the study and answer any questions they or their parent(s)/guardian(s) might have. As well, I will provide additional information in written form at that time which can be taken home. Once the study is complete, I will make information concerning the results available if participants so desire.

I_____ (parent of guardian) understand the contents of this document as explained to me. I hereby give my consent for _____ to participate in the study described above.

Signed: _____

Date: _____

Children's Hospital
Boston, Massachusetts
Informed Consent

Participant's Name:_____ **Date:**_____
Project Title: An Investigation of the Long-term Neuropsychological and Psychosocial Outcome of Maternal PKU Syndrome.

Protocol Number: 97-02-028

Consent Form Valid From April 24,1997 through April 23,1998

Description and Explanation of Procedure: The purpose of the present study is to increase our understanding of the memory, attention and psychosocial functioning of adults whose mothers had PKU or some degree of hyperphenylalaninemia (Maternal PKU). We are also evaluating a group of individuals whose mothers did not have PKU, but who may have some other types of difficulties or learning disabilities. In particular, we are interested in examining whether adults whose mothers had PKU differ from other individuals who may have learning difficulties due to other reasons. We are interested in studying short- and long-term memory abilities, intellectual abilities, attention, and social and emotional development. By giving the same tests to both groups, we will gain a clearer understanding of the pattern of strengths and weaknesses associated specifically with maternal PKU. Although we have some knowledge regarding the pattern of difficulties seen in children whose mothers had PKU, we know little about how these individuals function as adults. In order to develop interventions and support services for these adult individuals, if needed, we must first identify how their pattern of strengths and deficits may differ from individuals with other developmental or learning disabilities. This information will also help us to understand the long-term effects of phenylalanine on the developing brain.

The study includes a variety of tasks. Some require verbal responses and some involve putting together puzzles, copying geometric designs from pictures, or pushing a button in response to a specific letter being presented on a Computer screen. There are also questionnaires focused on social and emotional well-being. Some of the questions may be sensitive and you do not need to answer any questions which make you uncomfortable.

We will come to your home or some other location that is convenient to you. The research project will take between 3 1/2 and 6 hours of your time, depending on how many breaks you would like to have. You will be provided with a lunch break and/or several other breaks

Risks and Discomforts: You may become tired and/or anxious by the testing procedure. If this occurs, further rest breaks will be provided and if necessary, testing will be discontinued and rescheduled if possible.

You will be asked to provide information concerning your current medications. Ideally, all medications associated with cognitive change (e.g., Ritalin, Cylert) will be discontinued 24 hours prior to testing. The possible risks associated with discontinuing such medications are a decrease in attention

span and an increase in hyperactive behaviour. Decisions concerning the feasibility and ethics of discontinuing medications will be reviewed by Dr. Harvey Levy at the Children's Hospital and discussed with you and your physicians.

Potential Benefits: You may find it interesting to learn more about your individual strengths and weaknesses in areas such as memory, attention, level of academic achievement, and emotional functioning.

Anonymity: Although data from this study may be published, the confidentiality of all participants will be maintained. Neither your name nor any information identifying you will be released to anyone without your written permission, unless required by law.

I have fully explained to _____ the nature
participant
and purpose of the above-described procedures and the risks involved in its performance. I have answered and will answer all questions to the best of my ability. I will inform the participant of any changes in the procedure of the risks and benefits if any should occur during or after the course of the study.

_____ _____
Date Susan E. Waisbren, Ph.D. or her Representative

Consent: I have been satisfactorily informed of the above-described procedure with its possible risks and benefits. I give permission for my son/daughter/individual for whom I am legal guardian to participate in this study. I know that Dr. Susan Waisbren or her research assistant, Susan Brock, MA, will be available to answer any questions that I may have and may be reached at (617) 355-7346. If I feel my questions have not been adequately answered I may request to speak to a member of the Hospital Consent Committee by calling (617) 355-7052. I understand that I am free to withdraw this consent and discontinue participation in this project at any time, even after signing this form, and it will not affect my son/daughter's care. I have been given a copy of this form.

_____ _____
Date Signature of Participant

_____ _____
Date Witness to Signatures

APPENDIX I Checklist Of Measures

Checklist of Measures

_____ Structured Interview with Caregiver/Parent

_____ Young Adult Behaviour Checklist with Caregiver/Parent

_____ WAIS-R

_____ Young Adult Self-Report

_____ Beck Depression Inventory

_____ WRAT-3 - spelling & reading

_____ RAVLT - initial

_____ WRAT-3 - arithmetic

_____ Trails A & B

_____ RAVLT - recall/recognition

_____ WMS - R - initial

_____ Rey Complex Figure - copy

_____ WMS - R - recall

_____ Talland Letter Cancellation Test

_____ Underlining test

_____ Rey Complex Figure - recall

_____ Wisconsin Card Sorting Task

_____ Continuous Performance Task

_____ Laura's battery

APPENDIX J Computational Information

Computational Information for the RAVLT.

Number correct: A1
Number correct: A2
Number correct: A3
Number correct: A4
Number correct: A5
Number correct: A1 to A5 (total number of words recalled)
Number of perseverations: (across all trials A1 to A7)
Number of intrusions: (across all trials A1 to A7)
Number correct: B1 (interference list)
Number correct: A6 (immediate recall of list A)
Number correct: A7 (delayed recall of list A)
Percent recall: (number correct A6)/(number correct A5)
Learning index = A5-A1
List A recognition (number of hits)
List A recognition (total number false positives)
p(A) = signal detection measure of recognition performance; proportion of words recognized on List A = hit rate (HR); proportion of distracters responded to as list words = false positive rate (Fp)
p(A) = 0.5(1+HR-Fp) - varies between 0(random) and 1(perfect performance)

RAVLT Indices
(Interference and Efficiency Indices - <1=interference; >1=facilitation)
Proactive: B1: A1
Retroactive: A6: A5
Forgetting: A7: A6

APPENDIX K CPT Computational Information

Computational Information for the CPT.

The dependent variables from the CPT include: Reaction Time (centiseconds to respond to critical stimuli), Percent Omission Errors (number of missed critical stimuli/total number of stimuli - total number of critical stimuli * 100), Percent Commission Errors (responses to non-critical stimuli/total number of stimuli - total number of critical stimuli * 100), β (error bias) and d' (defined below), for the X task, the AX task, the degraded X task, and the auditory tones task.

β is a measure of the individual's error response bias relative to the total number of errors and ranges between -1 and +1. A negative number indicates more misses or omission errors whereas a positive number indicates more incorrect responses (responding to non-critical stimuli). Larger values of β indicate a higher number of errors relative to total errors. The larger the number the higher the number of errors relative to total errors. d' prime is a measure of how able the individual was to discriminate between critical and non-critical stimuli relative to the total number of critical stimuli.

SPSS Syntax Program

Do if number of critical stimuli does not equal 0.
Compute percent correct = (number correct divided by number critical) multiplied by 100.
Compute percent omissions = (number omissions divided by number critical) multiplied by 100.
Compute d' = (1 minus ((number incorrect minus number omissions) divided by (number critical))) multiplied by 100.
END IF.
Do if number critical stimuli = 0.
Compute percent correct = (number correct divided by one) multiplied by 100.
Compute percent omissions = (number omissions divided by one) multiplied by 100.
Compute d' = (1 minus ((number incorrect minus number omissions) divided by one)) multiplied by 100.
END IF.
Do if (total number stimuli minus number of critical stimuli) does not equal 0.

Compute percent commission errors = (number incorrect divided by (number stimulus minus number critical)) multiplied by 100.
Do if (total number stimuli minus number critical stimuli) does not equal 0.
Compute percent commission errors = (number incorrect divided by one) multiplied 100.
END IF.
Do if number incorrect = 0.
Compute BETA = (1 minus number omissions) divided by (1 plus number omissions).
END IF.
Do if number omissions = 0.
Compute BETA = (number incorrect minus one) divided by (number incorrect plus one).
END IF.
Do if (number incorrect does not equal 0) and (number omissions does not equal 0).
Compute BETA = (number incorrect minus number omissions) divided by (number incorrect plus number omissions).
END IF.

APPENDIX L Paired Samples t-Test

Paired Samples t-Test Analyses for FAS and IQ Matched Controls and MPKUS and IQ Matched Controls

Table 12.1 TLCT, Trails Test, and WCST Parametric and Nonparametric Comparisons of FAS Group and IQ Matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
TLCT	n=16	n=16		
Mean # Correct	37.17 (16.12)	38.06 (17.21)	-.235 (.81)	-.621 (.535)
Mean # Omission Errors	5.56 (4.54)	7.87 (7.50)	-1.143 (.271)	-1.862 (.063)
Mean # Commission Errors	3.63 (4.83)	1.28 (1.23)	-1.933 (.072)	-2.386 (.017)
Underlining Test	n=17	n=17		
Mean # Correct	45.88 (6.33)	47.75 (3.34)	-1.299 (.212)	-.592 (.554)
Mean # Omission Errors	4.94 (5.90)	3.92 (3.33)	.757 (.460)	-.024 (.981)
Mean # Commission Errors	1.71 (1.63)	1.34 (2.39)	1.34 (2.39)	1.421 (.155)

Trail Making Test	n=16	n=16		
Trails A Time	51.06 (27.60)	58.77 (30.87)	-1.025 (.322)	-.879) (.379)
Trails A Errors	1.18 (.91)	.75 (1.52)	.959 (.353)	1.211 (.226)
Trails B Time	63.00 (33.36)	59.11 (30.91)	.357 (.726)	.362 (.717)
Trails B Errors	1.81 (1.86)	1.56 (1.50)	.402 (.694)	.176 (.860)
WCST	n=16	n=16		
Categories Completed (Sets)	3.47 (2.34)	2.05 (2.22)	1.888 (.07)	1.740 (.082)
% Perseverative Errors	22.00 (10.43)	31.35 (18.54)	2.839 (.012)	2.438 (.015)
Failure To Maintain Set	1.588 (1.62)	.8824 (1.57)	1.396 (.182)	1.471 (.141)
% Correct Responses	59.14 (10.50)	46.68 (18.49)	2.710 (.015)	2.533 (.011)

Table 12.2 CPT and WAIS-R Parametric and Nonparametric Comparisons of FAS Group and IQ Matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
CPT	n=15	n=15		
X Task Reaction Time	43.00	43.46	-.169	-.409
	(7.57)	(8.70)	(.868)	(.683)
X Task Percent Correct	82.12	81.00	-.184	-.653
	(23.82)	(19.09)	(.856)	(.514)
X Task Percent Omission Errors	20.50	10.12	1.400	1.038
	(29.64)	(13.29)	(.182)	(.299)
X Task Percent Commission Errors	4.83	.600	2.089	2.589
	(7.98)	(.66)	(.055)	(.010)
X Task d'	96.12	107.87	-2.212	-1.541
	(17.68)	(13.86)	(.043)	(.123)
X Task β	-.0470	-.4083	2.309	2.244
	(.39)	(.53)	(.036)	(.025)
	n=16	n=16		
AX Task Reaction Time	37.58	36.94	.165	.118
	(12.02)	(9.33)	(.871)	(.906)
AX Task % Correct	74.95	80.07	-.749	-.776
	(24.48)	(21.13)	(.465)	(.438)
AX Task Percent Omission Errors	20.77	17.74	.520	.698
	(21.21)	(18.99)	(.610)	(.485)
AX Task Percent Commission Errors	5.55	3.35	.977	1.785
	(6.69)	(6.90)	(.343)	(.074)
AX Task d'	92.97	100.94	-1.067	-1.112
	(22.37)	(23.83)	(.302)	(.266)

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
CPT	n=15	n=15		
AX Task β	-1974 (.42)	-.2136 (.53)	2.759 (.014)	2.249 (.025)
DX Task Reaction Time	51.11 (7.39)	52.00 (8.97)	-.330 (.746)	-.199 (.842)
DX Task Percent Correct	70.11 (24.03)	58.00 (31.23)	1.678 (.113)	1.479 (.139)
DX Task Percent Omission Errors	29.88 (24.03)	41.88 (31.04)	-1.666 (.115)	-1.450 (.147)
DX Task Percent Commission Errors	7.65 (9.80)	4.77 (7.75)	.160 (.875)	.440 (.660)
DX Task d'	91.05 (33.87)	104.94 (58.46)	-1.284 (.217)	-1.729 (.84)
DX Task β	.0558 (.40)	-.1751 (.51)	1.678 (.113)	1.586 (.113)
Tones Task Reaction Time	46.80 (8.68)	46.66 (8.10)	.039 (.970)	.028 (.977)
Tones Task Percent Correct	52.43 (33.36)	63.33 (34.01)	-1.780 (.097)	-1.477 (.140)
Tones Task Percent Omission Errors	40.45 (32.57)	28.55 (33.44)	1.696 (.112)	1.475 (.140)
Tones Task Percent Commission Errors	7.65 (9.80)	4.77 (7.75)	.986 (.341)	1.791 (.073)
Tones Task d'	109.81 (35.09)	109.45 (28.30)	.027 (.979)	.825 (.410)
Tones Task β	-.1307 (.37)	-.3300 (.54)	1.065 (.305)	.966 (.334)

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
WAIS-R	n=17	n=17		
Arithmetic Subtest	4.00 (3.08)	4.88 (2.82)	2.252 (.039)	2.025 (.043)
Digit Span Subtest	6.64 (3.99)	8.35 (5.20)	-1.550 (.141)	-1.666 (.096)
WRAT-3	n=17	n=17		
Arithmetic Subtest	22.11 (9.40)	25.70 (9.97)	-1.908 (.075)	-1.682 (.093)

Table 12.3 RAVLT Parametric and Nonparametric Comparisons of FAS Group and IQ Matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
RAVLT	n=17	n=17		
Learning Index	4.41 (2.47)	6.00 (2.71)	-2.057 (.056)	-1.909 (.056)
Perseveration Errors	12.64 (17.70)	11.35 (11.09)	.434 (.670)	.000 (1.000)
Intrusion Errors	14.52 (14.52)	5.05 (3.96)	2.590 (.20)	2.528 (.011)
Immediate Recall (A6)	6.70 (3.03)	9.41 (3.20)	2.718 (.015)	2.287 (.022)
Percent Recall (A6/A5)	74.40 (32.80)	96.73 (30.50)	-2.376 (.030)	-2.215 (.027)
Proactive Interference (B1/A1)	2.69 (1.34)	1.42 (.75)	-1.707 (.10)	-2.664 (.096)
Delayed Recall (A7)	8.94 (3.15)	5.82 (3.52)	-3.253 (.005)	-2.629 (.0009)
Forgetting Index (A7/A6)	.91 (.37)	.95 (.20)	-.427 (.675)	-.545 (.586)
Recognition	2.42 (.58)	2.49 (.60)	-.147 (.885)	-.176 (.86)
Recognition (Signal Detection Of Recognition Performance)	.28 (.47)	.39 (.47)	-.954 (.354)	-.907 (.364)

Table 12.4 WMS-R Parametric and Nonparametric Comparisons of FAS Group and IQ Matched Control Group

Test & Subscale	FAS	Control	t (2 tailed)	z (2 tailed)
WMS-R	n=17	n=17		
Logical Memory I	13.70 (7.48)	16.52 (8.88)	-1.523 (.147)	-1.399 (.162)
Verbal Paired Associates I	14.05 (5.43)	15.29 (6.04)	-1.049 (.310)	-1.139 (.255)
Visual Paired Associates I	10.17 (4.85)	11.41 (4.43)	-.802 (.434)	-.985 (.325)
Visual Reproduction I	29.76 (8.01)	28.70 (8.49)	.969 (.347)	.798 (.425)
Logical Memory II	9.58 (6.82)	14.70 (8.34)	-2.466 (.025)	-2.199 (.028)
Verbal Paired Associates II	5.95 (1.34)	7.00 (1.45)	-3.816 (.002)	-2.835 (.005)
Visual Paired Associates II	4.41 (1.66)	4.41 (2.06)	.000 (1.000)	.770 (.442)
Visual Reproduction II	23.05 (11.66)	23.58 (11.22)	.306 (.764)	.095 (.924)
Rey Complex Figure				
Delayed Recall	13.00 (9.25)	12.70 (8.86)	.133 (.896)	.213 (.831)

Table 12.5 Underlining Test, WCST and Trails Test Parametric and Nonparametric Comparisons of MPKUS Group and IQ Matched Control Group

Test & Subscale	MPKUS	Control	t (2 tailed)	z (2 tailed)
Underlining Test	n=10	n=10		
Mean # Correct	43.25 (8.50)	46.31 (5.26)	-1.14 (.280)	-1.530 (.126)
Mean # Omissions	8.43 (8.49)	5.35 (5.25)	1.157 (.277)	1.478 (.139)
Mean # Commissions	2.35 (2.36)	2.05 (3.07)	.472 (.346)	6.63 (.508)
Trail Making Test	n=10	n=10		
Trails A Time	67.00 (46.05)	65.13 (28.78)	.156 (.880)	.051 (.959)
Trails A Errors	3.90 (4.95)	2.60 (4.52)	.719 (.490)	1.387 (.165)
Trails B Time	83.57 (38.94)	51.11 (20.98)	1.949 (.099)	1.521 (.128)
Trails B Errors	1.71 (1.49)	1.14 (1.06)	.703 (.508)	.750 (.453)
WCST	n=10	n=10		
Categories Completed (Sets)	4.40 (3.71)	2.80 (2.48)	1.50 (.168)	.982 (.326)
% Perseverative Errors	23.74 (19.07)	16.49 (8.17)	.935 (.374)	1.376 (.169)
Failure To Maintain Set	.50 (.97)	2.10 (2.02)	-2.02 (.074)	-2.384 (.017)
% Correct Responses	58.28 (20.99)	61.68 (10.29)	-.525 (.613)	-.764 (.445)

Table 12.6 CPT and WAIS-R Parametric and Nonparametric Comparisons of MPKUS Group and IQ Matched Control Group

Test & Subscale	MPKUS	Control	t (2 tailed)	z (2 tailed)
CPT	n=11	n=11		
X Task Reaction Time	47.45 (11.61)	47.27 (8.08)	.060 (.953)	.267 (.789)
X Task % Correct	68.00 (34.66)	72.36 (30.28)	-.335 (.744)	-.445 (.657)
X Task % Omission Errors	25.09 (27.57)	18.54 (27.72)	641 (.536)	.840 (.401)
X Task % Commission Errors	4.27 (8.02)	1.09 (.99)	1.588 (.143)	1.426 (.154)
X Task d'	106.00 (18.93)	112.36 (24.86)	-.652 (.529)	-.297 (.766)
X Task β	-.37 (.47)	-.34 (.52)	-.159 (.875)	-.255 (.799)
AX Task Reaction Time	43.54 (16.68)	42.72 (10.51)	.160 (.876)	.153 (.878)
AX Task % Correct	63.63 (38.81)	68.32 (30.62)	-.395 (.701)	-.400 (.689)
AX Task % Omission Errors	31.23 (33.22)	28.29 (28.89)	.281 (.784)	.889 (.374)
AX Task % Commission Errors	5.42 (10.04)	3.69 (2.65)	.619 (.550)	.622 (.534)
AX Task d'	104.10 (45.73)	106.59 (18.42)	-.205 (.842)	-.051 (.959)
AX Task β	.022 (.49)	-.14 (.36)	.827 (.428)	1.172 (.241)
DX Task Reaction Time	52.45 (8.93)	54.63 (13.46)	-.488 (.636)	-.102 (.919)

Test & Subscale	MPKUS	Control	t (2 tailed)	z (2 tailed)
CPT	n=11	n=11		
DX Task % Correct	66.54 (29.77)	55.27 (30.49)	1.245 (.242)	.891 (.373)
DX Task % Omission Errors	33.27 (29.68)	44.72 (30.49)	-1.267 (.234)	-.935 (.350)
DX Task % Commission Errors	11.45 (18.21)	15.36 (18.43)	-.788 (.449)	-.971 (.332)
DX Task d'	87.45 (71.06)	80.18 (68.92)	.218 (.832)	.000 (1.000)
DX Task β	-.033 (.50)	.10 (.44)	-.562 (.587)	N/A
Tones Task Reaction Time	43.09 (15.80)	49.18 (9.71)	-1.497 (.165)	-1.468 (.142)
Tones Task % Correct	36.11 (37.30)	54.29 (32.25)	-1.484 (.169)	-1.956 (.050)
Tones Task % Omission Errors	60.19 (38.33)	35.74 (31.19)	1.834 (.097)	2.045 (.041)
Tones Task % Commission Errors	5.86 (4.81)	6.57 (6.35)	-.288 (.779)	-.178 (.859)
Tones Task d'	136.73 (32.71)	106.63 (10.35)	3.404 (.007)	2.223 (.026)
Tones Task β	-.40 (.23)	-.19 (.44)	-1.352 (.206)	-1.245 (.213)
WAIS-R	n=12	n=12		
Arithmetic Subtest	3.75 (2.49)	4.33 (3.55)	.075 (.941)	.905 (.365)
WRAT-3	n=11	n=11		
Arithmetic Subtest	23.18 (13.30)	21.53 (14.07)	.881 (.399)	.000 (1.000)

Table 12.7 RAVLT Parametric and Nonparametric Comparisons of MPKUS Group and IQ Matched Control Group

Test & Subscale	MPKUS	Control	t (2 tailed)	z (2 tailed)
RAVLT	n=11	n=11		
Learning Index	4.36 (2.15)	5.27 (2.93)	-1.16 (.271)	-.801 (.423)
Perseveration Errors	8.827 (10.25)	4.727 (3.63)	.933 (.373)	.204 (.838)
Intrusion Errors	5.90 (6.83)	6.45 (8.73)	-.157 (.878)	-.210 (.833)
Proactive Interference (B1/A1)	2.69 (1.34)	1.42 (.75)	-1.707 (.10)	-2.664 (.096)
Immediate Recall (A6)	5.72 (3.60)	5.72 (4.79)	.000 (1.00)	.045 (.964)
Retroactive Interference (A6/A5)	73.65 (25.72)	51.37 (37.25)	1.483 (.169)	1.156 (.248)
Delayed Recall (A7)	5.45 (4.20)	6.90 (4.15)	-1.141 (.280)	-.972 (.331)
Forgetting Index (A7/A6)	.86 (41)	1.31 (1.67)	-.838 (.421)	-.255 (.799)
Recognition	12.27 (2.05)	14.27 (1.48)	-2.507 (.031)	-2.084 (.037)
Recognition (Signal Detection Of Recognition Performance)	.18 (.44)	-.032 (.79)	.989 (.346)	.756 (.450)

Table 12.8 WMS-R Parametric and Nonparametric Comparisons of MPKUS Group and IQ Matched Control Group

Test & Subscale	MPKUS	Control	t (2 tailed)	z (2 tailed)
WMS-R	n=11	n=11		
Logical Memory I	13.45 (9.59)	11.18 (9.47)	.828 (.427)	.833 (.405)
Verbal Paired Associates I	11.81 (6.94)	11.09 (9.07)	.309 (.763)	.423 (.673)
Visual Paired Associates I	9.18 (5.58)	8.27 (2.07)	.414 (.688)	.460 (.646)
Visual Reproduction I	22.18 (13.50)	24.36 (11.25)	-.652 (.529)	-1.557 (.119)
Logical Memory II	9.36 (8.42)	9.63 (9.44)	-.090 (.930)	-.805 (.421)
Verbal Paired Associates II	4.54 (2.50)	5.63 (2.83)	-1.150 (.277)	-1.247 (.212)
Visual Paired Associates II	3.72 (1.90)	3.36 (2.29)	.571 (.580)	.284 (.776)
Visual Reproduction II	22.18 (13.50)	24.36 (11.25)	-.652 (.529)	-1.51 (.130)
Rey Complex Figure				
Delayed Recall	11.72 (10.95)	8.90 (10.20)	.877 (.401)	.889 (.374)

APPENDIX M Block Analyses

Table 13.1 Underlining Test, Trail Making Test, WCST, and WAIS-R Parametric and Nonparametric Block Analyses

Test & Subscale	FAS	MPKUS	Control	F	χ^2
Underlining Test – 10 & 8					
Mean # Hits	43.25 (8.59)	41.46 (10.63)	46.13 (4.77)	1.876 (.182)	4.051 (.132)
	40.58 (5.44)	46.18 (5.62)	50.18 (.89)	8.072 (.005)	10.750 (.005)
Mean # Omissions	5.93 (7.31)	5.68 (5.01)	4.28 (3.17)	1.044 (.375)	6.889 (.032)
	11.08 (5.44)	3.66 (4.04)	1.52 (.88)	11.062 (.001)	10.516 (.005)
Mean # Commissions	1.48 (1.91)	3.73 (4.34)	1.91 (2.91)	1.693 (.212)	2.811 (.245)
	3.16 (2.48)	1.18 (.83)	.62 (.72)	5.668 (.016)	4.710 (.095)
Trails A Time - 10 Block	62.00 (49.80)	75.70 (57.64)	69.93 (47.30)	.439 (.652)	.684 (.710)
Trails A Time - 8 Block	46.37 (31.72)	60.25 (49.62)	55.29 (31.75)	.439 (.652)	.684 (.710)
Trails B Time - 10 Block	65.10 (45.66)	93.10 (50.17)	63.38 (42.01)	1.945 (.192)	6.821 (.033)
Trails B Time - 7 Block	49.14 (35.02)	76.28 (44.34)	45.68 (26.95)	1.881 (.195)	4.963 (.084)

Test & Subscale	FAS	MPKUS	Control	F	χ^2
WCST - 10 & 8 Block					
Categories Completed	3.00 (2.31)	4.20 (3.93)	3.60 (2.17)	.614 (.552)	.368 (.832)
	3.38 (2.45)	5.25 (3.69)	3.62 (2.32)	1.426 (.273)	2.600 (.273)
% Perseverative Errors	24.98 (12.40)	30.22 (25.65)	23.56 (12.66)	.491 (.620)	.200 (.905)
	24.02 (11.79)	21.12 (19.32)	21.43 (13.43)	.104 (.902)	.250 (.882)
Failure To Maintain Set	1.30 (1.63)	.40 (.96)	1.50 (1.71)	1.579 (.233)	3.697 (.157)
	1.25 (1.83)	.50 (1.06)	1.50 (1.92)	.805 (.467)	1.520 (.468)
% Correct Responses	58.50 (25.71)	60.80 (39.27)	64.30 (27.82)	.117 (.871)	.600 (.741)
	61.37 (27.92)	71.75 (36.03)	65.75 (29.17)	.301 (.745)	3.00 (.223)
WAIS-R	n=10	n=10	n=10		
Arithmetic Subtest	4.70 (3.77)	4.30 (2.35)	5.00 (3.55)	.510 (.609)	.074 (.964)
Digit Span Subtest	7.60 (4.86)	7.50 (6.29)	9.20 (6.62)	.590 (.405)	1.632 (.442)
WRAT - R					
Arithmetic - 10 Block	22.90 (11.66)	24.20 (13.75)	26.10 (13.30)	714 (.503)	1.459 (.482)
Arithmetic - 9 Block	24.00 (11.80)	26.55 (12.26)	28.22 (12.18)	1.137 (.345)	1.879 (.391)

Table 13.2 CPT Parametric and Nonparametric Block Analyses

Test & Subscale	FAS	MPKUS	Control	F	χ^2
CPT - 7 Blocks					
X Task Reaction Time	40.14	43.57	45.57	1.147	3.714
	(5.55)	(10.41)	(11.79)	(.350)	(.156)
X Task Percent Commission Errors	5.28	3.50	.71	1.371	6.083
	(10.29)	(6.94)	(.90)	(.291)	(.048)
X Task Percent Omission Errors	19.43	17.71	10.29	.557	.333
	(27.73)	(30.34)	(13.29)	(.587)	(.846)
X Task Percent Correct	78.29	78.00	70.57	.203	1.462
	(27.89)	(35.76)	(22.91)	(.819)	(.482)
X Task d'	95.62	89.86	108.14	1.402	5.333
	(30.25)	(49.66)	(18.78)	(.284)	(.069)
X Task β	-.2503	-.3802	-.5396	.883	1.680
	(.38)	(.51)	(.47)	(.439)	(.432)
AX Percent Correct	67.97	72.35	78.57	.510	.538
	(24.42)	(38.25)	(24.79)	(.613(	(.764)
AX Task Reaction Time	35.14	38.43	37.86	.173	2.000
	(13.04)	(16.43)	(10.27)	(.843)	(.368)
AX Task Percent Commission Errors	6.63	6.82	2.44	1.319	2.000
	(8.88)	(12.70)	(2.61)	(.304)	(.368)
AX Task Percent Omission Errors	28.80	23.96	19.35	.597	.963
	(24.48)	(32.96)	(22.17)	(.566)	(.618)
AX Task d'	95.62	89.86	107.14	1.080	1.407
	(30.25)	(49.66)	(18.78)	(.370)	(.495)
AX Task β	.007	.197	-.385	4.538	4.571
	(.32)	(.43)	(.55)	(.034)	(.102)

DX Task Reaction Time	50.14 (4.85)	47.14 (5.01)	50.00 (12.97)	.284 (.750)	.077 (.962)
DX Task Percent Correct	76.00 (26.98)	74.57 (30.95)	71.42 (35.32)	.088 (.916)	.364 (.834)
DX Task Percent Commission Errors	7.35 (10.98)	11.71 (20.93)	10.71 (20.58)	1.079 (.371)	2.160 (.340)
DX Task Percent Omission Errors	24.00 (26.98)	25.42 (30.95)	28.28 (34.74)	.078 (.926)	.857 (.651)
DX Task d'	94.57 (29.43)	78.57 (81.84)	85.43 (78.92)	.374 (.696)	.667 (.717)
DX Task β	.149 (.45)	.207 (.58)	.124 (.51)	.056 (.946)	.074 (.964)
Tones Task Percent Correct	55.01 (35.57)	49.42 (44.02)	69.49 (36.41)	.734 (.501)	2.571 (.276)
Tones Task Reaction Time	45.71 (8.90)	39.00 (17.78)	49.28 (10.59)	2.002 (.178)	2.571 (.276)
Tones Task Percent Commission Errors	10.95 (13.43)	4.72 (5.62)	3.33 (3.92)	1.500 (.262)	3.429 (.180)
Tones Task Percent Omission Errors	38.22 (32.09)	48.64 (46.67)	22.97 (31.70)	1.107 (.362)	2.571 (.276)
Tones Task d'	94.40 (40.53)	129.72 (36.74)	109.65 (19.11)	1.563 (.249)	2.889 (.236)
Tones Task β	.006 (.31)	-.320 (.34)	-.379 (.64)	1.653 (.232)	3.714 (.156)

Table 13.3 RAVLT Parametric and Nonparametric Block Analyses

Test & Subscale	FAS	MPKUS	Control	F	χ^2
RAVLT 10 and 9 Block Analyses					
Learning Index	3.60 (2.59)	4.50 (2.32)	5.50 (2.68)	1.822 (.190)	2.811 (.245)
	3.89 (2.57)	5.00 (1.80)	5.67 (2.78)	1.380 (.280)	2.182 (.336)
Perseveration Errors	18.30 (21.47)	6.40 (8.60)	7.00 (6.04)	2.227 (.137)	1.474 (.479)
	17.56 (22.63)	7.11 (8.81)	7.56 (6.13)	1.428 (.269)	.941 (.625)
Intrusion Errors	17.30 (18.14)	3.70 (2.98)	3.80 (3.46)	5.638 (.013)	6.000 (.050)
	15.56 (18.32)	4.11 (2.85)	4.22 (3.38)	3.720 (.047)	4.545 (.103)
Immediate Recall (A6)	6.90 (3.07)	5.50 (4.06)	8.00 (4.19)	3.857 (.040)	7.538 (.023)
	7.11 (3.18)	6.11 (3.79)	8.89 (3.30)	5.443 (.016)	8.667 (.013)
Percent Recall/ Retroactive	79.01 (23.74)	59.03 (28.01)	80.69 (42.50)	1.956 (.170)	4.667 (.097)
Interference (A6/A5)	76.68 (23.94)	65.58 (19.97)	89.66 (33.58)	2.989 (.079)	4.769 (.092)

Test & Subscale	FAS	MPKUS	Control	F	χ^2
RAVLT 10 and 9 Block Analyses					
Delayed Recall (A7)	5.50	5.50	8.00	2.586	4.514
	(3.27)	(4.53)	(3.77)	(.103)	(.105)
	5.78	6.11	8.89	3.279	5.688
	(3.35)	(4.34)	(2.67)	(.064)	(.058)
Forgetting Index (A7/A6)	.836	.833	.978	.329	.632
	(.36)	(.50)	(.48)	(.724)	(.729)
	.862	.925	1.08	.562	1.543
	(.37)	(.44)	(.36)	(.581)	(.462)
Recognition (number of hits)	13.20	10.90	13.80	3.200	8.647
	(2.53)	(4.28)	(2.49)	(.065)	(.013)
	13.56	12.11	13.67	2.239	7.267
	(2.40)	(2.03)	(2.60)	(.139)	(.026)
Recognition (Signal Detection Measure Of Recognition)	.20	.31	.09	.696	.389
	(.54)	(.27)	(.73)	(.512)	(.823)
	.20	.34	.20	.370	.563
	(.57)	(.26)	(.67)	(.697)	(.755)

Table 13.4 WMS-R and Rey Complex Figure Parametric and Nonparametric Block Analyses

Test & Subscale	FAS	MPKUS	Control	F	χ^2
WMS-R 10 and 9 Block Analyses					
Logical Memory I	13.50 (8.80)	14.40 (9.58)	11.60 (7.61)	.912 (.419)	.359 (.836)
	14.22 (9.01)	15.88 (8.85)	12.55 (7.41)	1.066 (.368)	1.086 (.581)
Verbal Paired Associates I	13.90 (6.87)	12.30 (7.30)	11.80 (7.62)	.970 (.398)	1.556 (.459)
	14.44 (7.06)	13.66 (6.24)	12.66 (7.54)	.595 (.564)	1.00 (.607)
Visual Paired Associates I	10.70 (5.59)	9.50 (5.93)	9.20 (5.57)	.552 (.585)	.389 (.823)
	11.55 (5.19)	10.55 (5.19)	10.11 (5.06)	.387 (.685)	.563 (.755)
Visual Reproduction I	28.50 (10.20)	24.10 (12.58)	25.80 (12.83)	2.540 (.107)	6.526 (.038)
	30.11 (9.37)	26.00 (11.72)	28.66 (9.64)	2.311 (.131)	5.882 (.053)
Logical Memory II	10.60 (8.04)	10.00 (8.62)	9.80 (7.71)	.053 (.948)	.211 (.900)
	11.11 (8.36)	11.11 (8.35)	10.88 (7.32)	.004 (.996)	.400 (.819)
Verbal Paired Associates II	5.90 (1.66)	4.70 (2.66)	6.50 (1.43)	4.846 (.021)	5.556 (.062)
	6.11 (1.62)	5.22 (2.22)	6.66 (1.41)	3.127 (.071)	4.000 (.135)
Visual Paired Associates II	4.10 (1.97)	3.90 (1.96)	4.00 (2.35)	.047 (.954)	.071 (.965)
	4.11 (2.09)	4.33 (1.50)	4.11 (2.47)	.080 (.924)	.583 (.747)
Visual Reproduction II	21.30 (13.89)	17.30 (14.88)	20.10 (11.87)	0.833 (.189)	2.737 (.255)
	23.67 (12.41)	19.22 (14.41)	21.55 (11.60)	1.891 (.183)	2.800 (.247)

Test & Subscale	FAS	MPKUS	Control	F	χ^2
Rey Complex Figure 10 & 9 Block					
Rey Copy	20.35 (11.71)	18.20 (13.74)	19.35 (10.38)	.551 (.586)	1.385 (.500)
	22.11 (10.93)	20.16 (12.99)	20.27 (10.57)	531 (.598)	.743 (.690)
Rey Recall	11.75 (10.28)	12.80 (10.92)	10.80 (10.65)	.350 (.709)	.211 (.900)
	12.83 (10.28)	14.22 (10.55)	11.77 (10.81)	.429 (.658)	.057 (.972)