THE RELATION OF CONTRAST SENSITIVITY

AND ADHD: DISCRIMINANT VALIDITY

AND CORRELATIONS WITH

LABORATORY MEASURES

By

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NOMENCLATURE

BHS	Behavioral Health Services
CS	contrast sensitivity
СРТ	continuous performance tests
СТ	computerized tomography
DA	dopamine
DAT1	dopamine transporter
DRD4	D4 receptor gene
ERP	event-related potential
FACT	Functional Acuity Contrast Test
fMRI	functional magnetic resonance imaging
MRI	magnetic resonance imaging
PET	positron emission tomography
Phe	phenylalanine
PKU	phenylketonuria
PSC	Psychological Services Center
rCBF	regional cerebral blood flow
SPECT	single positron emission computed tomography
Try	tyrosine

CHAPTER I

INTRODUCTION AND OVERVIEW

According to the current diagnostic criteria, Attention-Deficit/Hyperactivity Disorder (ADHD) is a persistent disorder seen primarily in childhood that is present before the age of 7 and results in significant impairment over a wide range of settings, including home, school, occupational, and social (American Psychological Association, 1994). In order for a child to meet diagnostic criteria for ADHD, he/she must display six or more symptoms of inattention and/or six or more symptoms of hyperactivity/impulsivity for at least 6 months. Additionally, these symptoms must not occur or be accounted for by another mental disorder and symptoms must be present in multiple settings. The diagnosis of ADHD is coded based on one of three types: ADHD, Predominately Inattentive Type; ADHD, Predominately Hyperactive-Impulsive Type; and ADHD, Combined Type (American Psychological Association, 1994). The prevalence rate of ADHD has been estimated to range from 3 to 5 percent of school-aged children being diagnosed with the disorder (American Psychological Association, 1994). In order to gain a better understanding of the etiology of ADHD, the first objective of this overview is to review the neurological correlates of the disorder.

Neurological functioning and impairment have been examined in an attempt to understand the etiology of ADHD. Neuroimaging and electrical waveform studies examining young children with ADHD have found deficits in a number of brain

structures and functions, with structural deficits primarily in the prefrontal or frontal cortex (See Klorman, 1991 and Nigg, 2001, for reviews). Studies using computerized tomography (CT) and magnetic resonance imaging (MRI) have also found evidence of brain abnormalities in the frontal cortex, primarily dysfunction in the frontosubcortical system of ADHD children (Faraone & Biederman, 1998). Finally, studies examining regional cerebral blood flow (rCBF) indicate a low neural activation in both hemispheres of the frontal lobe as well as the striatal regions in ADHD children as compared to normal controls (Bush, Valera, & Seidman, 2005; Lou, Henriksen, & Bruhn, 1984; Lou, Henriksen, Bruhn, Borner, & Nielsen, 1989). Overall, the research supporting the connection between frontal lobe dysfunction and ADHD is quite convincing.

Other research suggests that a dysregulation of catecholamines contribute to ADHD. One such catecholamine is the neurotransmitter, dopamine. Low levels of dopamine have been connected to motor problems as evidenced by the strong relation between dopamine deficiency and Parkinson's disease (Raskin, Shaywitz, Shaywitz, Anderson, & Cohen, 1984). Additionally, it is suggested that dopamine plays a role in sensory ability, attention, and emotional control as evidenced by the literature on dopamine and schizophrenia (Roth & Elsworth, 1995; Seeman, Guan & van Tol, 1995). Deficits in motor control, emotional regulation, and attention are all symptomatic of children with ADHD. This, coupled with medication response, has led researchers to examine the role of dopamine in ADHD. Dopaminergic genes, specifically DRD4 and DAT1 (DiMaio, Grizenko, & Joober, 2003; Faraone et al., 2005; Kirly et al., 2002) appear to be strong correlates of the disorder. DRD4 has been tied to the novelty-seeking trait seen in ADHD children and acts to mediate a blunted response to postsynaptic

dopamine (Ashgari, Sanyal, & Buchwaldt, 1995). DAT1 is the primary target gene for psychostimulant medication in ADHD (Volkow et al., 1998; Seeman & Madras, 1998) and children have shown significant behavioral improvements in attention and hyperactivity when taking psychostimulants (DuPaul & Barkley, 1993). Additionally, neuroimaging studies have indicated activation changes in ADHD children in response to psychostimulants. For example, functional magnetic resonance imaging studies (fMRI) have found that methylphenidate increases striatal activation in ADHD patients but decreases functioning in non-ADHD controls (Vaidya et al., 1998). Additionally, methylphenidate has shown increased frontal activation on Go/No-Go tasks in ADHD patients (Vaidya et al., 1998). Other research has supported interchange in dopamine markers in ADHD samples (Farone & Biederman, 1998).

This brief review of brain structure and function indicates that ADHD patients most likely suffer from frontal lobe impairment. Additionally, there is convincing evidence of dopaminergic dysfunction with ADHD, primarily supported by the effectiveness of psychostimulants and molecular genetic studies. Given that much research supports a biological etiology of ADHD, it seems appropriate for an objective diagnostic method to accompany current practice. Visual contrast sensitivity may provide such a measure. Contrast sensitivity is a measure of how dark black lines must be and how light the white background must be before a person can detect the black lines. Both Parkinson patients and children with PKU have lowered levels of dopamine and reduced contrast sensitivity (Bodis-Wollner, 1990; Bodis-Wollner, 1997; Diamond, Prevor, Callendar, & Druin, 1997; Kupersmith, Shakin, Siegel, & Lieberman, 1982; Nguyen-Legros, 1988). Therefore, the second objective will be to examine the current diagnostic

methods and address the need for an objective method of assessing the disorder, and the potential of contrast sensitivity to meet this need.

Adele Diamond and colleagues (Diamond, et al., 1997) examined contrast sensitivity and frontal lobe functioning in their work with children born with phenylketonuria (PKU). PKU is a rare disorder that also involves lowered levels of dopamine in the prefrontal cortex, especially when phenylalanine is increased over tyrosine. Diamond (1996) noted that the blood-retinal barrier is comparable to the bloodbrain barrier on measures of tyrosine (a precursor to L-Dopa or dopamine). So, Diamond and Herzberg (1996) used a contrast sensitivity test and found deficits in contrast sensitivity of PKU children as compared to their unaffected siblings and to normal children.

Given that this research by Diamond and Herzberg has yielded favorable results in assessing children with PKU using a visual contrast sensitivity test, research examining ADHD children on this same measure would be highly appropriate. In addition, the cognitive and behavioral manifestations of these two disorders are also similar, showing poor attention, concentration, and executive functioning (Antshel & Waisbren, 2003; Barkley, Grodzinsky, & DuPaul, 1992; Smith, Klim, & Hanley, 2000).

Current ADHD diagnostic methods consist of collecting self-report measures, other report measures, behavioral observations, and conducting interviews that rule out various related problems. Some researchers have begun using various tests purporting to measure frontal lobe (executive) functioning, including continuous performance tests (CPT), card playing tasks, go/no-go tasks, and stop-signal tasks. Many of these tasks can consistently discriminate between ADHD and normal controls but have not consistently

discriminated ADHD and other clinical groups (See Nichols & Waschbusch, 2004 for review). The laboratory task that has actually been normed and used in a clinical setting is several variations of the CPT. The CPT has been shown to discriminate between ADHD and non-ADHD populations in a research setting (Barkley, 1991; Grodzinsky & Diamond, 1992); however it appears to be less successful in discriminating ADHD and other clinical groups (McGee, Clark, & Symons, 2000; Halperin, Matier, Bedi, Sharma, & Newcorn, 1992). Comorbidity issues further complicate ADHD assessment. Approximately 35 to 60% of all ADHD children will also meet criteria for Oppositional Defiant Disorder (ODD) and 30 to 50% will eventually meet criteria for Conduct Disorder (CD) (Barkley, 1996). Some researchers have attempted to address the issue of comorbidity and discriminant validity by way of laboratory tasks. Hartung (2002) reviewed the extensive literature on laboratory tests and divided tasks into those that were purely motivational (Response Perseveration and the door-opening task), purely executive (stop-signal task and CPT), or a combination of both (go/no-go task) and assessed discriminant validity. From this review of the literature, she found several trends that indicated that tasks measuring motivation could better detect an ODD/CD sample, while those measuring executive functions could more correctly detect an ADHD sample. The combination task (both motivation and executive functioning) showed mixed results, identifying both ADHD and ODD/CD samples. Given the comorbidity rate, and the theories of motivational vs. executive inhibition etiology of ADHD and ODD/CD, it will be important to include both types of tasks in ADHD research and to identify a comorbid group.

Therefore, the current research program will attempt to assess ADHD, clinical control, and non-clinic normal control children on a contrast sensitivity test, the Functional Acuity Contrast Test (FACT) and various tasks of executive functioning and motivation. Four hypotheses are proposed for the current study. Hypothesis 1 states that the FACT will discriminate ADHD from non-ADHD samples. Hypothesis 2 states that the FACT will be highly correlated to stop signal and CPT tasks. Hypothesis 3 states that the FACT will be only moderately related to the go-no/go task. Hypothesis 4 states that the FACT will be unrelated to the door-opening task, which is proposed to be a purely motivational task.

The purpose of this literature review is to review current diagnostic methods for assessing ADHD and to determine if a contrast sensitivity measure and other laboratory tests will provide better understanding to the etiology of the disorder. To accomplish this task we must also examine the neuropsychological aspects of the disorder. First, an attempt will be made to describe PKU and Parkinson's Disease and how contrast sensitivity has been utilized for discriminant purposes. Second, this review will attempt to examine the evidence of a biological basis of ADHD, and tie the disorder to lower dopamine levels. Finally, a review of current diagnostic assessment will attempt to present the limitations in identifying and understanding ADHD.

CHAPTER II

REVIEW OF LITERATURE

Clinically Related Disorders

Phenylketonuria

Phenylketonuria (PKU) is a genetic metabolic disorder that is identified in infancy and is described by a severe imbalance between phenylalanine (Phe) and tyrosine (Tyr). More specifically, there is reduced activity of the phenylalanine hydroxylase (a catalyst enzyme that introduces hydrogen in the liver), which converts Phe to the dopamine precursor Tyr. The result of this is an increased Phe concentration in the bloodstream with Tyr levels in the low to normal range (Diamond et al., 1997). These children are treated with a diet low in Phe, which reduces this imbalance. If this diet is not started early enough or maintained over the course of their lifetime, the Phe levels rise to more than 10 times the normal amount and widespread brain damage will result in mental retardation for these PKU children. PKU affects approximately 1 in every 10,000 children (Guttler, 1988). Today, these children in the U.S. are nearly all detected early and continuously treated for PKU due to newborn screening programs (Stemerdink et al., 1999).

Treatment for PKU involves both diet and supplement. Getting the correct diet is a challenge in that Phe must be restricted, not eliminated, as the body needs the protein and amino acids. PKU children are also treated with a Tyr supplement, however, there is still a possibility of Tyr (and thus dopamine) depletion due to mechanisms that may interfere with Tyr crossing the blood-brain barrier and the brain neurons' sensitivity to the Tyr (Diamond et al., 1997). So, even with treatment, Phe levels can be elevated and Tyr levels can be low (Luciana, Sullivan & Nelson, 2001).

Although most children today are treated early and continuously for PKU, because there are still fluctuations in Phe and Tyr levels, a number of irreversible cognitive deficits can result. These deficits seem to be impacted by the Phe/Tyr ratio in that the higher the Phe levels the less access to Tyr for dopamine transmission. Therefore, when Phe levels are moderately elevated, Tyr levels are low, mild dopamine depletion occurs in the prefrontal cortex and specific prefrontal dysfunction is most likely (Diamond et al., 1997; Welsh, Pennington, Ozonoff, Rouse, & McCabe, 1990). Phe levels that are excessively high will then cause profuse damage that extends beyond the prefrontal cortex (Diamond & Herzberg, 1996). Treated PKU children have demonstrated IQ scores in the normal range of functioning, but these scores usually range from the 80s to 90s (Dobson, Kushida, Williamson, & Friedman, 1976) and are generally lower than matched controls (Diamond et al., 1997) and their siblings (Koch, Azen, Friedman, & Williamson, 1984; Williamson, Koch, Azen, & Chang, 1981). Additionally, younger PKU children show poorer performance on executive functioning tasks such as spatial working memory tasks, the Stroop test, the Tower of London planning task, and the Wisconsin Card Sort (Ris, Williams, Hunt, Berry, & Leslie, 1994; Stemerdink et al., 1999; Weglage, Pietsch, Funders, Koch, & Ullrich, 1996). Several studies have shown deficits in working memory and other executive functions, including attention and

response inhibition, in early treated PKU infants and young children (Diamond et al., 1997; Pennington, van Doorninck, McCabe, & McCabe, 1985; Spreen, Tupper, & Risser, 1984; Welsh et al, 1990) and older children and adults (Antshel & Waisbren, 2003; Stemerdink et al., 1999). Researchers have also reported a number of deficits involved in reaction time, attention allocation, and executive functioning for all age groups (Huijbregts, Sonneville, Licht, van Spronsen, Verkerk, & Sergeant, 2002; Waisbren, Brown, de Sonneville, & Levy, 1994). Two studies examining older children have failed to find these cognitive deficits between groups, (Luciana et al., 2001; Mazzocco, Nord, van Doorninck, Greene, Kovar & Pennington, 1994) but one study did find within-group differences in that those PKU children with high Phe levels had poorer patterns of performance on cognitive tasks (Luciana et al., 2001).

The prefrontal dysfunction hypothesis of PKU emerged from the research that shows cognitive deficits that are specifically localized to the prefrontal cortex rather than to general neurological deficits despite early and continuous treatment (Diamond et al., 1997; Stemerdink et al., 1999). As reviewed, moderately elevated Phe levels in PKU children leads to decreased Tyr, which then in turn appears to affect dopamine metabolism in the prefrontal cortex. Additionally, dopamine neurons appear to be extremely sensitive to even small reductions in Tyr (Bradberry, Karasic, Deutch, & Roth, 1989). Of course, lowered levels of dopamine have shown poorer cognitive performance (especially on executive functioning tasks) for nonhuman primates (Brozoski, Brown, Rosvold, & Goldman, 1979; Sawaguchi & Goldman-Rakic, 1991) and acute tyrosine depletions in humans have shown a relation with increased arousal and impaired cognitive functioning (McCann, et al., 1992; McCann, et al., 1995). Therefore, the

prefrontal deficit hypothesis posits that there are lowered levels of dopamine in the prefrontal cortex of PKU children, which results in irreversible cognitive deficits.

Based on this hypothesis, Diamond and Herzberg (1996) evaluated 47 children on a contrast sensitivity (CS) measure. Twelve of these children were early and continuously treated for PKU, 29 were children from the general population, and 6 were unaffected siblings of PKU children. Diamond and Herzberg found significant differences when comparing the PKU children to the normal controls or unaffected siblings, in that children with PKU displayed poorer CS.

Parkinson 's disease

Parkinson 's disease (PD) is primarily characterized as a motor disorder involving rigidity, tremors, and bradykinesia (Fahn, 2003). There are a number of other non-motor symptoms including cognitive, behavioral, and affective dysfunction (Burn, 2002; Glosser, 2001). The executive functioning of PD patients include poor visual-spatial ability (Crucian & Okun, 2003), poor cognitive sequencing (Fama & Sullivan, 2002), and poor working memory (Fournet, Moreaud, Roulin, Naegele, & Pellat, 2000). PD is strongly linked to neurological impairment, primarily dopaminergic deficiency beginning in the substantia nigra (Fahn, 2003) and the disorder appears to have a major impact on cognitive functioning through disruption of the basal ganglia (Crucian & Okun, 2003).

Similarly to PKU, researchers have also found CS deficits in PD patients as compared to normal controls (Bodis-Wollner, 1990; Bodis-Wollner, 1997; Kupersmith et al., 1982; Nguyen-Legros, 1988) and to aging individuals (Bodis-Wollner, 1997). Additionally, there is evidence that CS changes with motor impairment in Parkinson's

patients. More specifically, there is a change in the pattern of abnormality in spatial frequencies between the ON-states and the OFF-states of the disease (Bodis-Wollner, Marx, Mitra, Bobak, Mylin, & Yahr, 1987). Not only do PD patients demonstrate abnormal CS, but L-DOPA treatment with non-parkinsonian patients has resulted in improved CS scores as compared to controls (Nguyen-Legros, 1988).

Biology and ADHD

It has long been understood that there are biological associations to the disorder known as ADHD. Current technology has allowed ADHD researchers to focus on molecular biology, psychopharmacological responses, neuroimaging, and electrical cortical activity for determining the biological correlates of the disorder. Additionally, frontal lobe deficits have been examined using neuropsychological tests and family studies examining heritability also provide evidence for biological associations of ADHD. Each of these areas of research will be discussed.

Family, twin and adoption studies

Family, twin, and adoption studies have been used to determine the heritability of ADHD and examine genetic input versus environmental input. Parents of ADHD children have been found to be 2 to 8 times more likely to have the disorder than parents of children without ADHD (Faraone & Biederman, 1998), which suggests that there is some genetic contribution, but does not really specify how much. Examining heritability in both monozygotic and dizygotic twins allows for a quantitative analysis of genetic input. Spencer and colleagues (Spencer, Biederman, Wilens, & Farone, 2002) reviewed eight of

the most recent heritability studies and found that the average heritability of ADHD is .75, which means that 75% of the variance of this disorder is attributed to genetics. A more recent review indicated a similar heritability rate at .76 (Faraone et al., 2005). Furthermore, these researchers note that ADHD heritability is higher than many other mental illnesses that assume to have adequate heritability, including depression at .39 (Kendler & Prescott, 1999) and anxiety at .32 (Hettema, Neale, & Kendler, 2001) as well as some medical illnesses including breast cancer and asthma (Hemminki & Mutanen, 2001; Palmer et al., 2001). Finally, adoption studies also allow researchers to examine the genetic and environmental contribution of ADHD. Adoption studies have found that having biological parents with ADHD or antisocial personality disorder was more predictive of adopted children's ADHD than was any other factor (Cadoret & Stewart, 1991; Cantwell, 1975).

Dopamine and Molecular Genetics

Research has indicated neurochemistry imbalances in the pathophysiology of ADHD. Such research has examined neurotransmitters and molecular genetics. A neurotransmitter is a chemical that is released from neurons within the brain and is used to transmit information chemically from one neuron to another. Dopamine (DA), one of the small molecule neurotransmitters that have been identified, is synthesized from the dietary amino acid, tyrosine. Numerous studies have indicated that DA regulates motor and limbic system functioning (Deutch, 1993; Schultz, Dayan, & Montague, 1997; Wickelgren, 1997; Wise, 1996) and a few studies have examined the role of DA in cognitive functioning (Collins, Wilkinson, Everitt, Robbins, & Roberts, 2000; Nieoullon, 2002). Abnormal DA levels and transmission has been found in Parkinson's disease, Schizophrenia, Alzheimer's disease, Tourette's disease, Attention Deficit/Hyperactivity Disorder (ADHD), Huntington's disease, autism, and bipolar disorder. Some of these disorders have a motivational component, many express motor impairment, and all show cognitive impairment.

It has been hypothesized that ADHD is a result of abnormal DA and norepinephrine transmission (Nieoullon, 2002). Molecular biological studies have identified specific dopaminergic genes as contributing to ADHD (Comings, 1997). One of these specific genes includes the dopamine transporter gene (DAT1) that is involved in the re-uptake of DA from the synapse, and has been linked to hyperactivity (Faraone et al., 2005; Faraone & Biederman, 1998). Another variation involves the dopamine D4 receptor gene (DRD4) that is found more frequently in ADHD children than in normal controls and has an inhibitory effect on dopamine (Faraone et al., 2005; Faraone & Biederman, 1998). Other genetic variations related to ADHD include dopamine β hydroxylase (responsible for enzymatic conversion of dopamine to norepinephrine), the dopamine D2 receptor gene (DRD2) (Comings et al., 1996), and the dopamine D5 receptor gene (DRD5) (Daly, Hawi, Fitzgerald, & Gill, 1999).

A recent study examining the dopaminergic system genes in ADHD (Kirley et al., 2002) found the strongest evidence for problems within the DAT1 and DRD4 genes by examining DNA from 118 ADHD children ages 4-14, their ADHD parents (transmitted parental alleles), and their non-affected parents (nontransmitted parental alleles). The DRD4 has been associated with cognitive and attentional abilities and may have an association with the novelty seeking personality characteristic (Roman et al., 2001). The

DAT1 has been linked to hyperactivity (Giros, Jabar, Jones, Wightman, & Caron, 1996; Faraone & Biederman, 1998). With regard to DAT1, there was a significant preferential transmission between ADHD children and their ADHD parent. Specifically, this study and other research indicate that there is less transmission of DAT1 in areas such as the striatum and possibly higher cortical areas in children and parents with ADHD as compared to normal controls (Kirley et al., 2002; Tannock, 1998). Recently, one study found a 70% increase in DAT1 density of ADHD adults as compared to normal controls (Dougherty, Bonab, Spencer, Rauch, Madras, & Fischman, 1999). An increase in density of dopamine transporters leads to less dopamine available in the synapse for activation, which lends further support to the reduced dopamine hypothesis.

Many other studies have also found evidence to support the connection between ADHD and DAT1 (Cook et al., 1995; Curran et al., 2001; Daly et al., 1999; Gill, Daly, Heron, Hawi, & Fitzgerald, 1997; Kirley et al., 2002; and Waldman et al., 1998). Similar to DAT1, DRD4 appears to contribute to less dopamine transmission in children with ADHD as compared to normal controls (Faraone et al., 1999; Holmes et al., 2000; Kirley et al., 2002; LaHoste et al., 1996; Muglia, Jain, Macciardi, & Kennedy, 2000; Rowe et al., 1998; Roman et al., 2001; Smalley et al., 1998; and Swanson et al., 1998).

Although the evidence connecting ADHD to dopamine genes is compelling, it is still not considered definitive in the literature. This is due, primarily, to the host of studies showing conflicting findings. Although strong evidence suggests a connection between specific dopamanergic genes and ADHD, a number of studies have failed to find a relation with DAT1 (Asherson et al., 1998; Holmes et al., 2000; Palmer et al., 1999; and Roman et al., 2001) and with DRD4 (Castellanos et al., 1998; Comings et al., 1999;

Eisenberg, Zohar, & Mei-Tal, 2000; Hawi, McCarron, Kirley, Fitzgerald, & Gill, 2000; Kotler, Manor, Sever, Eisenberg, Cohen, Ebstein, & Tyano, 2000; and Todd et al., 2001).

There are also a number of methodological and practical problems in the molecular biology literature examining dopamine and ADHD. First, samples sizes in some studies are relatively small, resulting in low power to detect differences if they exist. Second, the samples used in the literature have high rates of comorbidity that have not been accounted for in any way. The comorbidity rates averaged 70% with approximately 30-50% being diagnosed with Oppositional Defiant Disorder (ODD) and 10-20% with Conduct Disorder (CD) (Castellanos, et al., 1998; Daly et al., 1999; Holmes et al., 2000; Palmer et al., 1999; Smalley et al., 1998). Given the nature of these disorders, it is highly possible that the comorbid condition of ADHD and ODD/CD is both structurally and functionally different than that of ADHD alone. Finally, there are few review articles available that attempt to summarize this conflicting body of knowledge. However, there has been two review articles and one meta-analysis by Faraone and colleagues (DiMaio et al., 2003; Faraone, Doyle, Mick, and Biederman, 2001; Faraone et al. 2005). The meta-analysis (Faraone et al., 2001) examined 22 casecontrol and family-based studies and resulted in small but significant relations between ADHD and DRD4 in 5 of 8 case-control and 9 of 14 family-based studies. The more recent reviews also indicate strong support for the relation between ADHD and DRD4 as compared to other genes (DiMaio et al., 2003; Faraone et al., 2005). So, despite conflicting research and the methodological problems in the field, genetic based evidence of ADHD is promising.

Psychopharmacology

Children with ADHD have been treated with stimulant medication for decades. Stimulant medications, such as methylphenidate (Ritalin) and dextroamphetamine (Dexedrine and Adderall) have been shown to effectively treat the disorder (Elia et al., 1990; Jonkman et al., 1997). The medications act to block the re-uptake of DA and norepinephrine in presynaptic terminals, and increase the release of DA and norepinephrine in the synapse (USP DI, 1999). The effective treatment of ADHD with stimulants and the mechanisms by which these medications work within the brain would support a hypothesis of diminished DA capacity.

A new non-stimulant medication, Atomoxetine (Strattera) works as a norepinephrine reuptake inhibitor and is used for those that are unresponsive to stimulant medication or for those that have comorbid internalizing conditions or substance abuse (Michelson et al., 2003). Physicians have also begun prescribing the antidepressants imipramine and buproprion SR as a second-line of defense. Imipramine is a tricyclic antidepressant (TCA) that blocks the re-uptake of norepinephrine (a derivative of DA) and serotonin in presynaptic terminals (USP DI, 1999). Buproprion SR is a unique new generation antidepressant that is more similar to selective serotonin-reuptake inhibitors (SSRIs) with regard to side effects but more like TCA with regards to mechanism of action, which seems to be a weak re-uptake inhibitor of DA and norepinephrine (USP DI, 1999). Therefore, it appears as though there may be other neurochemical issues and/or neurotransmitters involved in the etiology of the disorder, at least for a select group of children with ADHD.

Neuroimaging

Neuroimaging studies include functional magnetic resonance imaging (fMRI or MRI), single positron emission computed tomography (SPECT) and positron emission tomography (PET). These studies examine both structural and functional variances of ADHD children. The results of neuroimaging studies have been somewhat inconsistent in the literature. Some of these inconsistencies have shown discrepancies in children with ADHD for the caudate nucleus (Castellanos et al., 1996; Filipek et al., 1997), the corpus collosum (Lyoo et al., 1996; Baumgardner et al., 1996; and Hynd et al., 1991), the cerebellum (Berquin et al., 1998; Castellanos et al., 1996), and lateral ventricles (Castellanos et al., 1996).

The structural imaging literature has primarily used MRI to examine neuroanatomical differences between ADHD and normal control children. The MRI studies examining overall brain size have failed to find differences between ADHD children and normal controls when IQ was statistically controlled for (Berquin et al., 1998; Castellanos et al., 1996; Flilipek et al., 1997; Lyoo et al., 1996). Some of the most consistent findings noting discrepancies using structural MRI have been reported for the frontal lobe. First, the total frontal lobe volume and the right-side frontal lobe volume were significantly decreased in children with ADHD as compared to normal controls (Castellanos et al.; Filipek et al.; Hynd, Semrud-Clikeman, Lorys, Novey, & Eliopulos, 1990). Additionally, the children with ADHD had a reduced right side to left side asymmetry (R>L) than that seen in control children (Filipek et al.; and Hynd et al.).

The functional imaging literature has used a number of different techniques including fMRI, PET, and SPECT, all of which measure differential metabolic activity in

one form or another. Baumeister and Hawkins (2001) reviewed functional imaging studies and found many inconsistencies in the literature. The studies examining the frontal lobe primarily found decreased activity for ADHD children. However, there have been several reports of non-significant findings and one study even showed an increase in frontal lobe activity (Baumeister & Hawkins, 2001). Studies examining the caudate nucleus, occipital, temporal, and parietal lobes were less consistent (Baumeister & Hawkins, 2001).

Overall, the most consistent findings in the neuroimaging literature appear to involve deficits in frontal lobe structure and function in ADHD samples as compared to normal controls. Given that the frontal lobe is rich in dopaminergic transmission and important for executive functioning skills and motor control (Solanto, 1998), an examination of frontal lobe dopamine in ADHD children may be extremely beneficial.

Event-Related Potentials

Another method used to evaluate brain function has been to measure electrical activity through recording event-related potentials (ERPs) from the scalp. Klorman (1991) provided an overview of early ERP studies examining differences between children diagnosed with ADHD and normal controls and concluded that there were deficits in both behavioral and physiological measures. Children with ADHD had fewer correct hits and more errors to non-target stimuli than did normal controls on selective attention tasks. Also, the reaction times of ADHD children were slower and more variable. The physiological measures discussed in this review included P3b amplitude (theoretically measuring amount of processing), P3b latency, and a negative difference

waveform (Nd), which assesses attention. ADHD children performing the CPT had smaller P3b amplitudes for both targets and non-targets as well as longer P3b latency than normal controls. Studies on Nd resulted in smaller processing negativity (the difference between the attended target and non-target tones on selective attention tasks) for ADHD children relative to normals.

Jonkman and colleagues (1997a; 1997b) measured both auditory and visual selective attention in a study that lends support to the conclusions of Klorman's overview. They tested ADHD children and normal controls, ages 7-13, and found that ADHD children had fewer correct hits, more false alarms, and smaller P3b amplitudes than normals. The results of these studies suggest that ADHD children have poorer behavioral performance on tasks that require both a response to a target stimuli and a non-response (inhibition) to non-target stimuli. Furthermore, the ERP data suggest that ADHD children process stimuli to a lesser extent, and are slower in processing stimuli than normal controls. The Nd data also suggest that ADHD children process both targets and non-targets similarly, thus displaying a deficit in the ability to discriminate stimuli. Although there was inconsistency in the neuroimaging literature, the ERP literature shows consistent support of processing and performance deficits in children with ADHD as compared to normal controls.

Neuropsychological Tests and Executive Functioning

Researchers have also examined neuropsychological tests that are sensitive to executive functioning skills. Executive functioning has been described as a cluster of skills involving working memory, self-regulation, goal-directed planful behavior,

organization, response inhibition, and other higher-order cognitive processes. Research supports a strong connection between the frontal cortex and executive functioning (Barkley, 1997b; Roberts & Pennington, 1996; Travis, 1998; van der Molen, 2000). Aman, Roberts, and Pennington (1998) conducted a study examining frontal lobe deficits of ADHD children and found that ADHD children performed more poorly on executive function tests such as the Antisaccade and the Tower of Hanoi tasks as compared to normal controls. Additionally, unmedicated ADHD children performed more poorly on the Stopping task than did medicated children. These researchers conclude that these data support the frontal lobe deficit theory of ADHD.

Barkley and colleagues (1992) reviewed 22 neuropsychological studies examining the performance of ADHD children on executive functioning tasks. These tasks included the Wisconsin Card Sort Test, the Stroop Test, CPT, memory tasks, go-no/go tests, and motor tests. This review found that tests measuring response inhibition were more sensitive to discriminating ADHD from normal controls as compared to other neuropsychological tasks, but that most of the measures did not distinguish ADHD from other clinical groups. These researchers further highlighted the problem that comorbidity presents.

ADHD Assessment

Clinical Presentation

According to the Diagnostic and Statistical Manual, 4th Edition (DSM-IV), ADHD is pervasive disorder that is present before the age of 7 years and results in significant impairment over a wide range of contexts and situations, including home, school, occupational, and social. In order for a child to meet diagnostic criteria for ADHD, he/she must display six or more symptoms of inattention and/or six or more symptoms of hyperactivity/impulsivity for at least 6 months. Additionally, these symptoms must not be better accounted for by another mental disorder.

The diagnosis of ADHD is coded based on one of three types: ADHD, Combined Type (ADHD-C); ADHD, Predominately Inattentive Type(ADHD-PI); and ADHD, Predominately Hyperactive-Impulsive Type (ADHD-PHI). These three types appear to be highly subjected to the developmental nature of the disorder. The developmental trajectory of ADHD has shown that problems with inhibitory control arise around age 3 to 4 years, while the secondary problems related to attention arise around age 5 to 7 years (Hart et al., 1996). Additionally, it has been reported that the hyperactive/impulsive symptoms begin to drop off during middle childhood (Hart et al.). Therefore, diagnostically, a child is likely to be diagnosed with ADHD-PHI in preschool years, ADHD-C in early school years, and ADHD-PI type in middle childhood to adolescence.

Another important issue worth mentioning about the clinical presentation of the disorder is comorbidity with other mental disorders. It has been estimated that between 35 and 60% of clinic-referred children with ADHD will also meet criteria for Oppositional Defiant Disorder (ODD) and between 30 and 50% will eventually meet criteria for Conduct Disorder (CD) (Biederman, Faraone, & Lapey, 1992). With anxiety disorders the comorbidity rate has been estimated between 25 and 40% of clinic-referred children (Biederman et al.) and between 40 to 50% with mood disorders (Barkley, 1996). Additionally, when using a significant discrepancy score, 53% of ADHD children would also be classified with a learning disability (Lambert & Sandoval, 1980).

Diagnostic Interviews

Interviewing is one of the initial assessment methods used and provides basic demographic information; referral concerns; developmental, medical, school, and family histories; and a review of symptoms related to other major childhood disorders that may be confused with ADHD. Most assessments will include interviews for parent(s), teacher(s), and the child (depending upon the age). Many clinicians use unstructured interviews. However, unstructured interviews have the potential to be extremely unreliable based on a number of factors including lack of clarification of diagnostic criteria or decision rules and specific biases, assumptions, or errors on the part of the interviewer (Achenbach, 1985). From a research standpoint, unstructured interviews do not allow for standardization of interview presentation, which could impact group inclusion and the identification of comorbidity.

Several highly structured or semi-structured interviews have been developed that allow for classification of disorders according to DSM criteria. These structured interviews allow for a more standardized and reliable assessment for research purposes, however, they often generate information for group inclusion/exclusion rather than more qualitative information for formulating treatment recommendations (Mash & Terdal, 1997). Empirical research has found that the reliability of such structured interviews may vary within disorders and with the age of the child (Barkley, Fischer, Edelbrock, & Smallish, 1991; Edelbrock, Costello, Dulcan, Kalas, and Conover, 1985; Hinshaw, 1994). For example, children under the age of 10 have not shown to be reliable in reporting internal states, whereas children over 10 have shown to be better reporters of internal states than were their parents (Edelbrock et al., 1985). With regard to ADHD, it has been

reported that children below the age of 12 may not be reliable in reporting their own personal/family problems due to a decreased self-awareness and cognitive capacity (Hinshaw, 1994) and that ADHD children tend to underestimate the seriousness of their problems (Barkley, et al., 1991).

With regards to other informants, there is research to indicate that retrospective reports of childhood behavior provided by parents are less reliable than compared to nursery school, pediatric, and psychological records (Evans & Nelson, 1977). Finally, parent and teacher interviews can also be subject to demand characteristics in that an informant that wants a child treated may over-report severity levels and symptoms, whereas an informant who does not desire treatment may under-report (Mash & Terdal, 1997). Regardless of these concerns, parent and teacher reports are frequently used to determine ADHD status.

Behavior Rating Scales

Behavior rating scales are widely used in ADHD assessment and usually encompass both a general rating of childhood disorders, and a specific rating for ADHD symptoms. Most assessments will provide behavior-rating scales for parent(s), teacher(s), and the child (depending upon the age). Behavior rating scales are both convenient and useful as they provide acceptable reliability and validity and have adequate normative data. The information provided by behavior rating scales is often used to guide the clinical interview and screen for psychopathology.

A broad behavior-rating scale is often used to assess the major disorders known to affect children. A broad-based rating allows a clinician to determine if other disorders

should be assessed. Once the broad rating is reviewed, then more specific rating scales can follow to assess the specific symptoms related to the disorder. Again, some of the same problems seen with interviews are relevant to behavior-rating scales, including children under the age of 10 being poor reporters of internalizing disorders and ADHD children under the age of 12 underestimating their behavior and problems. Additionally, parent/teacher agendas may influence behavior-rating scales. However, one advantage to many behavior-rating scales is that they allow for built-in reliability and consistency measures. This allows for an item analysis to assess for informant negativity within parent/teacher reports, and consistency of responding in parent, teacher, and child reports.

One major concern in the use of informant behavior-rating scales has to do with the concordance of reporting. Mother and father reports have been estimated at 69% agreement (Achenbach, 1985) whereas parent and teacher reports have been estimated at 30% agreement (Achenbach, McConaughy, & Howell, 1987). One explanation for the lower parent/teacher agreement is that these ratings are context specific and that the behavior parents observe in an unstructured environment at home is different than the behavior teachers observe in a structured classroom setting. Therefore, impairment in behavior across settings will likely show a different symptom cluster at home as compared to school. This information should be considered when reviewing parent and teacher rating scales.

Laboratory Tests

Researchers have used various tests purported to measure frontal lobe or executive functioning in ADHD etiology research. Only one of the laboratory measures that will be reviewed, the continuous performance test (CPT), has been widely used in a clinical setting, although this task has limited research to support use in ADHD research [See Special Issue: (2005), Journal of Clinical Child Psychology, 34 (3)]. The other measures that will be discussed are laboratory tests used primarily in research with disruptive behavior disorders (ADHD, ODD, and CD). These measures include the card playing tasks, go/no-go tasks, and stop-signal tasks. Each of these four laboratory tests will be discussed.

For measuring sustained attention, the CPT is one of the most widely used in ADHD assessment. There are many different variations of the CPT that have been developed by researchers to assess slightly different functions. Most CPTs allow for assessment of hits (number of correct responses), omission errors (number of missed responses), and commission errors (number of incorrect responses to stimuli other than the target). CPTs have reliability discriminated between ADHD and non-ADHD populations (Barkley, 1991; Grodzinsky & Diamond, 1992), however, they appear to be less successful in discriminating ADHD and other clinical groups (McGee, Clark, & Symons, 2000; Halperin, Matier, Bedi, Sharma, & Newcorn, 1992). Additionally, CPTs have been shown to have poor negative predictive power in that the tasks can allow clinicians to rule in ADHD, but not to rule out ADHD based on a negative finding (Barkley & Grodzinsky, 1994; Matier-Sharma, Perachio, Newcorn, Sharma, & Halperin, 1995).

The card-playing task (also referred to as the door-opening task) is more often used in research with other disruptive behavior disorders, such as CD and ODD. As with the CPT, there are many variations. Most tasks require participants to select a card from

several choices, and they are rewarded for a correct response. Early in the task, all of their choices are rewarded, however, as the number of trials increases, the probability of a reward decreases. Many of these tasks implement response cost, where there is a chance for losing previously earned rewards. Participants are informed that they can stop playing the task at any time. The card-playing task is theorized to tap motivation in the orbitofrontal cortex and the amygdala (Fisher & Blair, 1998) and research suggests that it is a better discriminator between ADHD and CD/ODD in that the latter group will play significantly more cards that the former (Daugherty & Quay, 1991; O'Brien & Frick, 1996). The card-playing task also appears to discriminate between adults with Antisocial Personality Disorder (ASPD) and control prison inmates, in that those with ASPD will also play more cards (Newman, Patterson, & Kosson, 1987). Additionally, it has been shown that the ability to learn does not differ between those with ASPD and those without (Scerbo et al., 1990). Thus, the task appears to show motivational differences rather than differences in the ability to learn.

The go/no-go task has a number of variations but primarily requires participants to attend to and respond to a target (or go trial), while ignoring other stimuli (the no-go trials). The go/no-go task often includes a learning component, where the participant must learn which stimuli to respond to, and a reward component that rewards participants for correct responses and/or implements a response cost for incorrect responses. When the learning component is included, there is a significant demand placed on working memory, as participants must keep in mind those stimuli that are rewarded and those that are not. Additionally, this task taps into motivation when the reward/response-cost component is included. As a result, this task appears to identify both ADHD children and

CD/ODD children (Newman, Widom, & Nathan, 1985; Shue & Douglas, 1992; Milich, Hartung, Martin, & Haigler, 1994; Iaboni, Douglas, & Baker, 1995; and Hartung, Milich, Lynam, & Martin, 2002).

The stop-signal task in its various forms is a measure of impulse control and requires the participant to respond quickly to a target stimulus but later to withhold the response when a "stop" signal is given. This task primarily presents an increased prepotency of the target stimulus in that participant's first inclination is to respond to the target. However, they must inhibit responding to that target during the "stop" phases of the task. The stop-signal task also taps into some working memory ability by requiring participants to hold the instructions in mind as well as to change the instructions as needed (i.e., when the "stop" signal occurs). Most of the research that has been conducted on the stop-signal task suggests that the task discriminates between ADHD and normal controls as well as between ADHD and ODD/CD (Oosterlaan & Sergeant, 1998; Nigg, 1999; Schachar & Logan, 1990; Schachar & Tannock, 1995; Schachar, Mota, Logan, Tannock, & Klim, 2000; Slusarek, Velling, Bunk, & Eggers, 2001), although not consistent (Nichols & Waschbusch, 2004).

Direct Observations

Direct observations are recommended in ADHD assessment (Barkley, 1997a). The assumption is that direct observations are less subject to bias than are interview and behavior-rating scales where parents, teachers, and children can describe behavior in ways that are influenced by personal biases (Mash & Terdal, 1997). However, some biases still exist with direct observations, including observer bias, settings for

observations, and the observer's presence. To attempt to remedy these problems, systematic observation programs have been established to quantify direct observation and to stress the importance of multiple observations in multiple settings (Sattler, 2002). Many of these programs, however, are useful in research but may not be as practical in clinical settings.

Summary

Current ADHD diagnostic methods consist of conducting or collecting diagnostic interviews, behavior-rating scales, laboratory tests, and behavioral observations. ADHD assessment uses both broad- and narrow-based measures, assessing for a wide range of symptoms and functioning, as well as the specific symptoms needed to meet diagnostic criteria. There are a number of problems with current ADHD assessment methods. First, behavior-rating scales, self-report scales, clinical interviews and direct behavioral observations are subject to demand characteristics. Many of the rating scales have implemented reliability measures to assess for inconsistent responding or overly-negative responding to attempt to correct for some of these problems. Second, clinical interviews and direct observations are subject to clinician/observer bias. The use of structured or semi-structured interviews and systematic observation programs attempt to reduce this bias by setting more stringent decision rules. Finally, laboratory tests that have been normed for use in clinical settings often fail to provide good discriminant validity between ADHD and other clinical groups (e.g., CPT). Other laboratory tests that have been used to tap into executive functioning and motivation have been used primarily in research settings and are infrequently used in clinics (e.g., go/no-go, stop-signal, and card

playing tasks). There is less information available regarding the ability of these measures to discriminate between groups (See Nichols & Waschbusch, 2004 for review of CPT and stop-signal).

Comorbidity issues significantly complicate ADHD assessment, especially when using laboratory tests. However, it has been proposed that laboratory measures tapping into motivation and executive functioning may be helpful in discriminating ADHD from ODD/CD and identifying a comorbid group.

CHAPTER III

HYPOTHESES

The current research program attempted to assess ADHD children, other clinical children, and non-clinical normal control children on a contrast sensitivity test, (the Functional Acuity Contrast Test [FACT]), and various tasks of executive functioning and motivation. Four hypotheses were proposed for the current study. Hypothesis one stated that the FACT would discriminate ADHD from non-ADHD samples. Hypothesis two stated that the FACT would be highly correlated with stop-signal and CPT tasks. Hypothesis three stated that the FACT would be only moderately related with the go-no/go task. Hypothesis four stated that the FACT would be unrelated with the door-opening task, which is proposed to be a purely motivational task.
CHAPTER IV

RESEARCH DESIGN AND METHODS

Participants

Children ranging in age from 6 to 12 (grades 1 through 6) were recruited in two different locations. The first location was north central Oklahoma (primarily the town of Stillwater), and the second was a number of towns and cities in northeastern Oklahoma. The Stillwater site is located in the north central region of the state and home to Oklahoma State University (OSU). The ADHD sample was recruited from the Psychological Services Center (PSC) at OSU, from various community agencies (both clinic and non-clinic), and from north central Oklahoma public schools. From both recruitment locations, three groups were formed; ADHD (N=63), clinic controls (N=41), and non-clinic normal controls (N=36). At the Stillwater site, the normal control children were recruited from the community sample only, while the ADHD and clinic control children were recruited from both clinic and community samples. Demographic information for the participants used in the Stillwater site is presented in Table 1 (See Appendix).

The second location was northeastern Oklahoma and incorporated several rural towns and cities. Clinic-referred children were recruited from Cherokee Nation clinics located in northeastern Oklahoma. The patients were representative of the Cherokee

Nation 14-county jurisdiction and included both rural and urban Native American children. Although some patients were members of other tribes, most of the sample was of Cherokee descent. The normal control group was recruited from schools in the 14county jurisdiction with high populations of Native American students and at local tribal gatherings and were similar to those recruited from the tribal health facilities in this area with regard to tribal affiliation, acculturation, and social and economic status. Demographic information for the northeastern Oklahoma site is presented in Table 2 (See Appendix). Combined sample demographic information is presented in Table 3 (See

Participants recruited from the PSC at OSU consisted of children who had undergone assessment, who were on a waiting list for an assessment, or who were currently in treatment. Parents were provided with information about the study and were asked about their willingness to allow their child to participate. If they chose to participate, a member of the research lab contacted the parent to schedule an appointment. If a child had recently (in the last 2 months) undergone cognitive and/or achievement testing in the PSC, these scores were used in lieu of the IQ and achievement screening tests that were administered as a part of the research assessment battery. Also, children, parents, and teachers who had received the behavior-rating scales and structured clinical interview within the last 4 weeks as provided by a PSC Associate did not have to repeat these measures. In this case, a release of information was obtained, so that this information could be provided by the PSC for use in research.

Participants being recruited from the tribal health clinics were children referred to Behavioral Health Services (BHS) for ADHD or other clinical assessment. These

assessments are regularly provided by BHS at no cost to the family. Parents were informed of the study before the assessment began and were provided with information about both the research assessment protocol and the BHS standard assessment protocol. If parents chose not to allow their child to participate in the research study, then the standard BHS protocol was administered. If, however, parents chose to allow their child to participate in the research study, then he/she immediately began the research protocol that also served as an actual clinical assessment. After all of the materials were collected, a review summary was provided to the BHS licensed psychologist, who made appropriate diagnoses and treatment recommendations.

Initial Screening

At the Stillwater site, all children were assessed over two days. Each assessment session lasted approximately 1 to 1 ½ hours for normal control children and 1 ½ to 2 hours for clinic children. Children were assessed in the laboratory at OSU. Informed consent from the parents and assent from the child were obtained. Also, a release of information was obtained from the PSC, if needed. The initial screening consisted of a Wechsler Abbreviated Scale of Intelligence (WASI), the Wide Range Achievement Test (WRAT-R) Spelling subtest, the Gray Oral Reading Test (GORT-4), the NIMH Computerized Diagnostic Interview Schedule for Children (C-DISC), a parent-packet with various assessment measures (Demographic Information Sheet, Child Symptom Inventory for Parents (CSI-Parent), the Behavioral Assessment Scale for Children (BASC-Parent Report)), and a teacher packet including various assessment measures (CSI-Teacher and the BASC-Teacher Report).

These initial screening measures were used to ensure appropriate group inclusion. The three primary groups were ADHD, other clinic group, and a non-clinic normal control group. Children in the clinic group were those that had been diagnosed with depression, anxiety, learning, or oppositional/conduct disorders. Children who had comorbid ADHD/ODD or ADHD/CD were included in the ADHD group for the overall analysis. During this initial screening, ADHD children were allowed to continue current medication (if any) and their medication and dosage were noted. Additionally, children received a FACT at the initial screening and at the testing session so that test-retest reliability could be measured as well as any medication effects on contrast sensitivity (CS). After the FACT was administered, an evaluation of performance at each spatial frequency was conducted. If evidence of visual problems existed, then the child received a free vision exam by one of the research consultants, Brian Gumm, O.D. Children with neurological impairment resulting from injury or illness, prenatal substance exposure, and pervasive developmental disorder were excluded from the study based on an integration of information from parent report prior to scheduling the initial session (N=2). Children who were not at least in the average range of intellectual functioning (SS above 80) were also excluded from the study (N=4). If significant psychopathology was noted during the initial screening, appropriate referrals were made. At the northeastern Oklahoma sites the same initial screening was provided.

It is important to note that, although it is possible for children with a normal FACT score to be experiencing other visual pathology, this study was not interested in other visual pathology. The only interest here was in CS. This statement is made because optometry referrals were only made for individuals who showed abnormal CS. It is

highly unlikely that identification and treatment of some other visual pathology would then lead to a post-test abnormal reading on the FACT following a normal pre-test reading.

Testing Session

All eligible children returned for testing within one week of initial screening for both testing locations. There was an overall attrition rate of 5%, totaling seven children that did not return for the second session. At the second session, parent and teacher packets were collected. Parents were asked to withhold administration of stimulant medications from children the day of the testing session. Parents were reminded to withhold medication the day before testing via phone and compliance was confirmed the day of the testing session. The FACT was administered and a contrast reading was obtained. Following the FACT, children completed the tasks designed to tap into executive or motivational functioning, including a continuous performance test (CPT) (Halperin, Wolf, Pascualvaca, Newcorn, Healey, O'Brien, Morganstein, & Young, 1988), stop signal task (Logan & Cowan, 1984), the door-opening task (aka: card-playing task) (Daughtery & Quay, 1991), and the go-no/go task (Newman et al., 1985). These cognitive tasks were administered in a quasi-random order in that the executive functioning tasks were randomly administered first and the motivational tasks were randomly administered last. The motivational tasks had to be administered last to sustain motivation throughout all tasks. At the Stillwater site, parents were provided a brief report regarding their child's intellectual functioning, achievement status, and vision test status. At the northeastern Oklahoma sites, the same was provided for parents in non-

clinic settings. However, parents in the clinic received formal feedback and a more thorough report that included a diagnosis from the licensed psychologist. All children were paid twenty dollars for their participation and parents were paid five dollars for their travel expense.

During pilot testing of the FACT administration, it became evident that some children were showing major symptoms of hyperactivity and/or inattention that may have been interfering with their test performance. Therefore, all children were closely monitored for signs of hyperactivity and inattention (such as squirming in seat, rushing responses on gratings, and looking away from the sinewave board). When these symptoms were evident, two research team member's administered the FACT. One team member would concentrate on ensuring that the child examined and responded to each grating, redirecting the child as often as necessary and pointing to each grating throughout the test. The second team member would write down responses and would provide secondary observations to improve assurance that the child's hyperactivity and/or inattentive symptoms did not interfere with test performance.

Research Team

Doctoral students (one of whom is the principal investigator [PI]) administered assessments in both locations. These students underwent extensive training in administering the assessment protocol with close supervision throughout the process. Undergraduate students worked as assistants and job duties included administering computerized testing and the FACT for the participants. The undergraduate students underwent extensive training in the computerized structured interview, computerized laboratory tests, and FACT administration and were closely supervised by a doctoral level student at all times. Several undergraduate students were involved in data entry and scoring of assessment protocols and were closely supervised by the PI. All data was checked and re-checked three times. Finally, 20% of the data was randomly selected for a final recheck, which resulted in no found errors. Training for all research team members was ongoing throughout the entire project as team members were added during the study when the referrals increased.

Three consultants were also working on the research project. John Gastorf, Ph.D., is a licensed psychologist. He provided diagnoses at the BHS clinic in northeastern Oklahoma site and was supervising the doctoral students at the BHS sites. Dr. Gastorf has over 30 years experience working in outpatient and inpatient clinic facilities as well as in research positions. He is currently the director of Behavioral Services for Cherokee Nation. Cynthia Hartung, Ph.D., is an Assistant Professor in the Psychology Department at OSU and provided supervision to the doctoral students at the Stillwater site, including review of group inclusion decisions. The final consultant was the optometrist, Brian Gumm, O.D., who provided corrective lenses and visual examinations when necessary at the Stillwater site and trained the PI on FACT administration. Children from the northeastern Oklahoma site used Cherokee Nation Optometry Clinics for visual examinations when needed.

The researcher administering the screening session was blind to group inclusion. However, during the testing session the researcher knew to which group the child belonged as a feedback report was provided. Given that the laboratory tests are completely computerized and computer scored, it is unlikely that the researcher could

influence the outcome. However, there is always a possibility that instructions for each group could vary based on the researchers' knowledge of group inclusion. Therefore a script was provided which was used by researchers for administering all testing protocol. Additionally, all FACT administrations were conducted by research team members that were blind to group inclusion.

Measures

Diagnostic Interview Schedule for Children (DISC)

The DISC is a structured clinical interview that was developed by the National Institute of Mental Health (NIMH). The DISC includes both Youth and Parent Versions and elicits basic demographic information, a measure of three different time periods if needed (past 4 weeks, past 12 months, and "wholelife"), and is organized into six diagnostic modules (Anxiety, Mood, Disruptive, Substance Use, Schizophrenia, and Miscellaneous Disorders). This DISC-IV is set up to assess DSM-IV criteria. The C-DISC-IV is a computer version that allows the interviewer to enter and score information immediately. The computer version has been shown to reduce errors, data entry time, and training (3 days vs. 6), but does not reduce administration time. Because the administration time is lengthy, only the C-DISC Disruptive module was administered. Also, the time period selected was the past 12 months of behavior. As previously reviewed, children under the age of 10 are not reliable reporters of internalizing behaviors. Additionally, children with ADHD under the age of 12 tend to underestimate their behavioral problems. Therefore, the Youth version was not administered. One-year test-retest reliability coefficients (kappa) for the Parent Version were estimated at .79 for

ADHD, .54 for ODD, and .43 for CD diagnostic criteria (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). Validity data on the DISC-IV are nonexistent and validity estimates are extrapolated from previous versions of the DISC. Predictive validity scores (kappa) on the DISC-2.3 for the Parent Version were estimated at .72 for ADHD, .59 for ODD, and .74 for CD (Shaffer et al., 2000).

Wechsler Abbreviated Scale of Intelligence (WASI)

The WASI is a brief screening device to assess intellectual functioning (Psychological Corporation, 1999). The two-subtest form was used and includes the Vocabulary and the Matrix Reasoning Subtests. The WASI was normed for use with individuals ages 6 to 89, and takes approximately 15 minutes to administer. Approximately 700 participants were included in the normative data for children ages 6-12 years. The manual reports internal consistency of .89 for the Vocabulary subtest, .92 for matrix reasoning, and .96 for FSIQ-2. Test-retest (2 to 12 week interval) reliability was estimated at .85 for Vocabulary subtest, .77 for Matrix Reasoning, and .85 for FSIQ-2. Concurrent validity with the Wechsler Individual Scale for Children-3rd Edition (WISC) was .81 for the FSIQ-2. Predictive validity ranged from .63 to .72 on the composite scales of the Wechsler Individual Achievement Test (WIAT). An independent study reported concurrent validity between the WASI and the Kaufman Brief Intelligence Test (K-BIT) at .89 (Hays, Reas, & Shaw, 2002).

Wide Range Achievement Test (WRAT-R)

The WRAT-R is a brief screening device that assesses skills in reading, spelling, and arithmetic. The test can be administered to individuals ages 5 to 74 (Jastak & Wilkinson, 1984). Only the WRAT-R spelling test was administered and took approximately 10 to 15 minutes for the purpose of combining with the reading measure to rule out a reading disability. The WRAT spelling subtest measures a child's ability to copy marks resembling letters, write one's name, and write single words from dictation. The test was standardized on a national sample of 5600 participants, stratified by age, sex, race, geographical region, rural/urban residence. The WRAT-R provides standard scores (M=100, SD=15) and grade equivalents. The manual reports excellent internal consistency ranging from .97 to .99 for the Spelling subtests and adequate test-retest reliability, ranging from .79 to .96. Additionally, content validity, construct validity, and concurrent validity are all estimated to be in the acceptable to high range. Concurrent validity is measured with several achievement tests including the Peabody Individual Achievement Test, the California Achievement Test, and the Stanford Achievement Test.

Gray Oral Reading Test (GORT-4)

The GORT-4 measures oral reading rate, accuracy, fluency, and comprehension (Wiederholt & Bryant, 2001). The test was normed on 1677 persons in grades 1 through 12 and takes approximately 15-30 minutes to administer. Similar to the WASI and the WRAT-R, the GORT is presented in terms of a standard score of 100 and a standard deviation of 15. The GORT also provides percentiles and age and grade equivalents. Regarding reliability, the GORT-4 manual presents test-retest reliability (r = .91 to .95

with 2-week interval), internal consistency (r = .88 to .97), and criterion-related validity (r = .41 to .72) in the acceptable to highly consistent range. Much of the validity of the GORT-4 is based on the performance of previous versions, which have shown adequate concurrent and predictive validity with a number of highly used assessment measures, including Woodcock Word Attack subtest and the WRAT-R (Wiederholt & Bryant, 2001).

Behavioral Assessment Scale for Children (BASC)

The BASC rating scales were designed as an integrated system that facilitates differential diagnosis of a variety of emotional and behavioral disorders in children (Reynolds & Kamphaus, 1992). The BASC provides Parent Rating Scales (PRS) and Teacher Rating Scales (TRS) to rate the child's behavior, measuring a wide range of symptoms. There are 3 forms for the PRS and TRS that assess three different age ranges; 4- to 5-years, 6- to 11-years, and 12- to 18-years. These forms allow parents and teachers to rate the child on a four-point scale (never, sometimes, often and almost always) and derive T-scores that are then classified in the Average, At-Risk, or Clinically Significant range. The BASC self-reports were not used in this study due to reliability issues as discussed above. Additionally, the BASC provides validity scales that assess for consistency of responding and negativity of responses. The BASC has more than adequate normative data, assesses a wide range of behavioral, emotional, academic, and adaptive functioning, and allows for easy interpretation (Frick & Kamphaus, 2001).

Child Symptom Inventory (CSI-4)

The CSI-4 is a rating scale designed to assess specific symptoms of a wide range of childhood disorders founded on DSM-IV criteria (Gadow & Sprafkin, 1994). The disorder categories include ADHD, ODD, CD, Generalized Anxiety Disorder, Specific Phobia, Obsessive-Compulsive Disorder, Posttraumatic Stress Disorder, Tic Disorder, Schizophrenia, Depressive Disorder, Pervasive Developmental Disorders, Social Phobia, Separation Anxiety Disorders, and Elimination Disorders. The CSI-4 provides both Parent and Teacher Report Versions for measuring the behavior of children ages 5- to 14years. CSI-4 sensitivity for Parent Version were estimated at .80 for ADHD and .69 for ODD, while sensitivity for the Teacher Version were .60 for ADHD and .71 for ODD (no report was made for CD due to the low number of children with the diagnosis) (Gadow & Sprafkin, 1998). CSI-4 specificity rates were estimated at .74 for ADHD, .75 for ODD, and .83 for CD on the Parent Version and .86 for ADHD, .80 for ODD and CD on the Teacher Version (Gadow & Sprafkin, 1998). The CSI-4 was the first general rating scale to be tied specifically to the DSM-4, and covers many symptom areas that are missed by other global ratings scales. However, because it was designed as a link to DSM-4 criteria, it has limited normative data and is not recommended for normative interpretations (Frick & Kamphaus, 2001). By using both norm-referenced (BASC) and criterion-referenced testing we could provide an understanding of the participants functioning relative to other children as well as provide the categorical system that is needed for group inclusion.

Halperin's Continuous Performance Test (CPT)

The CPT developed by Halperin and colleagues (1988) presents 12 letters individually on a computer monitor in a quasi-random order. A total of 400 letters are presented over 12 minutes. There are 40 target stimuli presented (A followed by an X), 20 nontarget X's (X not preceded by an A), and 68 distractor As (A not followed by an X). Each letter is presented for 200 milliseconds with a fixed ISI of 1.5 seconds. Targets are presented with 10% frequency over the entire task. The test yields three composite scores: inattention, impulsivity, and dyscontrol. The inattention score is the number of missed targets plus the number of slow response time (RT) commission errors to X-only. The impulsivity score is the number of fast RT responses to letter combinations other than A-X (A-not-X commission errors) plus the number of A-only commission errors with long RT (>1.25 seconds). Commission errors are also broken down into type and include A-not-X errors, X-only errors, A-only errors, and random errors (responses to letters other than A or X). Halperin and colleagues argue that RT varies for each of these types of errors in that A-Not-X errors show shorter RTs (indicative of impulsivity) and that X-Only errors show longer RTs (indicative of inattention).

The normative data consist of several different samples, including 72 normal control children (Halperin et al., 1988), 85 normal control children (Newcorn et al., 1989), 54 clinical children (31 outpatient, 23 inpatient, with a wide mix of diagnoses) (Halperin, Wolf, Greenblatt, & Young, 1991), and final sample consisting of 31 ADHD children (20 of which had comorbid disruptive, mood, or anxiety), 53 clinical controls (CD or ODD, some with comorbid mood/anxiety), and 18 normal controls (Halperin et al., 1992). The CPT was normed on children ages 6.5- to 13-years. Halperin and

colleagues have reported that the CPT has discriminated between clinical and normal groups based on omission and X-Only errors of inattention. Additionally, these researchers found statistically significant differences on the measure of impulsivity (A-not-X errors) between participants with ADHD and normals, but not between clinical participants and normal controls. This would indicate that symptoms of inattention may discriminate clinical from non-clinical groups, while symptoms of impulsivity may discriminate ADHD from clinical as compared to the non-clinical group in laboratory settings. Composite measures of inattention, impulsivity, and dyscontrol, X-Only errors, and A-not-X errors were used as the dependent variables.

Stop Signal Task

In the stop-signal task (Logan & Cowan, 1984) participants respond to target stimuli, while occasionally stopping their responses after a stop signal is presented. Each trial begins with the participant watching the fixation point on the screen while a random presentation of the letters A through Z is viewed on the screen. The target stimuli are the letters X or O and the task requires that participants press the key corresponding to the target on the keyboard as quickly as possible. However, when the stop signal is presented the participant is to inhibit responding to the X or O. The stop signal is a 500 ms, 900Hz tone. The stop signal delay, which is the interval between the presentation of the go signal and the stop signal, varied depending upon the child's performance as modeled by Schachar and colleagues (Schachar et al., 2000). Using this modification, if a child responds when the stop signal is in effect, the stop delay will be shortened by 50ms. If a

child inhibits responding when the stop signal is in effect, the stop delay will be lengthened by 50ms. The dependent variable was the stop signal reaction time.

Door-Opening Task

The door-opening task (Daughtery & Quay, 1991) is a perseveration task that presents a maximum of 100 trials in which a child is allowed to play as long as he/she chooses. The object of the task is to stop playing before the probability of punishment exceeds the probability of reward. A door is presented on the computer screen and if the child chooses to open the door he/she will press the green button. At this time a happy face resulted in a reward and a sad face resulted in response cost. The probability of winning across the blocks of the task systematically decreased from 90% to 0%. The longer the child played, the greater the probability of losing. Children started with \$2.50 and earned 25 cents for each happy face and lost 25 cents for each sad face. Again, the child could stop playing the game at any time and the dependent variable was how many doors the child opened.

Go-No/Go Task

The go-no/go task (Newman et al., 1985) required children to learn which stimuli would be rewarded and which stimuli would be punished (mixed condition). The task presented 8 two-digit numbers as stimuli for each of 80 trials. The numbers were presented individually in a random order for each block for a duration of 2.5 seconds or until a response was made. Participants were given \$2.50 to start and earned 25 cents for responding to correct stimuli and lost 25 cents for responding to incorrect stimuli.

Omissions on any trial resulted in neither a gain nor loss of money. Errors of commission were the dependent measure.

Functional Acuity Contrast Test (FACT)

The FACT instrument contains visual stimuli arranged in 5 rows and 9 columns (Ginsburg, 1998). Each row contains 9 test patches of sinusoidal gratings of 3 different orientations (right, up, or left oriented). The progression of the grating size changes in steps between the rows and between each grating patch. The spatial frequencies also change between rows and are 1.5, 3, 6, 12, and 18 cycles per degree (cpd). The participant was to judge the orientation of each grating using 3-alternative forced choices and the last patch correctly identified was recorded for each spatial frequency (row). Before each use of the FACT, a light meter was used to ensure that each participant experienced the same lighting conditions. The dependent variable was the highest grading obtained as each spatial frequency.

CHAPTER V

RESULTS

Preliminary Analyses

An examination of site differences was needed before hypothesis testing could begin. One-way Analyses of Variance (ANOVAs) examining site by each dependent variable were employed. These analyses resulted in no significant site differences for any spatial frequencies on the FACT, for the hits and error measures on the CPT, for the number of doors opened on the Door-Opening task, for the hits and error measures on the Go/No-Go task or for the reaction time data or error measures of the Stop-Signal task. Therefore, all analyses for hypothesis testing were collapsed across sites.

Partial-order correlations were conducted between important demographic variables and the FACT. The variables included age and IQ. Only age showed consistent significant positive correlations with each spatial frequency of the FACT (r = .29 to .34, p<.01). IQ showed smaller, but significant, positive correlations on two (12 and 18 cycles per degree) of the five spatial frequencies (r = .17 to .21, p<.05). As a result of these correlations, age was used as the covariate in the Analyses of Covariance (ANCOVAs) examining the FACT, but IQ was not. The decision was made to exclude IQ as a covariate because IQ did not correlate with three of the five spatial frequencies (1.5, 3, and 6) and all five spatial frequencies were included in the ANOVA design. However, IQ was included as a step in the regression approach for 12 and 18 c.p.d.'s, as the spatial frequencies were examined separately in the regression design. To examine gender differences on the FACT, ANOVA was employed. The ANOVA resulted in no significant gender differences on the FACT. Therefore, gender was not included as a covariate in the analyses.

FACT By Group Analyses

Hypothesis one states that the FACT would discriminate between groups. Analysis of Covariance (ANCOVA) was employed to test this hypothesis. For all FACT analyses, participants who did not have a post-FACT score were excluded (n=24). Additionally, participants with abnormal pre- and post-test scores who had not received a vision exam were excluded from all analyses (n=3) and individuals with a score of zero on two or more spatial frequencies in the post test scores were excluded (n=1). This latter criterion was established to attempt to account for scores that reflected visual acuity problems rather than contrast sensitivity (CS) deficits. The resulting total number of participants used in the overall analyses was 112. The change in the number of participants as a result of the constraints of a particular analysis will be discussed.

As previously reviewed (see method section), ADHD group membership was defined in three different ways. ANCOVAs were conducted using each of the three definitions allowing for examination of conservative, moderate, and liberal diagnosing practices. Additionally, hypothesis one was also examined using a regression approach to attempt to address the concerns with categorically defining the ADHD group.

Several assumptions of ANCOVA were violated for the FACT analyses. First, the assumption that the scores are normally distributed within each group was not met. This violation of normally distributed scores is due to the very nature of the FACT. The FACT presents spatial frequencies that range from 1.5 to 18 cycles per degree (c.p.d.). As the spatial frequency increases, so does the difficulty level. Therefore, it is normal for children to get high scores in the beginning when the spatial frequencies are lower, but perform more poorly as the spatial frequency increases, thus resulting in skewed data. Second, the assumption of homogeneity of variance was also violated. However, the seriousness of this violation is minimal given that the ratio between the largest and smallest variance is approximately 2:1. Keppel (1991) recommends correcting alpha when this ratio is greater than 3:1. Additionally, Milligan, Wong, and Thompson (1987) recommend that if sample sizes are relatively equal (ratio of 4 to 1 or less) then the Fmax as great as 10 is acceptable (Fmax for the current study is estimated at 1.273). Third, the sphericity assumption was violated. The sphericity assumption posits that the pairs of the within-subject factor are homogenous. Again, this assumption violation is due to the nature of the FACT data. The normative data follow a non-normal distribution in that as the spatial frequencies increase, an individual's score will decrease. Therefore, the levels of the within-subjects factor for each participant are going be heterogeneous. It is important to remember as well that the within-subjects factor (FACT scores across all c.p.d.) are not the primary focus of this project. Nevertheless, a Geiser-Greenhouse correction is used when interpreting any within-subjects effects to account for positively biased results.

Violation of assumptions is even more serious when working with an unequal N design. Additionally, understanding the reason for the unequal N's will determine the type of procedure needed for correction. For the current data set, the ADHD group was significantly larger (n = 54) than the Clinic group (n = 27) and the Normal group (n = 27)31). One of the most important factors for determining the cause for the unequal N is the examination of attrition and missing data. There were 24 total children missing post-FACT data that were subsequently not included in the analyses. Of these 24 children, seven came to the first session only (5% attrition rate). An experimenter failed to give the FACT at both visits on 17 occasions (either forgot to get the pre-test measure at session 1 or the post-test measure at session 2). Of the seven children dropping out of the study, four were anticipated to be in the ADHD group and three were anticipated to be in the clinic group. Given the overall low attrition rate and that more than one group was represented in those who left the study, it is not assumed that the Unequal N's are due to the experimental conditions. There is evidence, however, to suggest that participant response was different for each group. Most children were recruited from a community sample (65%) as opposed to a clinic-recruited sample (35%). Of children recruited from a community sample, 42% were children meeting at least minimal criteria for ADHD (six or more symptoms at home or at school) as compared to 34% meeting criteria for the normal group and 24% for the clinic group. Toward the end of the study only children without ADHD were being recruited but researchers were still getting a high call rate from parents concerned about their child's ADHD status. It is assumed then, that unequal N in the current data set may be attributed to community response. Therefore, the least squares approach or SS Type III approach was used to correct for unequal N's. This

approach discards overlapping variance between effects rather than using the variance in any one effect (Page, Braver, & MacKinnon, 2003).

Again, three different definitions were used in classifying the ADHD group and each definition was analyzed separately using ANCOVA. The design was a 3x5 betweenwithin, with three groups serving as the between subject factor, five spatial frequencies serving as the within subjects factor, and age as the covariate. Definition one was the most liberal for determining ADHD diagnosis. This definition is based on an 'or rule' and defines ADHD as a total of six or more symptoms present in either parent or teacher report. This definition results in the higher rate of ADHD diagnoses in a population. The primary disadvantage of this definition is that it does not always ensure that symptoms are seen in multiple contexts. With this definition, a child could be included in the ADHD group based on the parent or teacher report alone. This analysis included the total N of 112 with 54 children in the ADHD group, 27 in the Clinic group, and 31 in the Normal group. This ANCOVA resulted in a significant main effect for group F(2, 108) = 3.60, p= .031 (Power = .655, Partial Eta Squared = .062), and a significant main effect for FACT, F(4, 436) = 15.60, p = .0001 (Geiser-Greenhouse correction with 1 and 108 df results in approximate *Fcrit* of 12.0 with p<.001), but no significant interaction (See Appendix, Figure 1). It is important to note here that a significant main effect for FACT indicates that the spatial frequencies are significantly different. This result is not meaningful for this study, except that a significant main effect for FACT indicates that the data in this sample follows the normative data for the test (i.e., children perform more poorly as the spatial frequency increases and becomes more difficult to discern). Planned comparisons were conducted using ANCOVA resulting in the finding of a significant

difference between the ADHD and Normal groups at 12cpd spatial frequency, F(1, 82) = 4.84, p = .031. No significant difference was found between the Normal and the Clinic groups and the difference between the ADHD and Clinic groups was approaching significance, F(1, 78) = 3.78, p = .055 (Power=.486, Partial Eta Squared = .043).

The second definition for determining ADHD diagnosis was the most conservative method. This definition is based on a modified 'and rule' and defines ADHD as a total of six or more symptoms present per parent report and six or more symptoms present per teacher report. It does not matter if the same symptoms are endorsed with the parent and teacher, as long as they each endorse a total of six. This definition results in the lowest rate of ADHD diagnoses in a population. The primary disadvantage of this definition is that it may only select the most severe ADHD children, missing many who are less severe or borderline. The participants meeting criteria for ADHD based on the first definition but not based on the second were excluded in this analysis. Therefore the total number of participants used in this analysis was 78, with the ADHD group dropping to 20 participants (Clinic and Normal number of participants remained the same). This ANCOVA resulted in a significant main effect for group F(2,74) = 6.02, p = .004 (Power = .87, Partial Eta Squared = .14), and a significant main effect for FACT, F(4, 300) = 17.23, p = .0001 (Geiser-Greenhouse correction with 1 and 75 df results in approximate Fcrit of 12.0 with p<.001), but no significant interaction (See Appendix, Figure 2). Again, paired comparisons were conducted using ANCOVA resulting in the finding of a significant difference between the ADHD and Normal groups at both 12cpd, F(1, 48) = 7.77, p = .008, and 18cpd, F(1, 48) = 4.52, p = .039. A significant difference was also found between the ADHD and Clinic groups at 18cpd,

F(1, 44) = 4.98, p = .031, and was approaching significance at 12cpd, F(1, 44) = 7.64, p = .064. No significant differences were found between the Clinic and Normal groups.

The final definition used for diagnosing ADHD was a more moderate method. This definition is a mix between a more liberal 'or rule' and a more conservative 'and rule' and defines ADHD as a total of six or more symptoms present in one context (parent or teacher) and three or more symptoms present in another context (teacher or parent). Again, it does not matter if the same symptoms are endorsed with the parent and teacher, just as long as one endorses a total of six symptoms and the other endorses a total of three. This definition results in a more moderate rate of ADHD diagnoses in a population and may be more appropriate when combining parent and teacher reports (Power, Costigan, Leff, Eiraldi, & Landau, 2001). This definition attempts to account for the shortcomings of the 'or rule' and the 'and rule.' Again, the participants meeting criteria for ADHD based on the first definition but not based on the third were excluded in this analysis. Therefore the total number of participants for this analysis was 86, with the number of participants in the ADHD group dropping to 28 (number of participants in the Clinic and Normal groups remained the same). This ANCOVA resulted in a significant main effect for group F(2, 82) = 5.98, p = .004 (Power = .87, Partial Eta Squared = .13), and a significant main effect for FACT, F(4, 332) = 17.00, p = .0001(Geiser-Greenhouse correction with 1 and 83 df results in approximate Fcrit of 12.0 with p<.001), but no significant interaction (See Appendix, Figure 3). Again, paired comparisons were conducted using ANCOVA resulting in a significant difference between the ADHD and Normal groups at 12cpd, F(1, 73) = 5.16, p = .026, and a significant difference between the ADHD and Clinic groups collapsed across all spatial

frequencies, F(1, 69) = 4.45, p = .038, but no significant difference between the Clinic and Normal groups.

Using three different methods for categorizing ADHD resulted in consistent findings of significant differences between ADHD and Normal groups and between ADHD and Clinic groups on the FACT. Therefore, hypothesis one stating that the FACT could discriminate among groups was supported.

FACT By Computer Task Analyses

Hypotheses two through four identified specific directional relations between the FACT and the computer tasks. Hypothesis two states that the FACT would be highly correlated with the Continuous Performance Test (CPT) and the Stop-Signal task. More specifically, poorer performance on the FACT would be related to poorer performance on the CPT and on the Stop-Signal (increased reaction time).

For correlations between the FACT and the CPT, four participants were identified as outliers. Three of the four participants were already accounted for by the various FACT exclusions (i.e., missing post FACT data or abnormal FACT scores without recent vision exam). The behavioral observations during the testing provided support for excluding the final outlier as the participant was holding down the space bar throughout the CPT. Finally, five participants had missing data on the CPT due to computer error. Therefore, 106 participants were used in the examination of the relation of the FACT and CPT. Pearson's product moment correlations indicated a significant relation between 6 c.p.d. and the CPT X-only errors, r = -.241, p = .006, and between 12 c.p.d. and the Xonly errors, r = -.179, p = .033. A significant relation was also found between 1.5 c.p.d.

and the CPT A-Not-X errors, r = -.304, p = .001, between 6 c.p.d. and the A-Not-X errors, r = -.260, p = .004, and between 12 c.p.d. and the A-Not-X-only errors, r = -.168, p = .043. (See Appendix, Table 4).

For the analysis between the FACT and the Stop-Signal task, participants were excluded if they inhibited less than 13% or more than 85% of stop trials or if Stop Signal Reaction Time (SSRT) was less than 50ms. Based on these criteria, 28 participants were excluded from the analysis and another nine participants had missing data due to computer/experimenter error. Therefore, 75 participants were included in the FACT and Stop-Signal analysis. Pearson's product moment correlations indicated only one significant correlation between 1.5 c.p.d. and SSRT, r = -.234, p = .022. No other significant correlations were found (See Appendix, Table 4). Analyses examining the correlations of the CPT and Stop-Signal task with the FACT provide moderate support for hypothesis two.

Hypothesis three states that the FACT would be only moderately related to the go-no-go task. In addition to the participants excluded due to FACT data, three participants had missing data on the Go-No-Go task due to computer error. Therefore, 109 participants were used in the examination of the relation of the FACT and the Go-No-Go task. Pearson's product moment correlations indicated that each spatial frequency on the FACT was significantly negatively related to errors of commission on the Go-No-Go task (See Appendix, Table 4). The FACT was completely unrelated to the errors of omission on the Go-No-Go task (See Appendix, Table 4). These results provide support for hypothesis three that predicts a moderate relation between the FACT and the Go-No-Go task.

Hypothesis four states that the FACT will be unrelated to the door-opening task, which is proposed to be a purely motivational task. Only participants meeting FACT exclusions were excluded from the FACT and Door-Opening task analysis. Therefore, 112 participants were used in the examination of the relation of the FACT and the Door-Opening task. Pearson's product moment correlations indicated no significant relations between any of the FACT spatial frequencies and the number of doors opened, providing support for hypothesis four (See Appendix, Table 4).

Regression Approach to examining FACT by ADHD

A regression approach was also taken to examine the relation of ADHD symptomatology and the FACT. This approach was conducted to supplement the ANCOVA approach in an attempt to address the original question while circumventing the assumption violations. However, examination of assumptions for regression analyses was similar to ANCOVA in that many assumptions were violated. Again, the data were not normal by distribution with negative skewness and positive kurtosis. This data could not be repaired with a logarithmic transformation, the transformation recommended for this type of normality violation (Fidell & Tabachnick, 2003). Also, the relationship between the regression variables is considered to be non-linear and the data can be described as heteroscedastic, or the variability in scores for one continuous variable is roughly the same as with the other continuous variable. As with the homogeneity of variance assumption in the ANCOVA, if sample sizes are relatively equal (ratio of 4 to 1 or less) then the Fmax as great as 10 is acceptable (Milligan, Wong, & Thompson, 1987). Therefore, no corrections were made for this assumption violation.

One regression was conducted for each spatial frequency on the FACT and involved three steps (with the exception of 12cpd, which used four steps as discussed below). Step one included those key demographic variables that were significantly correlated with the dependent variable, namely, age and IQ (IQ was only entered in step one on those spatial frequencies showing significant correlations, 12 and 18 c.p.d.). Step two included ADHD inattentive symptoms and ADHD hyperactive/impulsive symptoms. Step three included the interaction of inattentive symptoms and hyperactive/impulsive symptoms. Based on Figure 4 (See Appendix), it was evident that oppositional symptoms may account for significant variance at 12cpd. Therefore, ODD symptoms were entered in step two, three (two way interactions), and four (three way interaction between oppositional, inattentive, and hyperactive symptoms) at 12cpd. All data used for these analyses were centered to address issues of multicollinearity. Children's data were used in this analysis if they had both a parent and a teacher report. This criterion was set for two reasons. First, it could be an inaccurate representation of symptoms if Child A received an inattentive score of six with only a parent report and Child B received an inattentive score of nine with both a parent and teacher report. Child A appears to have fewer inattentive symptoms but this may only be due to this child lacking a teacher report. Second, the parent report of symptoms could have been used because most children had a parent report. However, this would restrict the range considerably (18 total symptoms possible for parent only report vs. 36 symptoms for both parent and teacher reports) and may be considered too restrictive for the regression analysis. Therefore, the number of participants included in the analysis was 73. The results of these regression analyses revealed that hyperactivity/impulsivity symptoms accounted for unique variance

at 1.5 and 3cpd spatial frequency. At 12cpd, the combination of hyperactive/impulsive and oppositional symptoms accounted for unique variance above and beyond the other variables (See Appendix, Tables 5 thru 7).

Exploratory Analyses of ADHD Subtype

Exploratory analyses were conducted to examine ADHD subtype. Subtypes were categorized as two groups based on the 'or rule': ADHD inattentive type (N=23) vs. ADHD hyperactive/impulsive or combined types (N=31). An ANCOVA was conducted examining the performance of these two groups (between-subjects factor) on the FACT at each spatial frequency (within-subjects factor) with age as the covariate. This analysis resulted in a non-significant finding for both the between subjects effect, F(1, 51) = 1.29, p = .26 (Power = .20), and the interaction, F(4, 208) = .45, p = .77 (Power = .16). However, non-significant findings may be a function of poor power to detect real differences.

Exploratory Analyses of Co-morbidity of ADHD and ODD/CD Symptoms

Exploratory analyses were conducted to examine the difference between children meeting criteria for ADHD without Oppositional Defiant Disorder (ODD; based on the 'or rule', N=33) and those meeting criteria for both ADHD and ODD (based on the orrule, N=21). ODD was considered present if either the parent or the teacher endorsed four or more symptoms. An ANCOVA was conducted examining the performance of these two groups (between subjects factor) on the FACT at each spatial frequency (within subjects factor) with age as the covariate. This analysis resulted in a non-significant finding for both the between-subjects main effect, F(1, 51) = .74, p = .394 (Power = .17), and the interaction, F(4, 208) = 2.28, p = .06 (Power = .66, Partial Eta Squared = .04). Again, non-significant findings may be a function of poor power to detect real differences. This is especially important given that the interaction was approaching significance (See Appendix, Figure 4).

Exploratory Analyses of FACT Data

In the original FACT analyses, three different definitions were used to define ADHD and each was separately analyzed. Many participants were completely excluded from the analyses when moving from the more liberal to the more conservative definition. Therefore, exploratory analyses were conducted to examine these participants who were excluded, which can be best described as a borderline ADHD group in that they may not meet full criteria. In order to ensure that the groups are equivalent, only participants with a parent and a teacher report were included. This way, if a child is in the borderline ADHD group it is because he/she is meeting borderline criteria rather than just missing a reporter. For example, a child may be experiencing severe symptoms of ADHD but only have one reporter and therefore, not meet the multiple context criteria to be classified in the ADHD group. This restriction of multiple reporters reduced the cell sizes substantially (n = 20 for ADHD group, n = 26 for Borderline ADHD group, n = 11 for Clinic group). An ANCOVA was computed to examine the differences of three clinical groups (ADHD, Borderline ADHD, and Clinic) on the FACT with age as the covariate. The Normal group was not included in this analysis because the clinical need in ADHD assessment is to discriminate the ADHD group from other clinical groups. Children

without clinical problems (Normal group) do not come into the clinic for assessment. Although it is important overall to ensure that the FACT does discriminate ADHD from Normal groups in the overall analysis, it is more important to examine the usefulness of the FACT in discriminating between clinical groups (ADHD vs. Clinic). Although the means followed the same pattern as other FACT by Group analyses, the ANCOVA results were not significant (See Appendix, Figure 5). The low subject number likely contributed to a low power (.27), which may have resulted in a non-significant finding.

CHAPTER VI

DISCUSSION

This research was conducted to examine the relation between visual contrast sensitivity (CS), as measured by the FACT, and ADHD. The results of this study suggest that the FACT significantly discriminates ADHD from normal controls and ADHD from other clinical controls. Additionally, the FACT is significantly correlated to laboratory measures of executive functioning, which is deficient in individuals diagnosed with ADHD (Aman et al., 1998, Barkley et al., 1992). Although much more work is needed, the results of this study support future research on the diagnostic utility of the FACT in ADHD assessment. More importantly, the results support the use of the FACT in ADHD etiology research. The results for the ADHD discriminant validity of the FACT and FACT correlations with laboratory measures will be discussed and an attempt made to address strengths and weaknesses and potential alternative conclusions. Implications for research directions will be addressed.

Initial Analyses

To ensure that the FACT scores and the computer task scores did not vary across data collection site, analyses were conducted to examine site difference by each spatial frequency of the FACT and site differences for each of the computer task scores. This resulted in no differences between sites and therefore, data were collapsed on all dependent variables. The lack of significant differences between sites suggests that there were no observed ethnic differences. Age, IQ, and gender were identified in the literature as important demographic variables to examine as contributors to variance. Results revealed that age accounted for significant variance in the FACT scores and, therefore, was used as a covariate in the analyses. IQ only accounted for a smaller amount of variability at two of the five spatial frequencies. Although IQ was not used as a covariate in analyses, it was included as a step in the regression approach for the two spatial frequencies at which significant differences were found (i.e., 12 and 18 cycles per degree). Gender did not account for significant variance in the FACT and therefore, was not included as a covariate in any of the analyses.

FACT and ADHD

There are two ways to examine the usefulness of the FACT in measuring ADHD, namely categorical and dimensional approaches. A categorical approach can address the utility of the FACT in discriminating ADHD from other categories (clinical and normal control) while a dimensional approach is helpful for examining the FACT's relation to ADHD symptoms (i.e., does poorer performance on the FACT correlate to greater symptom severity?). Both of these approaches were employed to examine the relation of the FACT to ADHD.

The categorical approach presented some obstacles in that there is disagreement about how to categorize or determine ADHD diagnosis. If an overly conservative method for determining ADHD diagnosis is used, then a significant finding could indicate that the FACT is only useful in clear cases of diagnosable ADHD, thus not including

participants of a milder severity which limits the clinical usefulness of the measure. If an overly liberal method for determining ADHD diagnosis is used, then a non-significant finding could be due to categorization of a group that is impure (i.e., too many false positives) which would not validly evaluate the usefulness of the FACT. To circumvent these problems, three different strategies were used to categorize ADHD. One method was very liberal, one was very conservative, and one employed more moderate criteria.

As reviewed in the results section, the liberal method used the 'or rule' to determine ADHD diagnosis. More specifically, ADHD was considered present if a parent or teacher endorsed six or more symptoms of inattention or hyperactivity. This liberal method only requires one person to endorse symptoms, which disregards the DSM-IV criterion requirement of multiple settings. The conservative method used the 'and rule' to determine ADHD diagnosis and required both a parent and teacher to endorse six or more symptoms of hyperactivity or inattention. This conservative method meets the DSM-IV requirement of multiple settings. Finally, the moderate method was employed to balance these two approaches and requires six or more symptoms of hyperactivity or inattention in one setting and three or more symptoms in another setting, thus meeting the DSM-IV criteria for multiple context without the very strict requirements used by the conservative method.

Each of these methods was analyzed separately and all produced significant results, supporting the hypothesis that the FACT could discriminate between ADHD and non-ADHD (clinical and normal control) groups. In other words, there were statistically significant differences between ADHD and both non-ADHD groups on the FACT in that

children with ADHD, overall, demonstrated poorer performance on the FACT. It is important to point out that the FACT could discriminate ADHD from normal controls on all three methods for determining group, however, the FACT only significantly discriminated the ADHD from clinical control group using the conservative and moderate methods. The liberal method was not significant at the .05 level for the FACT discrimination between ADHD and clinical controls, though closely approaching (p=.055).

The second way to address the primary question of the connection of the FACT to ADHD is the use of a dimensional approach, and thus employing regression analyses. Again, IQ was used as a step in the regression for two of the spatial frequencies, while age was used as a step in all regressions. After accounting for the variability in the FACT scores of these demographic variables, the hyperactivity/impulsivity symptoms were significantly related to contrast sensitivity (CS) for three spatial frequencies (1.5, 3, and 18 cpd) and were in the expected direction. Symptoms of hyperactivity/impulsivity accounted for unique variance in scores at certain spatial frequencies on the FACT above and beyond the variance that was already accounted for by age and/or IQ. In other words, the more hyperactive/impulsive symptoms endorsed by parents and teachers, the poorer the performance on the FACT.

Overall, these results of the relation between the FACT and ADHD are consistent and in the predicted direction. It was hypothesized that the FACT would discriminate the ADHD group from the normal control group and from the clinical control group. This was supported using the categorical approach and the relation between the FACT and symptoms of ADHD was further established using a dimensional approach. One

interesting finding that came out of these analyses was that hyperactivity/impulsivity symptoms accounted for unique variance in the FACT scores but symptoms of inattention did not. Therefore, the FACT might be a useful measure for tapping into the hyperactivity/impulsivity construct.

It was not expected that hyperactivity/impulsivity would have predictive value on the FACT over inattention symptoms. Based on the results of the regression analyses, hyperactivity/impulsivity accounted for unique variance in the FACT scores, but inattention did not. However, tasks of executive functioning are very broad. Executive functioning tasks generally load on multiple factors using factor analysis or principlecomponents analysis (Welsh, Pennington, & Groisser, 1991; Willcutt, Pennington, Boada, Ogline, Tunick, Chhabildas, & Olson, 2001), supporting the diversity of these measures. These tasks have also been shown to differentially relate to subtypes of ADHD (Chhabildas, Pennington, & Willcutt, 2001).Therefore, it could be expected that hyperactivity/impulsivity symptoms would differentially account for significant variance in the FACT. Even more interesting is that these same symptoms have been linked to the dopamine transporter (DAT1; Faraone & Biederman, 1998; Giros et al., 1996), the gene that is the primary target for stimulant medication (Volkow et al., 1998; Seeman & Madras, 1998).

Although the results of this study cannot make definitive statements about a connection of ADHD to dopamine or CS as a measure of retinal dopamine, the study can support these hypotheses. The research on brain structure and function indicates that ADHD patients most likely suffer from frontal lobe impairment (Castellanos et al., 1996; Filipek et al., 1997; Hynd, Semrud-Clikeman, Lorys, Novey, & Eliopulos, 1990).

Additionally, there is convincing evidence of dopamanergic dysfunction with ADHD, primarily supported by the effectiveness of dopamine agonists (psychostimulants) and molecular genetic studies (Comings, 1997; Comings et al., 1996; Cook et al., 1995; Curran et al., 2001; Daly, Hawi, Fitzgerald, & Gill, 1999; Dougherty et al., 1999; Elia et al., 1990; Faraone & Biederman, 1998; Faraone et al., 1999; Gill, Daly, Heron, Hawi, & Fitzgerald, 1997; Holmes et al., 2000; Jonkman et al., 1997; Kirley et al., 2002; LaHoste et al., 1996; Muglia, Jain, Macciardi, & Kennedy, 2000; Roman et al., 2001; Rowe et al., 1998; Smalley et al., 1998; Swanson et al., 1998; Tannock, 1998; Waldman et al., 1998). The most active and fastest firing dopamine neurons have been found in the retina (Iuvone et al., 1978; Fernstrom et al., 1986) and those projecting to the prefrontal cortex (Thierry et al., 1977; Bannon et al., 1981, 1983; Bannon and Roth, 1983; Roth, 1984; Tam et al., 1990) and these areas are specifically sensitive to even moderate reduction in tyrosine (Bradberry et al., 1989; Fernstrom et al., 1986; Fernstrom & Fernstrom, 1988). Tyrosine serves as a precursor to L-Dopa or dopamine. Parkinson Disease (PD) patients with extreme reduction in dopamine show poorer CS (Kupersmith et al., 1982; Bodis-Wollner et al., 1987; Bodis-Wollner, 1990) and CS improves when symptoms remit (Bodis-Wollner, Marx, Mitra, Bobak, Mylin, & Yahr, 1987). Children with PKU also show mild dopamine depletion in the prefrontal cortex, with elevated phenylalanine levels (Diamond et al., 1997) and reduced CS (Diamond & Herzberg, 1996). The results of the current study indicate that children with ADHD also have poorer CS. With the remarkable similarities between these disorders, a theoretical argument can be made for the connection of ADHD to dopamine and for CS as a measure of retinal dopamine. Additionally, the current findings that symptoms of hyperactivity/impulsivity account for
unique variance in the FACT may be indirectly related to the connection between these symptoms and DAT1 (Faraone & Biederman, 1998; Giros et al., 1996). However, research would be needed to directly relate the amount of dopamine turning over in the retina with CS functioning and to ADHD. Research would also be needed to establish a connection between DAT1 and CS.

The original idea for this study came out of the connection of various disorders to the neurotransmitter dopamine and related performance on tests of visual CS. Although the current findings could support the hypothesis that the FACT may be indirectly measuring retinal dopamine, there is another explanation for the finding. More specifically, the poorer FACT performance of children with ADHD may be due to hyperactive symptoms. In other words, children with ADHD may have a difficult time completing the FACT because of increased distractibility and a task that requires the ability to focus and sustain attention.

There are several points of discussion to dispute this idea. First, the disorders that inspired this study also showed poor FACT performance and at least one of these disorders, Parkinson's disease, is not associated with impulsivity. Second, during administration of the FACT, special attention was given to the child's task performance. When a child appeared to be rushing through the FACT or showed difficulty focusing on the task, administrators would redirect the child and ask for a response on each sinewave grating, pointing directly to each. Finally, it could be argued that if the FACT performance of children with ADHD was due to their hyperactive symptoms, then the differences between ADHD and other groups on the FACT would show up at all spatial frequencies. However, differences really emerged at the higher spatial frequencies.

Nevertheless, it is possible that poor performance on the FACT is due to symptoms of hyperactivity/impulsivity. This alternative explanation might also be supported by the regression results that suggest that symptoms of hyperactivity/impulsivity account for unique variance in the FACT. More research would be needed to determine what construct(s) or system(s) the FACT is measuring. remote

FACT and Laboratory Measures

Overall, the results of the relation between the FACT and computerized laboratory tasks were in the expected direction and supported the hypotheses. Hypothesis two stated that the FACT would be strongly related to the CPT and Stop-Signal tasks because these tasks are considered to be effective measures of executive functioning. The CPT showed a strong relation to the FACT in that increasing errors on the CPT were associated with poorer CS as measured by the FACT. This was seen for a number of CPT variables including X-only errors, A-not-X errors, and composite scores (inattention, impulsivity, and dyscontrol) at various spatial frequencies. The Stop-Signal task (stop-signal reaction time) was significantly related to the FACT at only one spatial frequency (1.5 cpd). The other spatial frequencies were in the expected direction but were not significant. This finding was contrary to the expectation that the FACT would demonstrate a stronger relation with the Stop-Signal task at various spatial frequencies. As a result of these analyses, hypothesis two was supported by the CPT data but only moderately supported by the Stop-Signal data.

Hypothesis three stated that the FACT would only be moderately related to the gono-go task because this task is proposed to involve some executive functioning

components but also a strong motivational component. This hypothesis was supported in that the go-no-go task was related to the FACT on commission errors, consistent with hyperactivity/impulsivity, but not to omission errors. Finally, hypothesis four stated that the FACT would be unrelated to the door-opening task because it is considered to be a motivational task rather than an executive functioning task. This hypothesis was supported in that no significant correlations were found between the FACT and the dooropening task.

The correlations between the FACT and the laboratory tasks suggest, as predicted, that the FACT may be related to executive functioning, which is proposed to be deficient in children diagnosed with ADHD. This was evident in the significant correlations between the FACT and most of the proposed executive tasks. However, there were some discrepancies, in that the stop-signal task was not as strongly related to the FACT as proposed. One possible explanation is that this limited result may be due to the small number of scorable data.

A second explanation examines the nature of this particular measure of executive function. The purpose of the stop-signal task is to inhibit responding to X's and O's when the participant hears a tone from the computer. However, sometimes the tone comes well after the response, at which point the participant must inhibit responding to the next stimulus. The next stimulus then, may not appear for several seconds and may cause some confusion for participants, particularly the younger ones, resulting in invalid data. However, exploratory analyses were conducted and found no age progression patterns when examining the percentage of stop-signal data retained at each age group. It may be that this task is inappropriate for this entire age group because it is too confusing, either

by poor computer design or inappropriate instructions for the task. More research is needed to determine the cause of the low rate of scorable data and the usefulness of this version of the stop-task for this age group.

When examining the various scores associated with the computer tasks it is possible to look at specific executive functions. More specifically, the CPT and the go-no-go tasks allow for an examination of both inattention and impulsivity. When examining the relation between the FACT and these specific functions, some discrepancies emerged. If commission errors on the go-no-go task are a measure of impulsivity, then the significant correlations found between the go-no-go commission errors and the various spatial frequencies on the FACT is also consistent with the regression data that shows hyperactivity/impulsivity symptoms account for unique variance on the FACT. Conversely, the lack of a significant relation between the FACT and the go-no-go omission errors is consistent with the failure of inattention symptoms to account for unique variance in the FACT on the regression analyses. The discrepancy, then, is seen when comparing the correlations between the FACT and the go-no-go task with those between the FACT and the CPT. The FACT was significantly related to both X-only errors (inattention) and A-not-X errors (impulsivity) on the CPT. This is contrary to the results of the go-no-go and FACT comparison that showed significant correlations that were specific to impulsivity (commission errors), not inattention (omission errors).

One possible explanation for this discrepancy is that the motivational component of the go-no-go task increased the desire to respond in hopes of earning money, therefore resulting in more errors of commission. However, when examining the mean number of responses for commission errors vs. omission errors and the mean number of responses

for A-not-X errors vs. X-only errors there were no differences. In other words, children made 71% more commission errors than omission errors on go-no-go and 71% more A-not-X errors than X-only errors on CPT. This finding was consistent when looking at both group means and overall means.

Another potential explanation for this discrepancy is that commission vs. omission errors on the go-no-go task are slightly different than A-not-X errors vs. X-only errors on the CPT. More specifically, commission errors are an incorrect behavioral response while omission errors are an incorrect failure to respond. The A-not-X errors and the X-only errors, on the other hand, are both errors in behavioral responding, like the commission errors on the go-no-go task. Even though the CPT X-only errors are considered to be a measure of inattention, these errors are similar to the CPT A-not-X errors and go-no-go commission errors in that they are all actual behavioral responses. The errors of omission are not provided as a separate score on Halperin's version of the CPT, but rather, as a part of the inattention score, which is a composite of omission errors and X-only errors.

To test this hypothesis, Pearson's product moment correlations were conducted examining the CPT and go-no-go outcome variables. The results indicate that CPT inattention composite score was not correlated with the go-no-go omission errors. Additionally, CPT X-only errors were significantly related to the go-no-go commission errors but not omission errors. These findings support the hypothesis that the inattention score on the CPT is different than the measure of inattention of the go-no-go through omission errors. However, the CPT inattention composite score was also not related to the go-no-go commission errors. These non-significant results could be due to the fact

that the CPT inattention score may be a measure of both inattention (omission errors) and impulsivity (commission X-only errors) and therefore is not strongly related to either one.

Special Issues

ADHD subtype was examined with the FACT. Subtypes were specified as ADHD inattentive type vs. ADHD hyperactive/impulsive and combined type. This decision to categorize into two groups was driven by the literature, which suggests that ADHD inattentive only subtype is uniquely different from subtypes involving symptoms of hyperactivity/impulsivity (Barkley, 1998; Carlson & Mann, 2000; Collings, 2003; Schmitz et al., 2002). Based on the results from the regression analyses, it might be expected that differences of FACT performance based on subtype would emerge. However, the results were non-significant which may suggest that ADHD subtype does not differ on FACT performance. Given that each of these subtypes shows a positive response to psychostimulant medication (Stein et al., 2003), it would be expected that the FACT would not discriminate among subtypes if this is truly a measure of retinal dopamine. This non-significant finding, however, may also be due to limited power to detect differences.

This study also attempted to examine a group of children that were diagnosed as Borderline ADHD. These were the children that met criteria for ADHD based on the 'or rule' but did not meet the more stringent criteria. These Borderline ADHD children were compared to children diagnosed with ADHD based on the moderate approach. This analysis also resulted in a non-significant finding. The results may support the use of the 'or rule' for determining ADHD status in research in that Borderline children based on

the 'or rule' were not significantly different on the FACT than were children diagnosed with ADHD based on more stringent criteria. However, low power may have contributed to this non-significant finding and definitive statements about the usefulness of the methods for categorical diagnosis cannot be made based on this study alone.

Issues of Co-morbidity

One of the goals of this study was to examine differences on the FACT score between children with ADHD and those with both ADHD and comorbid CD/ODD. The ANCOVA analysis resulted in a non-significant finding. However, it is important to note that the interaction was approaching significance (p=.06) and an examination of the means suggested that children with comorbid ADHD and CD/ODD (mean=6.905) perform more poorly than those with ADHD alone (mean=8.03) at 12 c.p.d. Regression analysis confirmed the impact of oppositional symptoms when combined with hyperactive symptoms at 12cpd. In other words, children with both hyperactive/impulsive symptoms and oppositional symptoms perform more poorly at 12cpd than do others. This would support the hypothesis that children with ADHD and comorbid ODD may be more severe cases which show major impairment at both 12 and 18cpd, while ADHD children without the co-occuring ODD condition show major impairment at only18cpd when compared to other clinical cases (See ANCOVA results).

Strengths/Weaknesses

This study is the first attempt to examine the usefulness of CS in understanding ADHD. This idea came from some clear connections in the literature on Parkinson's

Disease and PKU. This study was grounded in the literature and the hypotheses were supported. The results of this first attempt to study the connection between ADHD and CS are promising. Not only does this connection have the potential to contribute to our understanding of ADHD, but it may also assist in clinical diagnosis of the disorder.

This is the second known study of ADHD assessment to include a substantial American Indian population (Beiser, Dion, Gotowiee, 2000), and is the only known study to use an Oklahoma tribal sample. The literature on American Indian assessment is limited and these data have the potential to make considerable contributions. Although the FACT did not result in differences between American Indian and Caucasian samples, there are a plethora of other instruments (parent and teacher reports, structured diagnostic interviews, etc.) that could be examined to identify special issues in providing ADHD assessments to Oklahoma Cherokee children. Should the Cherokee Nation choose to pursue these research avenues, the results could contribute to the way in which children are assessed for ADHD within the tribe.

Finally, one of the major strengths of this study is that over half of the data were collected in a community clinic in which the results were actually used to provide clinical services. This is seen as strength because one of the major limitations of laboratory-based research is that it has poor external validity, limiting the generalizability and usefulness in a clinical setting. Conversely, working in a community setting may limit the control over extraneous factors, but it significantly improves the ability to generalize to real world clinical work.

There are several weaknesses in the current study. The most glaring is the violations of assumptions for the analyses. However, when examining the ADHD

literature, few studies were found that even reported testing for assumptions, and those that did, reported violations (Chhabildas, Pennington, & Willcutt, 2001; Hartung et al., 2002; Schmitz et al., 2002; Willcutt et al., 2001). Therefore, the nature and variability of ADHD may lend itself to variable and non-normal data. The current study cannot make definitive statements about this issue. However, the fact that the assumptions were violated means that the results in the current study must be interpreted with caution, particularly given that the violations may result in alpha inflation. Attempts were made to address alpha inflation, but these corrections cannot ensure complete confidence. Along these lines, the unequal N's can be seen as a weakness, particularly when examining the laboratory computer tasks. On the laboratory computer tasks, one participant may have valid data for one task but not another. Therefore, the number of participants that have data for all four laboratory tasks. However, this strategy would result in an extreme reduction in the number of participants used in the correlation analyses.

Another weakness may be the clinical significance of the findings. Although this is the first attempt to examine ADHD and CS and more research is needed before firm conclusions are reached, the issue of clinical significance should be at the forefront given the small effect sizes, at best, found in this study. The statistically significant differences between groups in this research study indicate efficacy in the use of CS as measured by the FACT. However, efficacy does not necessarily mean usefulness in the world of practice. Efficacy describes the statistically significant finding that the FACT can discriminate between the ADHD group and both non-ADHD groups in a research setting in which internal validity is controlled (i.e., client differences are accounted for). This

means that the study shows that in the highly controlled research environment children who experience a similar symptom presentation of ADHD with age and IQ statistically accounted for can be statistically distinguished from non-ADHD groups. We can take this one step forward and look at practical significance, which tells us whether or not the magnitude of effect was large enough to be meaningful. However, it may only be meaningful for the children falling into the usually restrictive demographic group. This does not mean that assessment measures that are empirically supported as efficacious will not also be effective in the real world. Clinical significance can be evaluated to demonstrate that the assessment measure can be used with many demographically different children with variations of the same disorder, thus showing usefulness. Clinical significance examines such things as the percentage of children with ADHD who actually perform more poorly on the FACT as compared to non-ADHD children and what the actual spread of scores look like for each of the various groups. All of this provides more qualitative information about whether or not the assessment measure is helpful in the real world. One easy way of examining clinical significance is to look at the magnitude of effect or effect size. Cohen (1969) provides general suggestions for interpreting effect size and specifies a standardized difference of |.2| as a small, |.5| as a medium, and 8 as a large effect size. The effect sizes in the current study for the main questions of discriminant validity of the FACT between groups ranged from .06 to .14. These are considered to be small effect sizes according to Cohen. However, these small effect sizes could be explained by the limited internal validity (but better external validity) of the current study.

Summary, Implications, and Future Directions

Overall, the results support the hypothesis that the FACT can discriminate between ADHD and Normal groups and between ADHD and Clinic groups. The FACT also appears to be related to laboratory tasks that measure attention and disinhibition. The results are a promising first start, particularly given the difficulty in discriminating ADHD from other clinical disorders. However, replication is needed and future research should give special attention to clinical significance and usefulness.

The idea for this study was inspired by the literature on children with phenylketonuria (PKU) and patients with Parkinson's Disease (PD). Both of these clinical populations show abnormal CS and appear to share some neurological and behavioral symptoms with ADHD. More importantly, PKU is associated with hallmark ADHD symptoms including deficits in working memory, attention and response inhibition and all three disorders have been tied to dopamine deficiency. The results of the present study provide further support for the connection between these disorders and warrant future examination of the relation between ADHD and PKU and subsequent neurological constructs.

The results of this study may also have some indirect implications for dopamine or CS as a measure of retinal dopamine. Children with ADHD most likely suffer from frontal lobe impairment with dopaminergic dysfunction. Patients with PD and children with PKU also show dopaminergic deficiency and poorer CS. The most active and fastest firing dopamine neurons have been found in the retina and those projecting to the prefrontal cortex. The results of the current study indicate that children with ADHD also have poorer CS. With the remarkable similarities between these disorders, a theoretical

argument can be made for the connection of ADHD to dopamine and for CS as a measure of retinal dopamine.

One potential concern that resulted from this study is whether the FACT is a measure of cognitive deficits or behavioral deficits. Cognitive deficits would involve frontal lobe executive dysfunction or dopamine deficiency/dysfunction. Behavioral deficits then, would involve the behavioral manifestations of ADHD, primarily hyperactivity/impulsivity. Future research should examine this issue and use of developmental paradigms with non-pathological children may be helpful. More specifically, taking out the psychological/pathophysiological component by using normal children and/or by using experimental methods one could attempt to isolate constructs. If the FACT is measuring cognitive deficits, then experimental manipulations should not result in changes in FACT scores. If however, the FACT is measuring more behavioral deficits, then the FACT is core may be sensitive to experimental manipulations.

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APPENDIX

Table 1.Demographic Information for the Stillwater Site

	Normal Control	ADHD	Clinic Control
Number of participants	N = 26	N = 30	N = 26
	n = 14	n = 20	n = 12
Male Female	n = 12	n = 10	n = 14
Mean Age	9.53 (1.79)	9.53 (1.82)	9.13 (1.81)
% of mothers obtaining Associates degree or beyond	67%	36%	30%
% of fathers obtaining Associates degree or beyond	64%	26%	11%
Mean IQ (standard score)	112.96 (11.60)	103.47 (12.84)	101.08 (15.98)
Mean GORT fluency score (scaled score)	11.48 (2.62)	8.33 (3.57)	7.83 (3.44)
Mean GORT comprehension score (scaled score)	12.52 (2.35)	9.40 (3.20)	9.42 (3.68)

Table 2.Demographic Information for the Northeastern Oklahoma Site

	Normal Control	ADHD	Clinic Control
Number of participants	N = 10	N = 30	N = 14
Mala	n = 3	n = 20	n = 6
Female	n = 7	n = 10	n = 8
Mean Age	9.83 (2.02)	8.56 (2.10)	9.51 (1.97)
% of mothers obtaining Associates degree or beyond	50%	29%	21%
% of fathers obtaining Associates degree or beyond	10%	13%	7%
Mean IQ (standard score)	100.60 (10.98)	98.50 (13.84)	93.29 (14.71)
Mean GORT fluency score (scaled score)	9.78 (4.44)	7.14 (3.55)	7.46 (4.93)
Mean GORT comprehension score (scaled score)	9.67 (3.46)	8.39 (3.50)	9.31 (3.28)

Table 3.Demographic Information for the Combined Sample

	Normal Control	ADHD	Clinic Control
Number of participants	N = 36	N = 60	N = 40
	n = 17	n = 40	n = 18
мане Female	n = 19	n = 20	n = 22
Moon Ago	0.62	0.05	0.26
Mean Age	(1.83)	(2.01)	(1.85)
% of mothers obtaining Associates degree or beyond	63%	36%	27%
% of fathers obtaining Associates degree or beyond	50%	20%	10%
Mean IQ (standard score)	109.53 (12.59)	100.98 (13.47)	98.35 (15.81)
Mean GORT fluency score (scaled score)	11.03 (3.21)	7.76 (3.58)	7.70 (3.96)
Mean GORT comprehension score (scaled score)	11.76 (2.92)	8.91 (3.36)	9.38 (3.50)

	1.5 c.p.d.	3 c.p.d.	6 c.p.d.	12 c.p.d.	18 c.p.d.
CPT X-only Errors	094	053	241**	179*	099
	N=106	N=106	N=106	N=106	N=106
CPT A-not-X Errors	304**	137	260**	168*	122
	N=106	N=106	N=106	N=106	N=106
Number of Doors Opened	.103	.046	.077	.118	.127
	N=113	N=113	N=113	N=113	N=113
Go/No-Go Errors of Commission	245**	254**	310**	262**	269**
	N=109	N=109	N=109	N=109	N=109
Go/No-Go	.112	.062	.069	.092	.072
Errors of Omission	N=109	N=109	N=109	N=109	N=109
Stop-Signal	234*	108	098	122	118
Reaction Time	N=75	N=75	N=75	N=75	N=75

Table 4.Correlations of Computer Tasks and FACT Spatial Frequencies

Notes. Significance tests are one-tailed. * p<.05, **p<.01

Variable	В	SE (B)	β	$\Delta \mathbf{R^2}$	F for $\Delta \mathbf{R}^2$
Step 1					
Age	.181	.044	.439**	.182	16. 986**
Step 2					
Age	.158	.044	.382**		
Inattentive Symptoms	.017	.018	.120		
Hyperactive Symptoms	150	.020	322*	.229	8.148**
Step 3					
Age	.159	.043	.384**		
Inattentive Symptoms	.023	.019	.162		
Hyperactive Symptoms	069	.024	446**		
Inattentive X Hyperactive	.005	.003	.189	.244	6.824**

Summary of Hierarchical Regression Analysis for Variables Predicting FACT scores at 1.5 c.p.d. (N=73)

*p < .05 **p<.01

Variable	В	SE (B)	β	$\Delta \mathbf{R^2}$	F for $\Delta \mathbf{R}^2$
Step 1					
Age	.242	.069	.383**	.134	12.169**
Step 2					
Age	.211	.070	.333**		
Inattentive Symptoms	.018	.029	.084		
Hyperactive Symptoms	063	.033	268	.161	5.602**
Step 3					
Age	.212	.070	.335**		
Inattentive Symptoms	.027	.030	.123		
Hyperactive Symptoms	090	.038	382*		
Inattentive X Hyperactive	.007	.005	.174	.171	4.708**

Summar	v of Hierarchical	Regression	Analysis for '	Variables Predicting FACT	scores at 3 c.p.d.	(N=73)

p < .05**p<.01

Variable	В	SE (B)	β	$\Delta \mathbf{R^2}$	F for $\Delta \mathbf{R}^2$
Step 1					
Age	.260	.068	.416**	.161	14.843**
Step 2					
Age	.230	.068	.367**		
Inattentive Symptoms	002	.029	009		
Hyperactive Symptoms	049	.032	210	.183	6.379**
Step 3					
Age	.230	.069	.368**		
Inattentive Symptoms	001	.030	002		
Hyperactive Symptoms	054	.037	230		
Inattentive X Hyperactive	.001	.005	.030	.172	4.732**

Summary of Hierarchical Regression Analysis for Variables Predicting FACT scores at 6 c.p.d. (N=73)

*p < .05 **p<.01

Variable	В	SE (B)	β	$\Delta \mathbf{R^2}$	F for $\Delta \mathbf{R}^2$
Step 1					
Age	.379	.104	.379**		
FSIQ	.045	.017	.281**	.230	11.755**
Step 2					
Age	.312	.100	.312**		
FSIQ	.035	.016	.215*		
Oppositional Symptoms	190	.071	339**		
Inattentive Symptoms	.011	.044	.032		
Hyperactive Symptoms	022	.051	060	.325	7.938**
Step 3					
Age	.243	.097	.243*		
FSIQ	.028	.016	.174		
Oppositional Symptoms	093	.088	165		
Inattentive Symptoms	002	.042	006		
Hyperactive Symptoms	022	.057	058		
Inattentive X Hyperactive	.007	.008	.115		
Hyperactive X Oppositional	042	.012	587**		
Inattentive X Oppositional	.028	.016	.310	.406	7.139**
Step 4					
Age	.247	.095	.248*		
FSIQ	.026	.016	.160		
Oppositional Symptoms	174	.098	309		
Inattentive Symptoms	033	.045	097		
Hyperactive Symptoms	023	.056	063		
Inattentive X Hyperactive	.004	.008	.072		
Hyperactive X Oppositional	054	.014	762**		
Inattentive X Oppositional	.024	.016	.269		
Inatt X Hyp X Oppositional	.004	.002	.421	.425	6.907**
*n<.05	.004	.002	.421	.423	0.907

Table 8 Summary of Hierarchical Regression Analysis for Variables Predicting FACT scores at 12 c.p.d. (N=73)

*p<.05 **p<.01

Variable	В	SE (B)	β	$\Delta \mathbf{R^2}$	F for $\Delta \mathbf{R}^2$
Step 1					
Age	.429	.121	.384**		
FSIQ	.032	.019	.178	.175	8.614**
Step 2					
Age	.392	.124	.351**		
FSIQ	.030	.020	.167		
Inattentive Symptoms	002	.053	006		
Hyperactive Symptoms	062	.057	148	.173	4.772**
Step 3					
Age	.388	.124	.347**		
FSIQ	.033	.021	.186		
Inattentive Symptoms	009	.054	023		
Hyperactive Symptoms	035	.067	084		
Inattentive X Hyperactive	007	.009	101	.168	3.912**

Summary of Hierarchical Regression Analysis for Variables Predicting FACT scores at 18 c.p.d. (N=73)

*p<.05 **p<.01



Figure 1. Means of each group (ADHD, Clinic, and Normal) at each level of the FACT based on the or-rule



Figure 2. Means of each group (ADHD, Clinic, and Normal) at each level of the FACT based on the and-rule



 $\underline{Figure~3}.$ Means of each group (ADHD, Clinic, and Normal) at each level of the FACT based on the moderate method



 $\underline{Figure~4}.$ Means of ADHD vs. ADHD/ODD at each level of the FACT based on the or-rule



Figure 5. Means of three clinical groups (ADHD, Borderline ADHD, and Clinic) at each level of the FACT based on the and-rule $\$

Oklahoma State University Institutional Review Board

Protocol Expires: 4/9/2004

Date: Thursday, April 10, 2003

IRB Application No AS0370

Proposal Title: THE RELATION OF CONTRAST SENSITIVITY AND ADHD: DISCRIMNATE VALIDITY AND CORRELATINS WITH LABORATORY MEASURES

Principal Investigator(s):

Jami Bartgis 215 N. Murray Stillwater, OK 74078

Reviewed and Processed as: Expedited (Spec Pop)

Approval Status Recommended by Reviewer(s): Approved

Dear PI :

Your IRB application referenced above has been approved for one calendar year. Please make note of the expiration date indicated above. It is the judgment of the reviewers that the rights and welfare of individuals who may be asked to participate in this study will be respected, and that the research will be conducted in a manner consistent with the IRB requirements as outlined in section 45 CFR 46.

As Principal Investigator, it is your responsibility to do the following:

- Conduct this study exactly as it has been approved. Any modifications to the research protocol must be submitted with the appropriate signatures for IRB approval.
- Submit a request for continuation if the study extends beyond the approval period of one calendar year. This continuation must receive IRB review and approval before the research can continue.
- Report any adverse events to the IRB Chair promptly. Adverse events are those which are unanticipated and impact the subjects during the course of this research; and
- 4. Notify the IRB office in writing when your research project is complete.

Please note that approved projects are subject to monitoring by the IRB. If you have questions about the IRB procedures or need any assistance from the Board, please contact Sharon Bacher, the Executive Secretary to the IRB, in 415 Whitehurst (phone: 405-744-5700, sbacher@okstate.edu).

Sincerely,

Carol Olson, Chair Institutional Review Board

		Institutiona	Review Bo	ard	
			Protoco	ol Expires:	4/9/2004
ate : Tuesday	r, June 03, 2003	IF	B Application No	AS0370	
roposal Title:	THE RELATION OF AND CORRELATIN	CONTRAST SENSITIVIT S WITH LABORATORY M	Y AND ADHD: DIS EASURES	CRIMNATE V	ALIDITY
Principal nvestigator(s) :					
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Stillwater, OK	74078			to March 10.	College and College
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Approvals are valid for one calendar year, after which time a request for continuation must be submitted. Any modifications to the research project approved by the IRB must be submitted for approval with the advisor's signature. The IRB office MUST be notified in writing when a project is complete. Approved projects are subject to monitoring by the IRB. Expedited and exempt projects may be reviewed by the full Institutional Review Board.



CHEROKEE NATION

P.O. Box 948 Tahlequah, OK 74465-0948 918-456-0671 Chad "Corntassel" Smith ውኩር Principal Chief

Hastings Shade O[®]W@\$h Deputy Principal Chief

July 30th, 2003

Jami Bartgis, MS 604 Kirby Lane Stillwater, OK 74074

Dear Ms. Bartgis:

We are in receipt of the revised version of your research proposal entitled "The Relation of Contrast Sensitivity and ADHD: Discriminate Validity and Correlations with Laboratory Measures". The Cherokee Nation Institutional Review Board had verified that you have complied with the recommended changes and your research proposal is granted **full** approval.

This IRB decision is in effect for one year, until June 18, 2004 and must be renewed annually thereafter. We are requesting that you submit a **progress report 60 days** prior to the anniversary of this approval. <u>Research will be stopped if the Cherokee Nation Institutional Review Board</u> does not receive the report in time for annual review.

The following items should be included in the progress report:

- 1. Any other affiliated Institutional Review Board approvals.
- 2. Any significant findings.
- 3. Any adverse reaction, injuries, catastrophic events. (These should have also been reported immediately to the Cherokee Nation Institutional Review Board.)
- 4. Any publications, presentations, abstracts that have arisen form this project. (These also require prior Cherokee Nation Institutional Review Board approval per our publication policy, which is enclosed.)
- 5. Any other information you feel is pertinent or important.

A final progress report notification to the Cherokee Nation IRB that the research is completed along with a final written progress report is also required.

No changes may be made to the protocol or consent form without prior approval from the Cherokee Nation Institutional Review Board.

Please feel free to contact me at 918-456-0671 x 2557 or Sohail Khan at 918-456-0671 x02602, if you have any questions or need assistance.

Sincerely,

Jeague, me

Gloria Teague, M.D. Chair, Cherokee Nation Institutional Review Board

Oklahoma State University Institutional Review Board

Protocol Expires: 4/9/2004

Date : Thursday, March 04, 2004

IRB Application No AS0370

Proposal Title: THE RELATION OF CONTRAST SENSITIVITY AND ADHD: DISCRIMNATE VALIDITY AND CORRELATINS WITH LABORATORY MEASURES

Principal Investigator(s) :

Jami Bartgis

215 N. Murray Stillwater, OK 74078

Reviewed and Processed as: Expedited (Spec Pop)

Continuation

Approval Status Recommended by Reviewer(s) : Approved

Signature l O lor

Carol Olson, Director of University Research Complian

Thursday, March 04, 2004 Date

Approvals are valid for one calendar year, after which time a request for continuation must be submitted. Any modifications to the research project approved by the IRB must be submitted for approval with the advisor's signature. The IRB office MUST be notified in writing when a project is complete. Approved projects are subject to monitoring by the IRB. Expedited and exempt projects may be reviewed by the full Institutional Review Board.

VITA

Jami D. Bartgis

Candidate for the Degree of

Doctor of Philosophy

Thesis: THE RELATION OF CONTRAST SENSITIVITY AND ADHD: DISCRIMINANT VALIDITY AND CORRELATIONS WITH LABORATORY MEASURES

Major Field: Clinical Psychology

Biographical:

- Education: Graduated from Vinita High School, Vinita, Oklahoma in May of 1994; received Bachelor's of Arts degree in Psychology from the University of Central Oklahoma, Edmond, Oklahoma in December of 1998; received Master's of Science degree in Psychology from Oklahoma State University, Stillwater, Oklahoma in August of 2002. Completed the requirements for Doctor of Philosophy degree with a major in Clinical Psychology at Oklahoma State University in December, 2005.
- Experience: Employed by Oklahoma State University, Department of Psychology, as graduate research assistant and Instructor. Employed by the University of Central Oklahoma, Department of Psychology, as an Instructor. Completed general clinical training at the Psychological Services Center at Oklahoma State University, Behavioral Health at the Cherokee Nation of Oklahoma, and Behavioral Health at the Indian Health Care Resource Center of Tulsa. Completed one-year of predoctoral internship in Clinical Psychology at the Louis de la Parte, Florida Mental Health Institute at the University of South Florida in August of 2005.
- Professional Memberships: American Psychological Association, Southwestern Psychological Association, Association for Advancement of Behavior Therapy, Society of Indian Psychologists

Name: Jami D. Bartgis

Date of Degree: December, 2005

Institution: Oklahoma State University

Location: Stillwater, Oklahoma

Title of Study: THE RELATION OF CONTRAST SENSITIVITY AND ADHD: DISCRIMINANT VALIDITY AND CORRELATIONS WITH LABORATORY MEASURES

Pages in Study: 123 Candidate for the Degree of Doctorate of Philosophy

Major Field: Clinical Psychology

Scope and Method of Study: The proposed research was designed to assess the relation between visual contrast sensitivity (CS) and Attention-Deficit/Hyperactivity Disorder (ADHD). The primary goal of the proposed research was to measure the utility of the CS in discriminating between ADHD, clinic controls, and non-clinic normal controls on the CS, and if differences existed, to determine the magnitude of the effect. Additionally, this project assessed the relation between CS and a number of executive functioning and motivational tasks. One hundred and forty children (age 6 to 12) were recruited from two different locations and comprised three groups: ADHD, Clinic Control, and Normal Control. Each child was assessed over two days. The initial screening involved administration of a Wechsler Abbreviated Scale of Intelligence (WASI), the Wide Range Achievement Test (WRAT) spelling subtest, the Gray Oral Reading Test (GORT), the NIMH Computerized Diagnostic Interview Schedule for Children (C-DISC), parent/teacher-packets with various assessment measures and the Functional Acuity Contrast Test (FACT). At the second testing session, children were again administered the FACT and then completed a number of tests designed to tap into executive functioning or motivation, including Halperin's CPT, Stop Signal Task, the Door-Opening Task, and the Go-No/Go Task.

Findings and Conclusions: The results of this study suggest that the FACT significantly discriminated ADHD from normal controls and ADHD from other clinical controls. Additionally, the FACT is significantly correlated to laboratory measures of executive functioning, which is deficient in individual diagnosed with ADHD. Therefore, the results of this study support the use of the FACT in ADHD etiology research. The results for the ADHD discriminant validity of the FACT and FACT correlations with laboratory measures will be discussed.