THE UTILITY OF CNS VITAL SIGNS AS AN INDICATOR OF ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

A Thesis
By
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FOREWORD

This thesis is written in accordance with the style of the *Publication Manual of the American Psychological Association (5th Edition)* as required by the Department of Psychology at Appalachian State University

I would like to express gratitude to my thesis chair, Will Canu, for his advice and encouragement throughout this process. I truly appreciate all that I have learned from him. Additionally, I would like to thank my thesis committee, Dr. Broman-Fulks, and Dr. Michael, my parents, John and Erlean Cook, and my classmates (Chelsea, Greg, Ina, Jessica, Laura, Martha, and Michael), who have all provided more support than I could have asked for. Finally, I dedicate this thesis to Joanna Yu. She makes all of the hard work worthwhile.

Running Head: UTILITY OF CNSVS IN ADULT ADHD

The Utility of CNS Vital Signs as an Indicator of Adult Attention-Deficit/Hyperactivity Disorder

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Abstract

While the expert consensus seems to be that 3 to 5% of adults suffer from Attention-Deficit/Hyperactivity Disorder (ADHD), the validity of this prevalence is still uncertain, given wide ranging estimates. One potentially important tool for accurately identifying ADHD in both children and adults is neurocognitive testing. The Central Nervous System Vital Signs (CNSVS) is a new, brief battery of computerized neurocognitive tests with putative value for the assessment of ADHD. Drawing from a community-derived sample of 702 adults (ages 18 to 85 years), this study examines whether the CNSVS differentiates individuals with clinically elevated ADHD symptoms (n = 61) from those with similarly elevated depression (n = 31) and anxiety (n = 21) and others with non-elevated scores (n = 589). Scores on the CNSVS were compared to self report measures of ADHD, depression, and anxiety to help establish the concurrent and convergent validity of this novel instrument. Overall, the CNSVS did not differentiate between ADHD, depression, anxiety, and control groups. An exploratory analysis did show a trend level difference between groups when restricting the age of participants to 40 years or younger, $\Lambda = .767$, F (3, 256) = 1.295, p = .086; however, ironically, the ADHD-U group fared *better* than peers in the comparison groups on two outcome variables, which accounted for this result. The findings are generally consistent with a body of prior research suggesting that measures of neurocognitive deficits in child, adolescent, and young adult ADHD groups inconsistently provide additional diagnostic certainty, and specifically indicate that the CNSVS battery does not effectively differentiate ADHD from other groups in a community sample across adulthood.

The Utility of CNS Vital Signs as an Indicator of Adult ADHD

Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by three key symptom clusters: developmentally inappropriate levels of (1) inattention, (2) hyperactivity, and (3) impulsivity. Affected individuals typically first display such symptoms in early childhood, and the condition is associated with broad reaching and persistent dysfunction in several domains of life (e.g., education, work, relationships; Fischer, Barkley, Smallish, & Fletcher, 2005).

Prevalence reports for ADHD in both school-aged children and adults vary widely. Estimates ranging from 3 to 5% (Buitelaar, 2002) to 8.7% (Froehlich et al., 2007) and even up to 10% (Scahill & Schwab-Stone, 2000) have characterized the proportion of school-aged children in the United States meeting *Diagnostic and Statistical Manual of Mental Disorders (4th edition, text revision*; DSM-IV-TR; American Psychiatric Association, 2000) criteria for the disorder. Similarly varied prevalence estimates are noted across countries and cultures (Faraone, Sergeant, Gillberg, & Biederman, 2003). Persistence of ADHD from childhood to adulthood varies with diagnostic methods as well. Barkley, Fischer, Smallish, and Fletcher (2002) note that self-report measures estimate persistence of ADHD into adulthood at 5 to 6%, whereas parent report measures increase the estimate to 46%. Barkley and colleagues (2002) further report that rate to increase to 66% for parent reports when developmentally referenced criteria are included. Several other studies have reported estimates of up to 80% persistence into adulthood (August, Stewart, & Holmes, 1983; Barkley, Fischer, Edelbrock, & Smallish, 1990; Claude & Firestone, 1995; Gittelmann, Mannuzza, Shenker, & Bonagura, 1985).

The identification of ADHD in adults is a problematic task, however. Barkley, Murphy, and Fischer (2008) point out that the current DSM-IV-TR symptom criteria was developed and normalized only on children. Accordingly, the appropriateness of these symptom criteria for adult populations is questionable. Barkley and colleagues (2008) maintain that symptom presentation in adult ADHD is significantly different from childhood, which would make the DSM-IV-TR symptom criteria inappropriate for at least some adult clients.

Domains of Impairment Associated with ADHD

Individuals with ADHD experience impairment in several areas of life. Children with ADHD have been shown to have more general health problems (Hartsough & Lambert, 1985). Later in life, impairment has also been found in driving-related activities, employment, substance use, and life expectancy (Barkley, 2006). Among the most commonly cited domains of impairment for individuals with ADHD are academics, physical safety and relationships.

Academics. Children with ADHD often suffer from poor academic performance and achievement (Barkley, 2006). Performance refers to actual productivity in school work, whereas achievement refers to grade level proficiency. Barkley (2006) cites several studies (Barkley, DuPaul, & McMurray, 1990; Brock & Knapp, 1996; Cantwell & Satterfield, 1978; Casey, Rourke, & Del Dotto, 1996; Dykman & Ackermann, 1992; Fischer, Barkley, Fletcher, & Smallish, 1990; Semrud-Clikeman et al., 1992) to establish that children with ADHD tend to score much lower on standardized achievement tests than do peers without ADHD. These studies found that children with ADHD scored 10-30 standard points below the mean for non-diagnosed classmates. Frazier, Demaree, and

Youngstrom (2004) conducted a meta-analysis of 24 studies testing reading achievement, 15 studies testing spelling, and 21 studies testing math achievement in groups of children with and without ADHD. This study calculated a weighted mean effect size for each academic area to illustrate the difference between the ADHD and control groups. Frazier and colleagues (2004) found an effect size of 0.64 (95% Confidence Interval [CI] of .53-.75) for measures of reading achievement, 0.87 (95% CI of 0.72-1.02) for spelling achievement, and 0.89 (95% CI of .78-100) for math achievement.

These findings contrast other research suggesting that children with ADHD tend to score no differently from peers without ADHD on measures of IQ (MTA Cooperative Group, 1999; Doyle, Biederman, Seidman, Weber, & Faroane, 2000). Using the Wechsler Intelligence Scale for Children (WISC-III), the MTA Cooperative Group found that the adjusted mean Full Scale IQ (FSIQ) score for children with ADHD was 98.45. Schuck and Crinella (2005) point out that when researchers do find lower IQ scores for children with ADHD there are only a few subtests depressing the scores. The subtests that children with ADHD tend to perform worse on include Arithmetic, Coding, Information, and Digit Span. These subtests are associated with executive functions (Loo et al., 2007). Schuck and Crinella (2005) compared FSIQ scores to three measures of executive functioning (Impulsivity, Perseveration, Fail set errors) in 123 males from 7-13 years old. The results showed relatively small correlations between measures of executive functioning and FSIQ scores (IMPULS, r = .07; PERSEV, r = –.22; and FAILSET, r = .19). Schuck and Crinella (2005) contend that children with ADHD may experience deficits in executive functioning that are not related to an overall IQ score.

Physical safety. Individuals with ADHD are also more likely to suffer from accidental injuries than unaffected peers. Szatmari, Offord, and Boyle (1989) studied a sample of 2,600 children, finding that 7.3% of children with ADHD suffered from an accidental poisoning and 23.2% suffered from bone fractures, whereas only 2.3% of control group children suffered accidental poisoning with 15.1% suffering from bone fractures. Barkley, Guevremont, Anastopoloulos, DuPaul, and Shelton (1993) surveyed parents about the driving experiences of their teenage and young adult children. The study found that teenagers and young adults with ADHD were more likely to have driven a car before obtaining a legal license, have their license suspended or revoked, receive repeated speeding tickets, and were four times more likely to be involved in an accident as compared to a non-diagnosed control group. Adults with ADHD are also more likely to have lower self esteem, less education, less marital success, greater difficulties in occupational functioning, and make poorer health choices (Murphy & Barkley, 1996).

Relationships. Social and peer relationships comprise another common domain of impairment for children and adults with ADHD. Several studies report findings that suggest approximately 50% of children diagnosed with ADHD suffer significant rejection by their peers (Gaub & Carlson, 1997; Guevremont & Dumas, 1994; Barkley, 1990). Unnever and Cornell (2003) conducted a study of 1,315 middle school students and found that children with ADHD were more likely to participate in bullying behaviors as well as be victimized by bullies. This study found that 13% of children with ADHD engaged in bullying as compared to 8% of non-diagnosed controls. Also, 34% of children with ADHD were victims of bullying as compared to 22% of non-diagnosed controls. Mikami and Hinshaw (2003) found that girls with ADHD had a tendency to

show more aggression and related difficulties sustaining relationships, reinforcing that significant relational impairment is not limited to males with the disorder.

Barkley (2006) notes that a longitudinal study examining social skills in children with ADHD (Weiss & Hechtman, 1993) found that by adulthood these individuals had more difficulty with heterosocial interactions as compared to non-diagnosed peers. Individuals with ADHD also show greater marital dissatisfaction and are more likely to enter into multiple marriages (Barkley & Murphy, 1996). Robin and Payson (2002) surveyed 80 married couples with one ADHD spouse and one non-ADHD spouse. This study found that sources of dissatisfaction in the marriage included inattention to the partner, careless or impulsive communication styles, forgetfulness, and outbursts of anger or frustration. Canu and Carlson (2003) examined heterosocial outcomes of male college students with ADHD Combined type (ADHD-C) and ADHD Primarily Inattentive type (ADHD-IA) as compared to a non-diagnosed control group. Using questionnaires and behavioral observations, this study found that the ADHD-IA group was passive and inexperienced in their social interactions, whereas the ADHD-C group reported a greater sexual drive and earlier dating experiences.

Behavioral Inhibition, Executive Functions, and ADHD

Behavioral inhibition is hypothesized to be the core deficit across the three symptoms clusters of ADHD (Barkley, 2006). The function of behavioral inhibition is to suppress both inappropriate responses to an environment and interference from extraneous stimuli (Schulz, Tang, Fan, Marks, & Cheung, 2005). Barkley (2006) proposes three interrelated processes that comprise behavioral inhibition. The first process is the inhibition of a prepotent or automatic response to an event. The second

process involves termination of an ongoing response, and the third process protects the time before a response from competing or distracting events. These three actions are believed to facilitate a period of delay between an event and the individual's response to the event. The period of delay is important because it allows for consideration of possible errors and greater flexibility to responses related to any particular task (Barkley, 2006).

The three behavioral inhibition processes are categorized as "executive" cognitive functions (Barkley, 2006). The primary purpose of executive functioning is to mediate an internal focus of behavior to develop appropriate responses to current and future events. Executive functions can be equated to self-regulation, in that they allow one to anticipate change in the environment and then guide the individual's response to optimize future outcomes. These subsequent behaviors are seen as goal-directed and intentional. Barkley theorizes that executive functions begin early in life as behaviors directed towards others and are internalized as the child develops. Four stages in the development of executive functioning are proposed: The internalization of behavior, a shift from controlling others to controlling oneself, a shift from present oriented behaviors to future goal-directed behaviors, and an increasing sensitivity to the importance of delayed consequences over immediate consequences.

Four cognitive functions that appear to support the process of behavioral inhibition include nonverbal and verbal working memory, self-regulated emotions or mood, and planning (Barkley, 2006). Nonverbal working memory is important in maintaining previously perceived information that will be used in the consideration of subsequent responses to the environment. The two sets of data that are processed by

nonverbal working memory are visual images and auditory stimuli. Verbal working memory, on the other hand, is best conceptualized as an internalization of speech. Internal speech is important for the development of self control and is also utilized in problem solving, reading comprehension, rule governed behavior, description, and reflection. The ability to regulate one's emotions is important because all external events elicit some sort of emotional response, which is often followed by an associated motor response. A period of delay, which is considered self-regulatory, permits such a prepotent response (e.g., hitting associated with anger) to be modified by the individual in consideration of future outcomes. Planning involves the analysis and synthesis of information. Analysis involves the separation of sequences of behavior into individual parts. Synthesis involves the reorganization of these sequences into novel responses. Together, all of these functions serve to inhibit inappropriate responses and maximize the benefits of future outcomes.

Working memory deficits associated with ADHD in neurocognitive tasks. Of the four executive functions that have been linked to ADHD, the preponderance of research has focused on working memory. Working memory both maintains and manipulates information in one's awareness. Such cognitive functions are seen as problematic for individuals with ADHD (Diamond, 2005). Baddeley (2003) proposed a model of working memory that is comprised of two independent functions that are overseen and maintained by a central executive (CE) system. The two systems are know as the phonological loop (PH), which processes auditory data, and the visuospatial sketch pad (VS), which processes visual information. Each has a unique mode of acquiring

information, a buffer which stores information temporarily, and a mechanism for rehearsal of information.

Rapport and colleagues (2008) measured VS working memory through a computerized task asking participants to encode and repeat a particular spatial sequence. PH working memory was measured through a computerized presentation of letters and numbers and asking the participants to repeat the sequence back. CE working memory was assessed by analysis of these two scores. The results of this study show that children with ADHD performed significantly worse than normal control participants for PH tasks with a Hedges' *g* effect size of 1.89 standard deviation units (95% CI = 1.80 - 1.98). Similar results were found for the VS tasks, where children with ADHD performed significantly lower than the control group (*g* = 0.89, 95% CI = 0.80-0.98).

Two separate meta-analyses also found significant working memory deficits for children with ADHD. Martinussen, Hayden, Hogg-Johnson, and Tannock (2005) analyzed 26 studies published from 1997 to 2003 and found an overall effect size for VS of 0.85 (95% CI = 0.62 – 1.08), and an effect size of PH of 0.47 (95% CI = 0.36 – 0.59) when comparing non-diagnosed to ADHD groups. Further, Martinussen and colleagues (2005) found these results to be independent of co-occuring learning disorders. Willcutt, Doyles, Nigg, Faraone, and Pennington (2005) analyzed 83 studies and found moderate executive functioning deficits in individuals with ADHD, with reported effect sizes for all studies falling between .46 and .69.

Schoechlin and Engel (2005) conducted a meta-analysis measuring neurological performance in adults with ADHD as compared to control groups. This analysis examined 24 empirical studies and compiled findings of 50 commonly used

neuropsychological tests. Poorer performance was found in the ADHD groups across 10 domains. These domains were Verbal Intelligence (d = -0.27), Executive Functions (d = -0.21), Visual/verbal fluency (d = -0.52), Visual/figural problem solving (d = -0.26), Abstract problem solving and working memory (d = -0.51), Simple attention (d = -0.38), Sustained attention (d = -0.52), Focused attention (d = -0.55), Verbal memory (d = -0.56), and figural memory (d = -0.18).

Behavioral inhibition deficits associated with ADHD in neurocognitive tasks. The Stoop Word-Color Test is often used as a measure of executive functioning deficits in individuals with ADHD, and is specifically designed to measure response (i.e., behavioral) inhibition. This is done by having individuals read the name of a color, though the word is printed in a different colored ink (e.g., the word green would be printed in red ink). This task requires information to be stored and processed simultaneously, engaging working memory. Several versions of the Stroop Test exist. The Golden version (Golden, 1978) poses three conditions to the participant. The first condition presents a card (word card) that measures the speed of reading the words written on it. Four different words (red, green, yellow, and blue) are printed on the card. The second card (color card) asks the participant to name the color of several Xs that are printed in red, green, yellow, and blue ink. The third card (color-word card) asks participants to read color words that are printed in a different color ink. For this task, interference occurs when the word on the third card is read incorrectly.

A popular measure of motor inhibition in individuals with ADHD is Conners' Continuous Performance Test (Conners, 1994). Conners' Continuous Performance Test (CPT) presents a target stimulus on a computer screen, with responses given through

pressing a button on a keyboard. This task is designed to measure inhibitory control as it requires the participant to correctly respond to stimuli presented rapidly while also inhibiting responses to non-targeted stimuli. Riccio, Reynolds, Lowe, and Moore (2001) conducted a meta-analysis and found a mean effect size of 1.46 for individuals with ADHD to have similar impairments, such as traumatic brain injury, when compared to control groups.

Most of the studies examining adult outcomes for those with ADHD have paid little attention to executive functioning and other cognitive deficits. Adults with ADHD are believed to have intellectual functioning that is roughly equal to that of the general population (Bridgett & Walker, 2006). Neurocognitive testing, however, has been shown to be an effective means for differentiating adults with ADHD from control groups. Lovejoy and colleagues (1999) showed that neuropsychological tests may be able to identify adults with ADHD. Using the Stroop task and other measures of executive functioning, this study found significantly poorer performance in tasks testing inhibition, shifting attention, and working memory. These finding suggests that there may be some use for neurocognitive tests as screening tools for ADHD in adulthood.

Assessment of Adult ADHD

ADHD is viewed primarily as a childhood disorder. However, evidence suggests a prevalence of approximately 4% among adults in the United States (Kessler et al., 2006). Still, *identifying* these adults with ADHD—particularly those not diagnosed in childhood—is often complicated, given that the onset of symptoms must be established as occuring before age seven. This is made more difficult in that diagnosing a referred adult with ADHD often relies on subjective, self-reports reports of past experience, as

many are unable to provide tangible evidence of the disorder in early childhood (McGough & Barkley, 2004). Further, as noted above, the DSM-IV-TR criteria are composed of symptoms that may be more developmentally appropriate for children than for adults (Barkley, 2006). Adults cannot be expected to have impairments in behaviors that they rarely exhibit (e.g., difficulty in playing quietly or running and climbing excessively). There is also evidence that a six symptom threshold is inappropriate for identifying ADHD in adults. A prevalence study of ADHD symptom criteria from the DSM-IV in a group of adults found that a six symptom threshold for a diagnosis was two to four standard deviations above the mean number experienced for adults with ADHD (Murphy, & Barkley, 1996). A later study confirmed this finding, noting the six symptom threshold for hyperactivity to be 3.5 standard deviations above the adult mean (Barkley, Fischer, Smallish, & Fletcher, 2002).

Barkley (2006) identifies three more issues that make identifying ADHD in adults difficult. First, individuals presenting for clinical services are apt to attribute inattention, hyperactivity, and impulsivity to ADHD rather than other conditions or exacerbating events. Second, from a professional diagnostic perspective, most of the Axis I disorders in the DSM-IV-TR include inattention as a symptom. Barkley identifies inattention as a "global marker" for any form of distress. Hyperactivity is also represented in both Axis I and Axis II conditions and is thus associated with complications in differential diagnosis. Finally, Barkley views ADHD as falling on a continuum, where the difference between an individual diagnosed with ADHD and an individual who does not receive a diagnosis is often arbitrary. Personal judgment is often used when making the final decision of a diagnosis, thus increasing the likelihood of error and inconsistency. Given

this set of diagnostic challenges, objective, standardized neurocognitive tests that measure underlying dysfunctions associated with ADHD would be ideal for the assessment of adult clients.

Central Nervous System Vital Signs battery and ADHD

The Central Nervous System Vital Signs (CNSVS) is computerized testing battery developed to be a brief measure of numerous clinical conditions. The benefits of such measures are that they allow for the assessment of neurological impairment in a relatively quick, efficient, and cost effective manner. They also allow for more consistency in administration and scoring, which may increase reliability. Finally, the CNSVS is intended to provide substantial and valid indicators of cognitive impairment. Initial research by the developers, Gualtieri and Johnson (2006a), suggests that the CNSVS is able to identify dementia, brain injury, depression, and ADHD. Their study used a community sample of 1069 participants with ages ranging from seven to ninety to create a normative database for scores on the CNSVS. In another study, Gualtieri and Johnson (2006b) used a cross-sectional design to examine the performance of individuals with ADHD from ages 10 to 29. This study found that individuals with ADHD performed worse than age matched controls on the CNSVS in the domains of psychomotor speed, reaction time, cognitive flexibility, and attention. These impairments were found across childhood, adolescents, and young adults.

The CNSVS is comprised of seven different computerized tests that are based on well established tests of executive functions and other neurocognitive abilities. The seven tests include Verbal Memory (VBM), Visual Memory (VSM), Finger Tapping Test

(FTT), Symbol Digit Coding (SDC), the Stroop Test, the Shifting Attention Test (SAT), and the Continuous Performance Test (CPT) (Gualtieri & Johnson, 2006a).

CNSVS Verbal Memory test and related measures. The VBM test requires a participant to learn word lists. A total of 15 words in all are presented with one word presented every two seconds (Gualtieri & Johnson, 2006a). The participants are then asked to remember the 15 words, which are randomly mixed into a list of 30 words for recognition. Participants are asked to press the spacebar every time they see a word from the original list. Recognition is tested again at the end of the CNSVS (approximately 20 minutes later) using the original 15 target words and 15 new non-target words. The Bushke Selective Reminding Test (Bushke & Fuld, 1974) is a 12 item list learning task, which is similar to the VBM, asks participants to perform a similar function. Participants in this task are tested for recall of words rather than recognition and are therefore not presented with words to cue memory. Solanto and colleagues (2007) found that individuals with ADHD combined type performed worse on Bushke indices of total recall, long-term storage and long-term retrieval, as compared to non-diagnosed peers (partial eta squared effect sizes = 0.093, 0.095, 0.099, respectively). Individuals with ADHD Inattentive (ADHD-IA) and Combined (ADHD-C) types also performed worse than controls on delayed recall (partial eta squared = 0.102). The California Verbal Learning Test (CVLT), which also measures an individual's aptitude for list learning (Delis, Kaplan, & Ober, 1987), has been shown to be sensitive to identifying adults with ADHD. Jenkins and colleagues (1998) found that adults who had been identified as having ADD as a child performed worse than adults without childhood ADD on CVLT learning trials (d = -0.71) and during delayed recall (d = -0.75). Gallagher and Blader (2001) also report

slower psychomotor processing and memory decrements for individuals with ADHD on the CVLT (Holdnack, Moberg, & Arnold, 1995 as cited by Gallagher and Blader, 2001). Lovejoy and colleagues also found that adults with ADHD performed more poorly on the CVLT than did controls (d = -0.52).

CNSVS Visual Memory test and related measures. The VSM test is similar to the VBM, except that participants are asked to remember geometric figures instead of words (Gualtieri & Johnson, 2006a). Like the VBM, the VSM requires participants to memorize 15 figures and then recognize them from a list of 30 figures. The recognition list contains 15 target figures and 15 non-target figures mixed randomly. A delayed recognition measure is also taken after five other tests have been given. The Benton Visual Retention Test is designed to measure an individual's ability to perceive and remember geometric figures (Golden, Espe-Pfeifer, & Wachsler-Felder**,** 2000). Dige and Wik (2005) found that adults who were diagnosed with ADHD performed more poorly than did controls on correct responses (d = 0.87) and errors (d = 1.65).

The CNSVS and other Stroop tests. As noted above, the Stroop Test has been published in several forms (Gualtieri & Johnson, 2006a). In the CNSVS, the Stroop Test has three components. The first part presents the words RED, YELLOW, BLUE, and GREEN one at a time in random order. The participant is asked to press the spacebar as soon as the word appears in order to produce a reaction time score. The second part of the test presents the same words. The words, however, are presented in colors. Participants are asked to press the spacebar only when the word presented matches the color that it is presented in. The score generated for this task is known as a complex reaction time. The final part of this test presents words in the same manner as the second

part of the test. Participants are asked to press the spacebar when the color and word are not matched. This final part also generates a complex reaction time. The reaction time for the third portion is generally 120 milliseconds longer than the reaction time in the second portion. The two complex reaction time scores are averaged together to determine an individual's speed of information processing. In their meta-analysis of neurological test performance of ADHD, Frazier and colleagues (2004) found an effect size of 0.56 between individuals with ADHD and non-diagnosed controls on the Stroop Task. This effect size was calculated specifically for the interference portion of the test. Lovejoy and colleagues (1999) found that adults with ADHD performed more poorly than did controls on the Stroop Neuropsychological Screening Test (Trennery, Crosson, DeBoe, & Leber, 1988). This study found a Cohen's *d* of -1.18. Though several studies have shown versions of the Stroop Test to be sensitive to executive functioning differences in individuals with ADHD, others have concluded that this measure cannot provide an accurate diagnosis of ADHD in itself (Homack & Riccio, 2004; Mourik, Oosterlann, & Sergeant, 2005).

CNSVS Shifting Attention Task and related measures. The SAT requires individuals to shift from following one set of instructions to another quickly. Participants are asked to match geometric figures by either shape or color, with the requirements changing randomly (Gualtieri & Johnson, 2006a). The test last for 90 seconds with the goal being for participants to match as many items correctly in the allotted time. The SAT measures correct answers, incorrect answers, and response time. The SAT closely resembles the Wisconsin Card Sorting Task (WCST), which measures one's ability to form and shift a cognitive representation (Berg, 1948). Solanto and colleagues (2007)

found that children meeting criteria for ADHD combined and ADHD inattentive performed more poorly than did controls (partial eta squared = 0.073) on the WCST. The also found that the two ADHD groups needed more trials to correctly identify a category (partial eta squared = 0.046), and were less perseverative in their responses (partial eta squared = 0.049). Further, Jenkins and colleagues (1998) found that adults who were identified with ADD as children performed more poorly on the WCST than did adults who were not identified with ADD as children (d = -0.395).

CNSVS and other Continuous Performance Tasks. The CPT measures sustained attention and vigilance (Gualtieri & Johnson, 2006a). In the CNSVS version of the CPT, participants are required to respond to the presentation of the letter "B" but not the presentation of any other letter. The test presents 200 letters of the course of five minutes. The target stimulus "B" is presented 40 time in all. Though the presentation is randomized, the targets stimuli are presented 8 times for every minute of the test. The test records three scores. The first is the number of correct answers. The two error scores are responses to incorrect stimuli (impulsivity), and target stimuli that are not responded to (inattention). Research suggests that CPTs are able to discriminate individuals with ADHD from non-diagnosed control groups (Fischer et al., 2005; Preston, Fennell, & Bussing, 2005). These studies, however, also revealed that CPTs are not as useful in discriminating individuals with ADHD from groups with sub-clinical symptoms of inattention and hyperactivity or between subtypes of ADHD. Solanto and colleagues (2007) found that individuals with ADHD-C had slower reaction times to targets, greater deleterious effects in reaction times as the task progressed, and greater deficits in an index of attentiveness. Fischer and colleagues (2005) found that individuals with ADHD

made significantly more commission and omission errors. They also found that both types of errors did not differentiate individuals with ADHD from individuals with sub-clinical symptoms of hyperactivity. Preston and colleagues (2005) conclude that CPTs may still be useful in research to identify sample groups.

Other CNSVS neurocognitive measures. The SDC is a timed task that requires participants to refer to a key that connects numbers (2-9) with corresponding symbols (Gualtieri & Johnson, 2006a). The number/symbol pairs are presented at the top of the screen while a row of symbols without a corresponding number are presented below. Participants are asked to type in the proper number for each symbol. The test last for 120 seconds with the correct score being measured by the number of correctly coded symbols. Participants are also given a practice trial in order to learn how to complete the task. Loo and colleagues (2007) used the Symbol Digit Coding subtest of the Wechsler Adult Intelligence Scale (WAIS-III) to compare Finnish adolescents with ADHD to a control group. This study found that the ADHD group performed worse than controls on this task (Cohen's *f squared* = 0.37).

The FTT measures an individual's fine motor control and, while commonly used in neuropsychological research (Gualtieri & Johnson, 2006a), analogous tasks have not previously been used to examine differences between ADHD and other groups. In the FTT, participants press a spacebar with their right index finger as often as the can in 10 seconds. They repeat the process with their left index finger. There is one practice trial and three test trials. A participant receives a score based on the average number of taps in all six trials.

The Current Study

In the present study, a community sample of 1044 young to elderly adults underwent and administration of the CNSVS. The primary purpose of this study was to replicate that normative data on the CNSVS. The first hypothesis is that results from this study will resemble that of Gualtieri and Johnson (2006a) in terms of mean scores on the subtasks showing mild cognitive deficits. The utility of the CNSVS as a measure of ADHD in adulthood will also be examined. The second hypothesis is that adults with ADHD will have deficits in executive functioning as measured by the CNSVS, as compared to other participants. Individuals with ADHD will be identified according to scores on self-report diagnostic measures; scores on the latter will also be directly correlated with relevant scores on the CNSVS, providing further evidence for convergent validity.

Method

Participants

One-thousand-forty-four individuals, ranging from 18 to 85 years of age (female to male ratio is approximately 3:2), participated in the study, which was part of a larger investigation examining the effects of an antioxidant regimen on physical and psychological health. From this participant pool, 702 were included in the current analyses. Participants were excluded for having incomplete CNSVS data (n = 48), ADHD data (33), or BSI data (49). Another 72 participants were excluded for having elevated depression *and* anxiety in the absence of elevated ADHD symptoms (see below). Finally, 140 participants were excluded for reporting subclinical levels of anxiety or depression in the absence of ADHD (see further details on exclusion criteria below).

All data utilized here were collected at baseline, before randomized intervention or placebo exposure. Participants were volunteers from the community, who learned of the study via print, email, and other advertisements, and were financially compensated for their participation ($300 for three-month intervention trial).

Design

Participants completed study measures in two cohorts of similar size (e.g., approximately 520), one of which completed the study in the winter of 2008, and another in the autumn of that same year. The criterion groups in this study include an ADHD Primarily Inattentive type group (ADHD-IA; n = 34), an ADHD Combined and Primarily Hyperactive-Impulsive type group (ADHD-HI, n = 27), two clinical comparison groups (depression, CCD, n = 31 and anxiety, CCA, n = 21), and a control group (n = 589). These groups were identified by self-report surveys, which assessed symptoms of ADHD and other psychological disorders (see below for complete details; also see Table 1for further demographic and diagnostic description).

ADHD was defined using current (i.e., past six months) self symptom reports. Individuals were included in the ADHD groups based on Barkley and Murphy's (2006) 1.5 standard deviation cutoff for ADHD symptom prevalence (see below), with those in the ADHD-IA group reporting only elevated IA symptoms and those in the ADHD-HI group reporting elevated HI symptoms with or without elevated IA. In addition, participants had to endorse experiencing impairment related to their current ADHD symptoms as being either "often" or "very often." The potential symptomatic expression of other common disorders (i.e., anxiety, depression) was measured using the Brief Symptom Inventory (BSI, see below; Derogatis, 1993). Individuals without ADHD (as

defined previously) who reported elevated BSI depression were assigned to the CCD group, and those with elevated BSI anxiety were assigned to the CCA group. For sake of comparative clarity, participants with both elevated anxiety and depression, in the absence of elevated ADHD symptoms, were excluded from analysis. Given the substantial Axis I comorbidity rates for individuals with ADHD, those who met criteria for inclusion in one of the ADHD groups who also have elevated (i.e., *t* score $\geq$ 65) BSI depression or anxiety were not excluded and were retained as ADHD participants. Of the participants included in the ADHD groups, 18 (29.5%) reported elevated levels of anxiety and depression, 8 (13.1%) reported elevated levels of anxiety, and 7 (11.5%) reported elevated levels of depression. In all, 33 (54%) participants in the ADHD-U group reported comorbid anxiety, depression, or both. The control group was composed of participants who scored within one standard deviation of the mean for depression, anxiety, and ADHD as measured by the BSI and the ADHD self report survey.

Measures

ADHD Self-report (*Current Symptom and Childhood Symptom Scales,* Barkley, Murphy, & Fischer, 2006; adult executive dysfunction symptoms, Barkley et al., 2008). The ADHD self report survey consists of three portions. The first portion assesses current gross ADHD impairment according to DSM-IV-TR symptom criteria as well as sluggish cognitive tempo, a cognitive style often associated with the Primarily Inattentive ADHD Type (Barkley & Murphy, 2006). There are 22 items in this portion with 4 response options (*Never, Sometimes, Often, Very Often*), including one that broadly asks for frequency of impairment due to these symptoms. The second portion assesses current ADHD symptoms using seven additional items identified recently by Barkley and

colleagues (2008) as being more developmentally appropriate for adults with ADHD. The final portion of the survey assesses child symptoms according to the DSM-IV-TR criteria including age of onset. Clinically-elevated (+1.5 *SD*) symptom thresholds are normed across age groups and symptom clusters (Inattention, Hyperactive-Impulsive, Total ADHD Score). For the Inattention cluster, ages 17-29 years have a cutoff of 13, ages 30-49 have a cutoff of 12, and ages 50+ have a cutoff of 10. For the Hyperactive-Impulsive cluster ages 17-29 have a cutoff of 16, ages 30-49 have a cutoff of 13, and ages 50+ have a cutoff of 10. For the Total ADHD Score, ages 17-29 have a cutoff of 28, ages 30-49 have a cutoff of 24, and ages 50+ have a cutoff of 18. Items assessing inattentive symptoms, hyperactive/impulsive symptoms, and adult symptoms are listed in Appendix A. For this sample, Inattentive symptoms have a Cronbach's alpha (α) of .89 while the α for Hyperactive symptoms is .85.

Brief Symptom Inventory. The BSI provides a broad picture of an individual's current symptoms and the severity of those symptoms. The BSI is a self-report measure with 53 items rated on a 5 point scale. The scale measures the level of distress that each item holds for the participant and ranges from "not at all" (0) to "extremely" (4). The BSI is a measure of current psychological symptom experience and therefore does not measure chronic or persistent symptoms. It is appropriate for use on clinical and medical populations as well as community respondents (Derogatis, 1993). This scale was designed to be a short form of the *Symptom Checklist-90-Revised* (Derogatis & Cleary, 1977). Derogatis (1993) reported correlations between the two measures as .95 for both the anxiety and depression clusters. The BSI includes 9 symptom scales; those used in the current study are depression (α= .85, 2-week test-retest = .84) and anxiety (α= .81, 2-

week test-retest r = .79; Derogatis, 1993). Items assessing symptoms of depression and anxiety are listed in Appendix A.

CNSVS. As described in detail above, the CNSVS is a computerized testing battery comprised of abbreviated versions of seven commonly used neurocognitive tests that takes about 30 minutes to complete (Gualtieri and Johnson, 2006a). The tasks include verbal memory, visual memory, finger tapping, symbol-digit coding, the Stroop Test, shifting attention, and a CPT. These tests tap a range of cognitive functions such as memory, reaction time, and attention. Participants are guided through the tasks with comprehensive on-screen instructions and practice elements on more difficult tasks. Gualtieri and Johnson (2006a), the authors, propose that these domains are sensitive to detecting mild cognitive impairment.

Gualtieri and Johnson (2006a) report test-retest reliability and concurrent validity data for the CNSVS. On the individual subtests of the CNSVS, reliability coefficients range from .31 (Stroop errors) to .88 (CPT reaction time). The authors measured concurrent validity by comparing performance on the CNSVS tasks to that on other empirically-supported tests measuring memory, psychomotor speed, executive functioning, and attention. A range of correlation coefficients were found for memory (0.07-0.95), psychomotor speed (0.19-0.74), executive functioning (0.3-0.66), and attention (0.06-0.94), suggesting that, generally speaking, the CNSVS taps constructs similar to those measured by conceptually related instruments.

Procedures

Participants attended a single, group data collection session (i.e., baseline) in the morning after having fasted since midnight. The full, treatment-study protocol involved a

physical evaluation including having their blood drawn before participants proceeded to a computer lab where they were given verbal instructions concerning the CNSVS. Subsequent completion of the CNSVS generally took about 20-30 minutes, as expected. All participants completed a paper version of the BSI the same day. The ADHD survey was taken online within the week prior to the baseline data collection, with some participants completing it at a computer station at baseline. The study adhered to American Psychological Association (APA, 2002) ethical guidelines. The study received approval from the institutional review board of Appalachian State University on April 27, 2009.

Analyses

CNSVS raw scores were used in all analyses. First, a Multivariate Analysis of Variance (MANOVA) examining potential between group differences across the seven CNSVS subtests (dependent variables) was conducted. Follow up Analysis of Variance (ANOVA) procedures were conducted to further explore overall group differences on each of the CNSVS subtests. Tukey post-hoc tests were conducted to examine pairwise differences between each group on the individual CNSVS subtest variables. These comparisons included: ADHD-IA/ADHD-HI, ADHD-IA/CCD, ADHD-IA/CCA, ADHD-IA/Control, ADHD-HI/CCD, ADHD-HI/CCA, ADHD-HI/Control, CCD/CCA, CCD/Control, and CCA/Control. Each Tukey test compared the differences between two means to determine whether the difference is statistically significant. Finally, effect sizes for group differences were calculated to illustrate their practical significance, employing Cohen's *d*. Correlations were also run to demonstrate how individual ADHD traits are associated with the subtests of the CNSVS.

Results

Demographic Analyses. In order to document whether the comparison groups differed, demographically, age and education level were used as dependent variables in cross-group ANOVA analyses, and gender was similarly examined in a chi-square analysis. Comparison groups did not differ by age, F (3, 699) = 0.52, p = .67. They did, however, differ by level of education, F (3, 699) = 2.67, $p < .05$. Tukey post-hoc comparisons show that education level of participants significantly differed only between the CCA and CCD group, however, $p < .05$, d = 0.7. Individuals in the CCA group tended to have more education than did individuals in the CCD group. Groups also differed according to gender, χ^2 (1, N =700) = 16.79, $p < .01$. Head to head group differences in terms of gender are as follows: ADHD-U and CCA χ^2 (1, N = 87) = 3.32, p = .07, ADHD-U and CCD χ^2 (1, N = 77) = 6.87, $p < .01$, ADHD-U and Control χ^2 (1, N = 652) = 36.79, $p < .01$, CCA and CCD χ^2 (1, N = 50) = 3.92, $p < .01$, CCA and Control χ^2 (1, N = 624) = 21.97, $p < .01$, CCD and Control χ^2 (1, N = 613) = 6.87, $p < .01$. The ADHD-U group had the smallest proportion of male participants (27.87%). The CCA group had the highest percentage of males (66.67%), while the CCD group and Control groups measured at 60% and 39.29%, respectively.

Primary Analysis. An initial MANOVA was conducted to determine if group differences existed between the five groups (ADHD-IA, ADHD-HI/C, CCD, CCA, and non-diagnosed peers, hereafter described as Control). The following variables were included in the MANOVA: Verbal Memory comprehensive score, Visual Memory comprehensive score, Right Finger Tapping average (number of taps), Left Finger Tapping average, Symbol Digit Coding Correct Responses, Stroop Simple Reaction Time,

Stroop Complex Correct Responses, Stroop Complex Commission Errors, Stroop Correct Responses, Stroop Reaction Time for Correct Response, Stroop Commission Errors, Shifting Attention Correct Responses, Shifting Attention Errors, Shifting Attention Reaction Time for Correct Responses, CPT Correct Responses, CPT Omission Errors, CPT Commission Errors, and CPT Reaction Time for Correct Responses. This omnibus MANOVA did not return a statistically significant result, Wilks' Lambda, $\Lambda = .907$, F (4, 699) = .974, $p = .538$.

A follow up MANOVA was conducted to determine if the two ADHD groups differed significantly, using the same outcome variables as noted above. The overall MANOVA was not significant, $\Lambda = .827$, F (1, 59) = .529, $p = .923$. Given that the two ADHD groups did not differ, they were combined into one group (ADHD-U) for subsequent analyses. A second, omnibus MANOVA was conducted to examine whether differences existed between the larger, undifferentiated ADHD group (ADHD-U), CCD, CCA, and the Control group. Again, the MANOVA was not significant, $\Lambda = .907$, F (3, 699) = 1.2, $p = .13$. Though this result does not approach statistical significance, it appears to suggest that the added statistical power of a larger ADHD group helped to signal that potential group differences may exist that are of smaller magnitude, and that cannot be statistically detected in the current sample. Cohen (1992), in fact, indicates that to achieve a statistical power of .80 for detecting "small" group differences using a four-group ANOVA, with alpha set at the traditional threshold (i.e., .05), one would need comparison groups of 274 or more participants-- obviously much larger than the ADHD-U cell size. Means and standard deviations including the ADHD-U group are provided in

Table 2. Means and standard deviations by gender including the ADHD-IA, ADHD-HI, and ADHD-U groups are provided in Table 3.

ANOVAs were conducted across all groups for each dependent variable. A significant difference was found for Verbal Memory, F (3, 699) = 3.011, p = .03. There were no other statistically significant or trend level ($p < .1$) differences across the CNSVS subtests. See Table 4 for more detail regarding these ANOVA results.

Pairwise Comparisons. As noted above, planned Tukey post-hoc comparisons were made across all groups on variables for which group differences (at the typical or trend levels) were detected. For Verbal Memory, a trend towards significant differences (i.e., $.1 > p > .05$) was found between ADHD-U and CCA, p = .058, d = 0.52, and ADHD-U and CCD, p = .08, d = 0.6. The ADHD-U group actually performed *better* on this task than the other three groups.

No other significant or trend level differences were found. Effect size differences between ADHD-U and the three comparison groups on all dependent variables are listed in Table 5.

Correlational Analysis: Inattention and Hyperactivity-Impulsivity and CNSVS Scores

A correlational analysis was conducted to examine the association between ADHD symptom clusters (Inattention, Hyperactivity/Impulsivity), in general, and the CNSVS subtests. A trend towards significance was found between Inattention and Verbal Memory, r (702) = .071, p = .06.

Significant correlations were also found between Hyperactivity/Impulsivity and Verbal Memory, r (702) =. 09, p = .01, Visual Memory , r (702) = .127, p = .001, Symbol Digit Coding Correct Responses , r (702) = .163, $p < .001$, Stroop Reaction

Time for Correct Responses , r (700) = -.09, p = .018, Shifting Attention Correct Answers, r (702) = -.08, p = .05, and Shifting Attention Errors, r (702) = -.08, p = .038. Further, a trend toward significance was found between Hyperactivity/Impulsivity and Stroop Correct Responses, r (700) = .07, p = .08, and Stroop Commission Errors, r (702) = -.068, p = .07. A list of correlations between ADHD symptom clusters and all CNSVS variables is provided in Table 6.

Exploratory Analysis: ADHD Effects in Younger Adult Subsample

Given that differences between individuals with ADHD and others may gradually dissipate and become less evident with age (Mannuzza et al., 1993, 1998), further analysis was conducted with an age restricted sample. Cases were restricted to individuals age 40 and under, corresponding to the recruitment demarcation for "young" adulthood in this sample. This age cutoff was chosen because it corresponds to age-norm categories utilized with the measure of current ADHD symptomatology in this study (Barkley & Murphy, 2006). A post-hoc MANOVA was conducted to determine differences between the four groups (ADHD-U n = 24, CDA n = 11, CDD n = 8, Control n = 215). Results show a trend towards significance, Λ = .767, F (3, 256) = 1.295, p = .086. Tukey post hoc analysis showed significant differences on Stroop simple reaction time between the ADHD-U (M = 330.42, SD = 112.43) and CCA (M =272.27, SD = 19.4; p = .034) and control groups (M = 278.48, SD = 51.38; p < .001; CCD M = 273.68, SD = 37.75). A trend towards significance was found on Stroop simple reaction time between the ADHD-U group and CCD; p = .09.

Exploratory Analysis: Effects in a Group with Clinical-level Childhood ADHD

In order to create a more stringently "clinical" ADHD group—with elevated symptoms dating back to childhood—an exploratory MANOVA analysis was conducted with the ADHD-U group restricted such that individuals had to report not only significant adult symptoms and related impairment, but also clinically significant childhood ADHD symptoms. The threshold for child impairment was based on Barkley and Murphy's (2006) 1.5 standard deviation cutoff for ADHD symptom prevalence (elevation on either the HI or IA scales). This procedure identified 15 participants (25%) from the ADHD-U group who reported more persistent ADHD symptoms. The results of this analysis were not statistically significant, $\Lambda = .922$, F (3, 654) = .947, $p = .58$. See Table 7 for means and standard deviations for both exploratory analyses.

Discussion

Summary of Findings

Contrary to the initial hypothesis, adults identified with clinically elevated ADHD symptoms did not show neurocognitive deficits, relative to a non-diagnosed control group, according to the CNSVS. In fact, individuals did not meaningfully differ across the ADHD-U, CCD, CCA, and control groups. Only the Verbal Memory task differentiated between the ADHD-U and other groups.

Somewhat surprisingly, the ADHD-U group performed *better* than the CCD and CCA groups on the Verbal Memory task. In fact, many of the differences between the ADHD-U and comparison groups were not in the expected direction. Participants from the ADHD-U group actually performed better than the CCA, CCD, and control groups on

subtests for Finger Tapping, Symbol Digit Coding, the Stroop tasks, the Shifting Attention task, and the CPT.

There was little relation between the CNSVS and symptoms of Inattention and Hyperactivity/Impulsivity. Though several of the CNSVS variables significantly correlate with Inattentive and Hyperactive/Impulsive symptoms, the strength of these associations is small. It appears that only a small portion of the variance in CNSVS scores is related to the variance in ADHD symptoms, in this sample.

Two post hoc analyses were conducted to explore whether the CNSVS might be a more sensitive ADHD indicator in selected subsamples. First, all groups were restricted to only include individuals who were 40 years of age or younger. Theoretically, restricting the age range could have increased the ability of the CNSVS to detect group differences, as some ADHD symptoms are thought to decrease with age (Mannuzza et al., 1993, 1998). This analysis did show a trend towards statistical significance ($.05 < p < .1$). Further analyses showed the ADHD-U group to differ from the CCA and control groups. Significant differences were found on Stroop simple reaction time, and a nearly significant difference was found between the ADHD-U group and the CCD group on this variable. The ADHD-U group tended to perform worse on this task, which suggests that it may be useful for distinguishing individuals with ADHD in young adulthood. A second post hoc analysis was conducted in which the total ADHD-U group was restricted to individuals reporting clinically-elevated current *and* childhood symptoms, meeting a stricter diagnostic threshold which, again theoretically, could have increased the likelihood for the CNSVS subtests to differentiate the groups. However, no significant differences between groups were found in this analysis.

Differences from Gualtieri and Johnson's Research

Understanding the failure to find differences between individuals identified with highly elevated ADHD traits (i.e., at minimum, a high risk for clinical diagnosis) and non-symptomatic and clinical control groups first necessitates a careful consideration of the differences between the current study and those conducted by Gualtieri and Johnson (2006a, 2006b) that established the initial CNSVS norms and its putative utility at identifying cases of ADHD.

Sample size and power. Significant differences in performance may have been found between the ADHD-U group and the other groups had the ADHD-U group been larger. Indeed, Gualtieri and Johnson (2006b) used an ADHD group composed of 175 participants, while our sample included just 61 participants. This is not an unusual limitation in the related literature; in fact, Barkley (2006) identifies small sample size as a common shortcoming amongst studies examining the neurocognitive functioning of adults with ADHD. Effect sizes for group differences noted for CNSVS variables in Gualtieri and Johnson (2006b) ranged from .24 (small) to .52 (moderate). In the current study, there are actually *fifteen* pairwise effect sizes—in comparisons between the ADHD-U and clinical control groups that could theoretically aid in differentiating ADHD from other conditions in adulthood-- that fall into this range, yet none were statistically significant. The fact that this study demonstrated some similar effect sizes on non-significant pairwise comparisons, as compared to Gualtieri and Johnson (2006b), suggests that the cell sizes here resulted in suboptimal power.

Power analyses conducted with G*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009) indicated that with power set at 0.95 and an alpha (α) level of 0.05 the

necessary sample size required to detect moderate effects (f^2 = .15) on the initial MANOVA was 100 for each group, and that follow-up pairwise (*t*) analyses would need 88 participants for each group to detect differences of a similar magnitude (*d* = .5). Power is unfortunately less than optimal for almost all analyses reported herein. In fact, for the detection of moderately sized differences between the ADHD-U (*n* = 61) and the CCA (*n* = 21) groups, α would need to be set at 0.26 to achieve a power of 0.8. Similarly, an α level of 0.16 is necessary for the same power in comparisons between the ADHD-U group and the CCD (*n* = 31). Finally, to, again, detect moderate pairwise differences, an α level of 0.004 is required to achieve a power level of 0.8 given samples sizes for the ADHD-U group and the control group (*n* = 589). Comparisons between the ADHD-U group and the control group may then have adequate power to find statistical differences with moderate effect sizes. Unfortunately, several group effects from Gualtieri and Johnson (2006b) were in the small range, and to achieve a power of 0.8 to detect such differences, even between the ADHD-U and control group, α must be set at 0.5 or higher, which seems an unacceptable compromise for empirical research.

Diagnostic Procedures. Participants in the Gualtieri and Johnson (2006b) study were compiled from case files for children, adolescents, and young adults who underwent a full psychological evaluation at the North Carolina Neuropsychiatry Clinic. All participants underwent an administration of the CNSVS as part of the evaluation and received a primary diagnosis of ADHD. Diagnoses were made by experienced clinicians based on DSM-IV-TR criteria. All cases were reviewed by a senior psychiatrist as well. Individuals with comorbid disorders were excluded from the sample. Conversely, those assigned to our ADHD-U group were identified only via self-report measures, and

participants reporting significant symptoms of depression and anxiety were not excluded. Consequently, these less-stringent inclusion criteria may have resulted in false positive inclusions in the ADHD-U group, which may have diminished the group's mean cognitive impairment (i.e., executive dysfunction) and thereby limited the ability to find expected differences on the CNSVS subtests.

Evidence exists to suggest this may, indeed, be a valid criticism. Some community-based research suggests that "normal" adults often report having significant levels of ADHD symptoms at some time in their life. In a sample of 719 non-diagnosed adults, Murphy, Gordon, and Barkley (2002) reported that a large majority of individuals reported at least six symptoms of ADHD occurring "at least sometimes" in both childhood (80%) and adulthood (75%). Further, 25% of their sample reported a similar quantity of symptoms as occurring "often or very often" in childhood, while 12% of the sample reported symptoms as occurring "often or very often" in adulthood. Given that prevalence estimates for ADHD are much lower in childhood and adulthood, there may be a tendency for adults to over report symptoms of ADHD. However, our ADHD-U group is approximately 6% of the sample, which is in line with the expected base rate of ADHD in adulthood (Kessler et al., 2006) and seems, at least on the surface, to suggest that we did not egregiously over-classify participants into ADHD groups.

On another tack, of the participants in the ADHD-U group, 18 (29.5%) reported elevated levels of anxiety and depression, 8 (13.1%) reported elevated levels of anxiety, and 7 (11.5%) reported elevated levels of depression. In all, 33 (54%) participants in the ADHD-U group reported comorbid anxiety, depression, or both. This is not necessarily unexpected given comorbidity estimates from epidemiological research. For instance, in

a large-scale study with participants representative of the United States as a whole Kessler and colleagues (2006) found that 18.6% of individuals identified with ADHD were also identified as having major depressive disorder, and 47.1% met criteria for an anxiety disorder. Nevertheless, inclusion of participants with co-occurring symptoms of anxiety and depression into the ADHD-U group may have somewhat hindered the CNSVS's ability to distinguish performance across the three clinical groups, as compared to the "pure" ADHD sample employed by Gualtieri and Johnson (2006a, 2006b).

Age Range. The normative study for the CNSVS by Gualtieri and Johnson (2006a) included ADHD groups with a mean age near thirteen years. The other Gualtieri and Johnson (2006b) study included slightly older participants, typically in their late teens (*M* age = 18.5 years). On the other hand, our sample included adults of all ages, with those in the ADHD group averaging right around forty-five years of age. This must, of course, be taken into consideration when interpreting the current findings, given that converging evidence suggests that ADHD symptoms ameliorate as individuals develop in adulthood. For instance, in two separate cohorts, research has shown that only 31% and 43% of hyperactive children continued to be significantly impaired in *early* adulthood (mean age = 18.5 years; Gittelman et al., 1985; Mannuzza et al., 1991), as measured with a structured interview using DSM-III criteria. Eight years later—and while probands were still by and large in their twenties—follow-up established that those meeting impairment criteria for hyperactivity fell to 8% and 4% respectively (mean age = 26 years; Mannuzza et al., 1993, 1998).

More recent research has shown that such findings likely underestimate the persistence of ADHD in adulthood. As cited earlier, Barkley and colleagues (2002)

found that 66% of children with ADHD were also diagnosed in adulthood, and their findings may be more accurate as they used developmentally referenced criteria to identify ADHD. Still other researchers have derived mixed findings regarding age effects. For instance, Fischer and colleagues (2005) found that hyperactive children who still had a diagnosis of ADHD in young adulthood did continue to show deficits in executive functioning when compared to controls, although improvement in attention and inhibition was seen across groups.

While the evidence, therefore, is somewhat ambiguous with regard to how persistent ADHD symptoms tend to be beyond adolescence, it is important to note that virtually all of the "long-term" follow-up research on ADHD has really only measured the persistence of ADHD symptoms into early, or, at most, middle adulthood, and little is known concerning the persistence of symptoms further along the lifespan. Hyperactive symptoms may, in fact, continue to normalize over time, and related impairment in neurocognitive functioning may also subside. The inattention that is obvious in some individuals with ADHD at younger ages could possibly ameliorate in later life, as well, in comparison to non-diagnosed age-mates. Simply put, there may only be very small and difficult-to-detect differences that discriminate between those with ADHD and those without, by mid- or late adulthood.

A limitation, however, of the existent literature is that research examining such symptom amelioration has focused primarily on hyperactivity. Inattentive symptoms are more likely to persist into adulthood (Spencer, Biederman, & Mick, 2007). Nigg and colleagues (2005) suggest that individuals with ADHD-IA should show more deficits in executive functioning than should individuals with the hyperactive type. Extrapolating

from Nigg's assertion as well as evidence that the IA and HI symptom clusters' persistence varies across time, one would expect that the CNSVS subtests would distinguish between the ADHD-IA and ADHD-HI groups in an adult sample. However, this was not the case. Whether or not ADHD subtypes actually do continue to differ in neurocognitive impairment in adulthood will be discussed in more detail later.

Medication. To determine if treatment altered the performance of the ADHD-U group, current self-reported medication usage was informally examined, post hoc. Only four individuals in the ADHD-U group self-reported being currently on an ADHD medication on an open-ended question regarding general, current pharmacological treatments; to the extent that this one-item, face valid measure of current usage tapped the possibility of ADHD medication effects in this sample, ongoing treatment seems a quite unlikely explanation for the better performance of the ADHD-U group, relative to Gualtieri and Johnson's (2006b) sample.

Educational Attainment

The high level of educational attainment for individuals in the ADHD-U group represents a unique characteristic of this community sample. Barkley (2006) points out individuals with ADHD tend to obtain less education than do control groups. In one sample, Barkley (2006) notes, 32% of individuals identified as being hyperactive did not finish high school. Further, only 21% of this hyperactive group enrolled in college, as compared to 78% of the control group. In another study of young adults with ADHD, it was again found that the ADHD groups had significantly less education; only 6.3% of participants in the ADHD-IA group graduated from college, while 7.3% of participants in the ADHD Combined type graduated from college (Murphy et al., 2002). The ADHD-U

group included 36 participants (59%) who reported completing 4 or more years of college, which stands in stark contrast to this trend of educational underachievement.

Consequently, it seems likely that the participants identified in the ADHD-U group are "high functioning"—or even sub-clinical-- relative to other individuals with ADHD. Indeed, individuals in the ADHD-U group actually performed significantly *better* on the CNSVS Verbal Memory task than the CCD and CCA groups, and indistinguishably from the non-clinical control group. This unexpectedly high level of educational attainment and cognitive functioning in the ADHD-U group may be in part due to the nature of the community from which the sample was taken. Boone, North Carolina, is a small college town with many of its residents associated with Appalachian State University and other organizations that provide professional services to the surrounding rural area (e.g., hospital, county-level governance, law offices). Many individuals across the comparison groups have achieved high levels of education, and this likely represents a bias toward high intellectual ability in this community sample. Differences in executive functioning between individuals with ADHD and other groups may have been more difficult to detect due to this trend.

Testing Protocol

The CNSVS test protocol calls for individual administration. However, due to the size of the testing group and relatively limited administration time, we administered the CNSVS in a group format, utilizing a computer lab to test up to about 30 participants at a time. The seating in this environment was such that many individuals had a participant on both their left and their right, engaged in the same CNSVS battery but often completing a different subtest, concurrently. In addition, as testing was implemented

continuously in this computer lab, the vast majority of the participants completed the CNSVS battery as others came or went. Spacing was maintained as much as possible (e.g., every other computer used). While the CNSVS was designed to be taken without even a test administrator present, its administration in the current study represents a substantial deviation from test protocol, and these environmental differences may have caused distraction and some added difficulty for participants. Generally speaking, the influence of having multiple individuals in the testing environment—other participants and "helpful" research assistants, alike—may have diluted the sensitivity of the battery. Further, participants were in unique circumstances, nutritionally, as they had fasted the entire morning and had undergone a physical evaluation prior to administration of the CNSVS. Perhaps this could have had a sort of leveling affect, as low energy might have contributed to inattention or sluggishness across groups. In any event, these circumstances deviate from standard protocol and should certainly be weighed when interpreting the data.

Though there is no published research that has specifically examined how group administration of a computer-based, neurocognitive testing battery designed for individual usage effects outcome scores, there is ample evidence suggesting that mode of administration and social environment does affect task and test performance, in general. In a study examining such factors, Whitener and Klein (1995) found that measures of self esteem were significantly affected by whether they were administered in group or individual settings. While self-esteem questionnaires have little in common with neurocognitive testing batteries, it still seems plausible that performance on the CNSVS

in the current study may have been altered, as compared to that of Gualtieri and Johnson's (2006a, 2006b), simply via the experience of being in a group, as well.

Research for standardized testing may provide more relevant comparisons. Mode effects have been found in studies measuring computerized vs. pencil and paper test administrations. Keng, McClarty, and Davis (2008) found that adolescents generally performed better on pencil and paper version compared to computerized versions of an aptitude test. In measuring differences between neurocognitive testing modes for individuals with schizophrenia, O'Halloran and colleagues (2007) found that standard paper and pencil administrations and computerized administrations ranged in intraclass correlation between 0.61 and 0.95. These findings suggest that altering test mode can, at least at times, produce significant variability in test performance.

Another consideration involves the influence of external distracters in testing situations. Tinius (2002) found that adults with ADHD (*M* age = 31.8 years) tended to have high variability in reaction time on the CPT. The author concluded that adults with ADHD were susceptible to distraction from external stimuli. Indeed, one might expect that increased external distracters would impair performance across groups. However, there appears to be little difference between the mean performance across subtests when comparing the ADHD group employed by Gualtieri and Johnson (2006b) and the one identified for this study. This suggests that there was not a systematic downward shift in performance across groups in the current study. Further, while higher *standard deviations* in the sample might indicate increased situational distraction, our groups were equivalent to, and sometimes smaller than, those derived in Gualtieri and Johnson's study (2006b). Overall, quantitative analysis of the testing results along these lines seems to

suggest that distraction due to the testing format, itself, may not have detracted meaningfully from the ability to detect ADHD-related differences in this study.

Neurocognitive Deficits and ADHD

The current findings bring in to question whether or not the CNSVS, or neurocognitive test batteries in general, are sensitive to identifying adults with or at elevated risk for ADHD. While neurocognitive testing is generally not viewed as appropriate for diagnosing ADHD (Seidman, 2006), much research suggests that individuals with ADHD do tend to perform worse on such measures (as noted previously; see Barkley, 2006, for an overview). However, results from studies specific to adults have been mixed.

Studies measuring differences between adults with ADHD and non-diagnosed peers using CPT tasks have been particularly inconclusive. While several studies have shown adults with ADHD tend to perform more poorly on CPT tasks (Schoechlin, & Engel, 2005; Murphy, Barkley, & Bush, 2001; Barkley, Murphy, & Kwasnik, 1996), Preston and colleagues (2005) found that CPT variables did not distinguish between an ADHD group and individuals with subclinical ADHD symptoms. McGee, Clark, and Symons (2000) questioned whether CPT tasks were more indicative of reading disorders rather than ADHD. The authors found that a CPT could not discriminate between ADHD and Reading Disordered (RD) groups. They also found that a measure of phonological awareness was statistically related to a CPT index score (albeit rather weakly, $r = -.23$). The current study also suggests, overall, that the CPT may provide poor discriminant validity for ADHD, at least in adulthood.

Contrary to research cited earlier which supports the use of the Shifting Attention task to distinguish ADHD from controls (e.g., Solanto et al., 2007; Jenkins et al., 1998), this measure may, in fact, not be appropriate for assessment of this population in adulthood. The majority of the extant research on measures similar to the CNSVS Shifting Attention task has focused on the Wisconsin Card Sorting Task (WCST), which is thought to measure cognitive flexibility. Frazier and colleagues (2004) conducted a meta-analysis of studies measuring differences on WCST performance between children with ADHD and non-diagnosed peers. The authors found mean weighted effect size differences between groups to be 0.35 for perseveration scores, 0.29 for categorization (i.e., rule detection), and 0.15 for the number of set failures (i.e. failed to recognize a new set of task-oriented rules). None of these effect sizes were statistically significant. Barkley (2006) concludes that the experience of ADHD is not likely to have an adverse affect on the cognitive function measures by the WCST. Similarly, the Shifting Attention task of the CNSVS may represent a cognitive function that is not deficient in adults with ADHD.

There is also some question as to whether or not individuals with ADHD differ consistently from their non-ADHD peers in executive functioning. Doyle, Biederman, Seidman, Weber, and Faraone (2000) found children with ADHD did perform worse than non-diagnosed peers on a testing battery including a Stroop task, a CPT, and the WCST. However, individuals within the ADHD group showed marked variation in terms of the extent of their individual deficits on these executive functioning and attention tasks. To wit, some suggest that deficits in executive functioning are most profound in individuals with ADHD-IA (Sonuga-Barke, 2002). Nigg and colleagues (2005) found that measures

of executive functioning were uniquely sensitive to identifying deficits in individuals with ADHD-IA, as opposed to those with prominent hyperactivity-impulsivity, who tended to register deficiencies more on measures of psychomotor speed. Further, Seidman (2006) suggests that individuals primarily suffering from hyperactive-impulsive symptoms are more likely to exhibit impairment in brain reward systems that are independent of executive functioning. The current study did not reveal any differences between the ADHD-IA and ADHD-HI groups. The authors of the CNSVS (Gualtieri & Johnson, 2006a, 2006b) did not establish differences between these groups, per se, but findings from the current study underscore that this neurocognitive battery may not be sensitive to the unique deficits of the ADHD types.

Implications of Exploratory Analyses

While creating more stringent standards for inclusion in the ADHD-U group should have derived a group that more closely resembled the clinical populations used by Gualtieri and Johnson (2006a, 2006b), analyses still mostly resulted in null findings, with the only exception being Stroop simple reaction time. Low power can partially explain this finding, as the ADHD-U group was reduced to a mere 25% of its original size. However, the overall MANOVA did not even approach trend level significance, which fits with other data presented here that suggests that neurocognitive differences between individuals with ADHD and other groups may not be robust in middle and older adulthood—or, at the least, that the CNSVS battery is not sensitive enough to detect them.

Given that neurocognitive deficits have been shown for individuals with ADHD into young adulthood, it was hypothesized, post-hoc, that the CNSVS would be better able to distinguish the age-restricted ADHD-U group from the other groups. While a

trend toward statistical significance was found in this exploratory analysis, further examination showed that differences on Stroop simple reaction time drove this difference and were, in fact, *not* in the expected direction. As noted previously, this may be a consequence of the relatively high functioning of the ADHD-U group used in these analyses. In addition, as in the previous exploratory analysis, the sample size was significantly reduced, which may have decreased the power to detect smaller differences that would be more in line with expectations (i.e., signaling impairment in the ADHD-U group relative to others). Further, Gualtieri and Johnson (2006b) identified young adulthood as being ages 20-29 years, as compared to the 40-or-below criterion employed herein. Still, the age-restricted analysis suggests that, even before middle age, the CNSVS may not differentiate ADHD from other groups.

Limitations and Future Directions

Much of the preceding discussion has focused on limitations and qualifications regarding the current study and interpretation of its findings. However, it is important to highlight the most salient of these, for clarity's sake. First, self report measures alone are not ideal in identifying ADHD. A full psychological evaluation may have allowed for more accurate assignment to groups. One piece of evidence that suggests that diagnostic uncertainty exists herein, given the criteria we used to identify "ADHD" participants, is that when childhood symptoms were taken into consideration—a requirement for strict *DSM-IV-TR* diagnosis—the ADHD-U group decreased to just a quarter of its original size. This indicates that some of our identified ADHD group participants either do not meet full diagnostic criteria for ADHD, do not accurately recall the extent of their childhood symptoms, currently exhibit ADHD symptoms that are extensive but due to another, non-

neurological cause, or a combination thereof. Given this likely degree of heterogeneity and resulting "subclinical" or even false-positive "ADHD" cases, detection of "true" group differences was likely made more difficult.

Second, Gualtieri and Johnson (2006a, 2006b) used samples ranging from childhood to young adulthood. Our study used a sample of individuals ranging across the adult lifespan, and this difference does not lend easily to direct comparison of results. Third, as noted above, although the sample as a whole was quite large, its community-derived nature equated to relatively few individuals with ADHD traits that are clinically elevated. The consequence: Low statistical power that limits of the ability to detect differences between the ADHD-U and other groups. Perhaps a larger sample size would allow for the detection of differences that are smaller in effect size. However, as stated earlier, Cohen (1992) suggests clinical group cell sizes would need to be substantially larger to achieve statistical significance in *F* tests, given the effect sizes in the current study.

Fourth, the demographic composition of the sample differs significantly from that of both the general U.S. population and that of the larger group of individuals with ADHD. For instance, educational attainment amongst the ADHD-U group is far better than what would be expected in a community sample of individuals with ADHD. Higher attainment of education may indicate that our ADHD group is high functioning relative to most in that population. Furthermore, the ethnic distribution in this sample is far from diverse. Consequently, for these and other reasons (e.g., doubts regarding the "clinical" nature of ADHD-identified individuals), generalization of these findings to the population of ADHD individuals should be done only with great caution.

Clinical Implications. The current study suggests several important implications regarding ADHD in adulthood. First, contrary to previous studies examining neurocognitive deficits in younger populations, the CNSVS did not differentiate subtypes of ADHD in adulthood. Perhaps subtype classifications become less meaningful, from a cognitive functioning perspective, as those with ADHD progress through adulthood. Future research examining the nature of symptom expression specific to adults with ADHD would be helpful.

Interestingly and despite the preponderance of null findings in the study, medium effect sizes between the ADHD-U group and the CCA and CCD groups were found for several CNSVS subtests. These subtests include both Verbal and Visual memory, Finger tapping, Shifting attention and several Stroop tasks. Future studies with large samples of rigorously identified adults with attention-deficit, mood, and anxiety disorders may productively include this brief CNSVS battery in their study protocol to enable a targeted examination of whether a subset of CNSVS tests has some clinical utility for differentiating these conditions.

Finally, the current study underscores the considerable challenge of diagnosing ADHD in adulthood. Diagnostic criteria require that ADHD symptoms be present in childhood. For individuals who present for psychological evaluation in adulthood, obtaining and substantiating such information is often difficult. Further adding to these difficulties is the relatively unknown course of ADHD throughout the lifespan. One may expect that neurocognitive deficits that have been found in younger individuals with ADHD would persist throughout adulthood, and therefore provide a robust indicator of chronic psychological disorder. However, there is not a great deal of research supporting

this contention. The current study suggests that neurocognitive deficits may not persist--at least in "higher-functioning" cases, or precisely those that might present in adulthood for diagnosis-- further disrupting the ability to identify ADHD in adulthood.

Conclusions. Neurocognitive testing batteries have been shown to be sensitive to identifying deficits in children, adolescents, and, to an extent, young adults with ADHD. However, more research on neurocognitive functioning across the lifespan is necessary. Research examining neurocognitive deficits in ADHD is especially lacking for those over the age of 40. Given that ADHD symptom experience may not be consistent across the lifespan, performance on neurocognitive batteries may also vary as individuals age. Results from the current study suggest that the CNSVS may not be useful in distinguishing adults with ADHD. Longitudinal research, which follows children diagnosed with ADHD across the lifespan, may provide further understanding into the sensitivity of neurocognitive measures, including the CNSVS.

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Table 1

Means and Standard Deviations for Demographic Variables across Groups

	ADHD-IA (n = 34)	ADHD-HI (n = 27)	CCA (n = 21)	CCD (n = 31)	Control (n = 589)
Age	45.67 (14.69)	45.89 (13.87)	45.27 (13.96)	42.7 (16.63)	46.01 (16.81)
Education in Years	16.03 (2.79)	16.12 (2.37)	15.97 (2.43)	14.45 (2.93)	15.71 (2.71)
Gender (% Male)	38.24%	14.8%	66.67%	60%	39.29%
Inattention	13.91 (2.77)	13.42 (5.13)	7.1 (3.84)	6.2 (3.14)	3.63 (2.94)
Hyperactivity-Impulsivity	8.58 (2.62)	14.43 (4.64)	5.93 (3.47)	6.6 (3.8)	3.87 (3.07)
BSI Anx. Scale Score	63.97 (9.76)	59.04 (10.7)	67.57 (3.2)	54.35 (8.42)	47.21 (7.13)
BSI Dep. Scale Score	61.36 (12.15)	60.52 (8.67)	53.9 (5.63)	66.55 (5.25)	46.26 (8.07)

Note. ADHD-IA = ADHD Inattentive group, ADHD-HI = ADHD Hyperactive/Impulsive or Combined type group, CCD = Depression Clinical Comparison group, CCA= Anxiety Clinical Comparison group. ADHD symptoms based on current self symptom reports (Barkley and Murphy, 2006). BSI Anx. = BSI Anxiety, BSI Dep. = BSI Depression. BSI Scale scores measure current Depressive and Anxious symptoms (Derogatis, 199).

Table 2

Means and Standard Deviations for CNSVS across Groups

Dependent Variable	ADHD-U (*n* = 61)	Anxiety (*n* = 21)	Depression (*n* = 31)	Control (*n* = 589)	ADHD-GJ (*n* = 175)
Verbal Memory	53.7	51	50.75	52.61	51.62
	(4.94)	(5.36)	(4.91)	(4.83)	(5.69)
Visual Memory	45.82	44.83	44.25	45.8	46.73
	(5.23)	(5.99)	(5.19)	(5.22)	(5.85)
FT Right	56.9	60.72	59.27	58.28	--
	(10.96)	(7.5)	(8.36)	(9.03)	
FT Left	55.19	57.91	55.77	55.11	--
	(7.84)	(6.7)	(9.16)	(8.05)	
SDC Correct	53.61	55.03	49.7	53.92	54.17
	(13.69)	(13.14)	(17.98)	(14.02)	(13.48)
Stroop Simple RT	318.98 (110.12)	279.33 (32.99)	293.55 (74.56)	303.98 (75.09)	314.37 (119.75)
Stroop Complex Corr.	11.9 (0.35)	11.97 (0.18)	12.00 (0.00)	11.82 (1.19)	--
Stroop Complx. Com.	0.3 (0.62)	0.27 (0.52)	0.45 (0.61)	0.38 (0.75)	--
Stroop Correct	23.46	23.6	23.9	23.42	--
	(2.75)	(1.13)	(0.3)	(2.92)	
Stroop RT	710.26	695.3	686.2	699.08	--

Correct	(149.75)	(122.41)	(119.82)	(137.38)	
Stroop Com.	1.31	2.1	1.65	1.7	
Errors	(1.54)	(2.83)	(1.18)	(2.44)	--
SAT Correct	48.31	53.37	50.35	49.68	46.19
	(10.48)	(8.2)	(10.8)	(10.97)	(10.18)
SAT Errors	6.43	5.17	6.75	7.07	12.43
	(6.05)	(6.68)	(4.99)	(8.02)	(11.38)
SAT RT Correct	1143.39	1066.37	1116.63	1084.29	
	(161.33)	(180.42)	(198.81)	(209.21)	--
CPT Correct	39.33	39.63	39.45	39.2	38.9
	(3.25)	(1.33)	(1.28)	(4.45)	(2.24)
CPT Omission	0.67	0.37	0.55	0.52	
Errors	(3.25)	(1.3)	(1.28)	(3.01)	--
CPT Comm.	1.93	4.57	0.85	1.95	
Errors	(12.01)	(21.19)	(1.63)	(11.63)	--
CPT RT Correct	441.56	432.6	436.2	429.61	
	(70.38)	(101.57)	(46.87)	(62.1)	--

Note. FT Right = Right Finger Tapping average (number of taps), FT Left =Left Finger Tapping average, SDC Correct = Symbol Digit Coding Correct Responses, Stroop Simple RT = Stroop Simple Reaction Time, Stroop Complex Corr. = Stroop Complex Correct Responses, Stroop Complx. Com. = Stroop Complex Commission Errors, Stroop Correct = Stroop Correct Responses, Stroop RT Correct = Stroop Reaction Time for Correct Response, Stroop Com. Errors = Stroop Commission Errors, SAT Correct

= Shifting Attention Correct Responses, SAT Errors = Shifting Attention Errors, SAT RT Correct = Shifting Attention Reaction Time for Correct Responses, CPT Correct = CPT Correct Responses, CPT Omission Errors = CPT Omission Errors, CPT Comm. Errors = CPT Commission Errors, CPT RT Correct = CPT Reaction Time for Correct Responses, and ADHD-GJ = ADHD group data from Gualtieri and Johnson (2006b), where available.

Table 3

Means and Standard Deviations for CNSVS across Gender for ADHD-IA, ADHD-HI, and ADHD-U groups

	ADHD-IA Male	ADHD-IA Fem.	ADHD-HI Male	ADHD-HI Fem.	ADHD-U Male	ADHD-U Fem.
Verbal Memory	52.23	53.4	53.5	54.79	52.54	54.16
	(5.56)	(5.73)	(4.8)	(3.86)	(5.27)	(4.8)
Visual Memory	45.77	45.55	46.75	45.92	46	45.75
	(6.41)	(5.58)	(0.5)	(4.91)	(5.57)	(5.16)
Ft Right	56.13	57.68	61.75	55.85	57.45	56.68
	(13.67)	(8.87)	(6.23)	(11.81)	(12.39)	(10.5)
Ft Left	57.08	54.15	58.17	54.53	57.33	54.36
	(6.62)	(6.92)	(3.05)	(9.58)	(5.9)	(8.39)
SDC Correct	48.85	53.4	50.5	56.88	49.24	55.3
	(14.78)	(12.8)	(16.76)	(13.31)	(14.73)	(13.05)
Stroop Simple RT	315.62	325.2	298.75	319	311.65	321.82
	(172.47)	(82.18)	(50.74)	(100.45)	(151.15)	(91.59)
Stroop Complex	11.92	11.9	12	11.88	11.94	11.89
Corr.	(0.28)	(0.31)	(0.00)	(0.45)	(0.24)	(0.39)
Stroop Correct	23.54	22.9	24	23.79	23.65	23.39
	(1.13)	(4.69)	(0.00)	(0.66)	(0.99)	(3.19)
Stroop RT Correct	774.85	680.75	697	702.08	634	607.57
	(219.53)	(79.43)	(126.99)	(151.09)	(156.63)	(81.98)

Stroop Com. Errors	0.23	0.15	0.5	0.42	1.41	1.27
	(0.44)	(0.49)	(0.58)	(0.78)	(1.06)	(1.7)
SAT Correct	48.23	47.85	51	48.29	48.88	48.09
	(11.1)	(10.89)	(11.61)	(10.27)	(10.91)	(10.43)
SAT Errors	6.46	6.9	4	6.42	5.88	6.64
	(7.52)	(6.71)	(2.58)	(5.17)	(6.7)	(5.86)
SAT RT Correct	1146.19	1133.5	1174.33	1144.97	1152.81	1139.76
	(162.85)	(132.3)	(243.74)	(177.74)	(176.58)	(157.05)
CPT Correct	39.77	39.9	40	38.5	39.82	39.14
	(0.44)	(0.31)	(0.00)	(5.12)	(0.39)	(3.81)
CPT Omission	0.23	0.1	0	1.5	0.18	0.86
Errors	(0.44)	(0.31)	(0.00)	(5.12)	(0.39)	(3.8)
CPT Comm. Errors	0.31	0.2	0.25	4.54	0.29	2.57
	(0.63)	(0.41)	(0.5)	(19.09)	(0.59)	(14.13)
CPT RT Correct	418.92	445.9	408	455.79	416.35	451.3
	(39.88)	(57.83)	(621.2)	(90.06)	(44.05)	(70.38)

Note. Fem. = Female, FT Right = Right Finger Tapping average (number of taps), FT Left =Left Finger Tapping average, SDC Correct = Symbol Digit Coding Correct Responses, Stroop Simple RT = Stroop Simple Reaction Time, Stroop Complex Corr. = Stroop Complex Correct Responses, Stroop Complx. Com. = Stroop Complex Commission Errors, Stroop Correct = Stroop Correct Responses, Stroop RT Correct = Stroop Reaction Time for Correct Response, Stroop Com. Errors = Stroop Commission Errors, SAT Correct = Shifting Attention Correct Responses, SAT Errors = Shifting

Attention Errors, SAT RT Correct = Shifting Attention Reaction Time for Correct Responses, CPT Correct = CPT Correct Responses, CPT Omission Errors = CPT Omission Errors, CPT Comm. Errors = CPT Commission Errors, CPT RT Correct = CPT Reaction Time for Correct Responses.

Table 4

Analysis of Variance Results: ADHD-U Comparisons

Dependent Variable	*F* value	*p* value
Verbal Memory	3.01	0.03*
Visual Memory	0.89	0.45
FT Right	1.25	0.29
FT Left	1.25	0.29
SDC Correct	0.62	0.61
Stroop Simple RT	1.83	0.14
Stroop Complex Correct	0.38	0.77
Stroop Complex Com. Errors	0.57	0.64
Stroop Correct	0.22	0.88
Stroop RT Correct	0.18	0.91
Stroop Com. Errors	0.78	0.51
SAT Correct	1.52	0.21
SAT Errors	0.78	0.51
SAT RT Correct	1.77	0.15
CPT Correct	0.12	0.95
CPT Omission Errors	0.08	0.97
CPT Comm. Errors	0.52	0.67
CPT RT Correct	0.65	0.59

Note. FT Right = Right Finger Tapping average (number of taps), FT Left =Left Finger Tapping average, SDC Correct = Symbol Digit Coding Correct Responses, Stroop

Simple RT = Stroop Simple Reaction Time, Stroop Complex Corr. = Stroop Complex Correct Responses, Stroop Complx. Com. Errors = Stroop Complex Commission Errors, Stroop Correct = Stroop Correct Responses, Stroop RT Correct = Stroop Reaction Time for Correct Response, Stroop Com. Errors = Stroop Commission Errors, SAT Correct = Shifting Attention Correct Responses, SAT Errors = Shifting Attention Errors, SAT RT Correct = Shifting Attention Reaction Time for Correct Responses, CPT Correct = CPT Correct Responses, CPT Omission Errors = CPT Omission Errors, CPT Comm. Errors = CPT Commission Errors, and CPT RT Correct = CPT Reaction Time for Correct Responses.

* $p < .05$.

Table 5

Effect Size Differences between ADHD-U and Other Groups (Cohen's d)

Dependent Variable	Anxiety	Depression	Control
Verbal Memory	0.52†	0.6†	0.22
Visual Memory	0.18	0.3	0.01
FT Right	-0.41	-0.24	-0.14
FT Left	-0.37	-0.07	0.01
SDC Correct	-0.12	0.24	-0.02
Stroop Simple RT	0.49	0.27	0.16
Stroop Complex Correct	-0.25	-0.4	0.09
Stroop Complex Com. Errors	0.05	-0.24	-0.12
Stroop Correct	-0.07	-0.22	0.01
Stroop RT Correct	0.11	0.18	0.08
Stroop Com. Errors	-0.35	-0.25	-0.19
SAT Correct	-0.54	-0.19	-0.13
SAT Errors	0.19	0.2	-0.06
SAT RT Correct	0.45	0.15	0.32
CPT Correct	-0.12	-0.05	0.03
CPT Omission Errors	0.12	0.05	0.05
CPT Comm. Errors	-0.15	0.13	-0.01
CPT RT Correct	0.1	0.09	0.18

Note. FT Right = Right Finger Tapping average (number of taps), FT Left =Left Finger Tapping average, SDC Correct = Symbol Digit Coding Correct Responses, Stroop Simple RT = Stroop Simple Reaction Time, Stroop Complex Corr. = Stroop Complex

Correct Responses, Stroop Complx. Com. Errors = Stroop Complex Commission Errors, Stroop Correct = Stroop Correct Responses, Stroop RT Correct = Stroop Reaction Time for Correct Response, Stroop Com. Errors = Stroop Commission Errors, SAT Correct = Shifting Attention Correct Responses, SAT Errors = Shifting Attention Errors, SAT RT Correct = Shifting Attention Reaction Time for Correct Responses, CPT Correct = CPT Correct Responses, CPT Omission Errors = CPT Omission Errors, CPT Comm. Errors = CPT Commission Errors, and CPT RT Correct = CPT Reaction Time for Correct Responses.

† $p < .10$.

Table 6

Correlations between ADHD Symptoms and CNSVS Scores (Pearson's r)

Dependent Variable	AHDH-IA Symptoms	ADHD-HI Symptoms
Verbal Memory	0.07†	0.09**
Visual Memory	0.03	0.13*
FT Right	-0.03	0.06
FT Left	0.01	0.06
SDC Correct	-0.04	0.16*
Stroop Simple RT	0.01	-0.06
Stroop Complex Correct	-0.03	-0.06
Stroop Complex Com. Errors	-0.03	-0.01
Stroop Correct	-0.01	0.07†
Stroop RT Correct	-0.01	-0.09**
Stroop Com. Errors	-0.03	-0.07†
SAT Correct	-0.03	0.08**
SAT Errors	-0.02	-0.08**
SAT RT Correct	-0.06	-0.01
CPT Correct	-0.03	-0.04
CPT Omission Errors	0.06	0.08
CPT Comm. Errors	0.02	0.02
CPT RT Correct	0.05	0.01

Note. ADHD symptoms based on current self symptom reports (Barkley and Murphy, 2006). ADHD-IA= Inattentive symptoms, ADHD-HI= Hyperactive/Impulsive symptoms.

FT Right = Right Finger Tapping average (number of taps), FT Left =Left Finger Tapping average, SDC Correct = Symbol Digit Coding Correct Responses, Stroop Simple RT = Stroop Simple Reaction Time, Stroop Complex Corr. = Stroop Complex Correct Responses, Stroop Complx. Com. Errors = Stroop Complex Commission Errors, Stroop Correct = Stroop Correct Responses, Stroop RT Correct = Stroop Reaction Time for Correct Response, Stroop Com. Errors = Stroop Commission Errors, SAT Correct = Shifting Attention Correct Responses, SAT Errors = Shifting Attention Errors, SAT RT Correct = Shifting Attention Reaction Time for Correct Responses, CPT Correct = CPT Correct Responses, CPT Omission Errors = CPT Omission Errors, CPT Comm. Errors = CPT Commission Errors, and CPT RT Correct = CPT Reaction Time for Correct Responses.

** $p < .01$. * $p < .05$. † $p < .10$.

Table 7

Group Means (SDs) for CNSVS Variables with Age and (ADHD group only) Childhood Symptom Restrictions Applied

Dependent Variable	ADHD-U (n = 24)	Anxiety (n = 11)	Depression (n = 8)	Control (n = 215)	ADHD-CL (n = 14)
Verbal Memory	54.25	52.45	51.75	53.58	54.43
	(3.98)	(5.66)	(3.15)	(4.48)	(2.98)
Visual Memory	46.33	45.27	47	47.93	48.07
	(5.47)	(6.2)	(3.7)	(5.11)	(3.6)
FT Right	60.1	62.61	63.13	62.53	59.52
	(9.27)	(7.78)	(6.26)	(6.89)	(9.08)
FT Left	56.47	59.21	60.38	57.4	55.81
	(8.29)	(6.81)	(6.21)	(6.96)	(7.81)
SDC Correct	62.08	61.82	60.38	64	58.43
	(11.03)	(10.94)	(11.82)	(10.3)	(15.48)
Stroop Simple RT	330.42	272.27	273.88	278.48	279.57
	(112.43)	(19.4)	(37.75)	(51.38)	(42.79)
Stroop Complex	11.92	12	12.00	11.97	11.93
Corr.	(0.41)	(0.00)	(0.00)	(0.19)	(0.27)
Stroop Complx.	0.21	0.45	0.25	0.31	0.36
Com.	(0.51)	(0.69)	(0.46)	(0.69)	(0.5)
Stroop Correct	23.96	23.73	24	23.79	23.93

	(0.2)	(0.47)	(0.00)	(1.61)	(0.27)
Stroop RT Correct	665.04	660.36	643	668.08	683.93
	(98.77)	(74.8)	(71.84)	(112.19)	(154.91)
Stroop Com. Errors	1.04	1.18	1.62	1.51	1.71
	(1.16)	(0.75)	(1.18)	(2.08)	(1.2)
SAT Correct	53	56.36	55.5	55.12	50.93
	(6.76)	(9.38)	(7.39)	(7.45)	(11.13)
SAT Errors	4.79	4.09	4.5	5.55	5.21
	(3.41)	(2.91)	(2.33)	(5.63)	(5.22)
SAT RT Correct	1066.63	1012.63	1067.48	999.2	1115.81
	(124.41)	(193.53)	(213.14)	(130.37)	(201.15)
CPT Correct	39.42	39.82	39.88	39.61	38.36
	(1.06)	(0.4)	(1.81)	(2.45)	(1.15)
CPT Omission	0.58	0.18	1.12	0.39	0.64
Errors	(1.06)	(0.41)	(1.81)	(2.45)	(1.15)
CPT Comm. Errors	0.58	0.45	1.75	1.27	0.43
	(1.06)	(0.69)	(2.32)	(7.33)	(0.94)
CPT RT Correct	437.79	421.91	428.38	416.38	423.29
	(90.58)	(27.97)	(65.87)	(49.56)	(58.17)

Note. FT Right = Right Finger Tapping average (number of taps), FT Left =Left Finger Tapping average, SDC Correct = Symbol Digit Coding Correct Responses, Stroop Simple RT = Stroop Simple Reaction Time, Stroop Complex Corr. = Stroop Complex Correct Responses, Stroop Complx. Com. = Stroop Complex Commission Errors, Stroop

Correct = Stroop Correct Responses, Stroop RT Correct = Stroop Reaction Time for Correct Response, Stroop Com. Errors = Stroop Commission Errors, SAT Correct = Shifting Attention Correct Responses, SAT Errors = Shifting Attention Errors, SAT RT Correct = Shifting Attention Reaction Time for Correct Responses, CPT Correct = CPT Correct Responses, CPT Omission Errors = CPT Omission Errors, CPT Comm. Errors = CPT Commission Errors, CPT RT Correct = CPT Reaction Time for Correct Responses, ADHD-CL = ADHD-U subgroup meeting ADHD impairment criteria for childhood

Appendix A—IRB Approval

To: Will Canu
Psychology
CAMPUS MAIL

From: _____
Jay W. Cranston, M.D., Chair, Institutional Review Board

Date: 4/27/2009

RE: Notice of IRB Exemption

Study #: 09-0234
Study Title: The Utility of CNS Vital Signs as an Indicator of Adult ADHD
Exemption Category: (4) Collection or Study of Existing Data

This submission has been reviewed by the above IRB Office and was determined to be exempt from further review according to the regulatory category cited above under 45 CFR 46.101(b). Should you change any aspect of the proposal, you must contact the IRB before implementing the changes to make sure the exempt status will continue. Otherwise, you will not need to apply for annual approval renewal. Please notify the IRB Office when you have completed the study.

CC:
Jared Cook, Psychology

Appendix B—Diagnostic Items

ADHD Self-Report Items

Items Assessing Inattention:

- Failed to give close attention to details or make careless mistakes in my work.
- Had difficulty sustaining my attention in tasks or fun activities
- Didn't listen when spoken to directly
- Didn't follow through on instructions and failed to finish work
- Had difficulty organizing tasks and activities
- Avoided, disliked, or was reluctant to engage in work that requires sustained mental effort
- Lost things necessary for tasks or activities.
- Was easily distracted.
- Was forgetful in daily activities.

Items Assessing Hyperactivity/Impulsivity:

- Fidgeted with hands or feet or squirm in seat.
- Left my seat in situation in which sitting is expected.
- Felt restless.
- Had difficulty engaging in leisure activities or doing fun things quietly.
- Felt "on the go" or "driven by a motor."
- Talked excessively.
- Blurted our answers before questions have been completed.
- Had difficulty awaiting turn.

- Interrupted or intruded on others.

Items Assessing Adult Symptoms:

- Am often easily distracted by extraneous stimuli.
- Make decisions impulsively.
- Have difficulty stopping activities or behavior when I should do so.
- Start a project or task without reading or listening to directions carefully.
- Show poor follow-through on promises or commitments made to others.
- Have trouble doing things in the proper order or sequence.
- More likely to drive a motor vehicle much faster than others (excessive speeding).

BSI Items

Items Assessing Depression:

- Thoughts of Ending your Life
- Feeling Lonely
- Feeling blue
- Feeling no interests in things
- Feeling hopeless about the future
- Feelings of worthlessness

Items Assessing Anxiety:

- Nervousness or shakiness inside
- Suddenly scared for no reason
- Feeling tense or keyed up
- Spells of terror or panic
- Feeling so restless you couldn't sit still

Appendix C—Consent

Consent Form for Human Subjects

Quercetin, Upper Respiratory Tract Infection, Inflammation, Mental Vigilance, Blood Lipids, Pharmacokinetics: A Community Clinical Trial

Primary Investigator: David C. Nieman, Dr. PH, Director of the Human Performance Laboratory, Appalachian State University (ASU); niemandc@appstate.edu
Research Project Managers:
Sarah Gross, MS; Melanie Austin, MS
Co-Investigators:
Dru Henson, PhD (immunologist)
Jean-Pierre Kinet, MD (immunologist)
Steven McAnulty, PhD (oxidative stress)
John Quindry, PhD (oxidative stress researcher)
Josh Broman-Fulks, PhD and Will Canu, PhD (psychologists)
Tom Lines (CEO, Quercegen Pharma)

I. PURPOSE OF THIS RESEARCH PROJECT

Quercetin is a unique molecule found in some plant foods such as apples, berries, peppers, black tea, and onions. Quercetin is a powerful antioxidant (5 times more powerful than vitamin C), reduces inflammation, helps regulate the immune system, prevents some types of viruses and bacteria from multiplying, and has caffeine-like effects on the brain. Few studies with humans, however, have been conducted and most of these quercetin-related effects have come from laboratory cell culture and animal studies. Most people ingest about 20 mg of quercetin a day (the equivalent amount found in two large apples). Scientists have shown that people eating high compared to low amounts of quercetin have a reduced risk of developing heart disease, type 2 diabetes, asthma, lung cancer, colorectal cancer, and prostate cancer. In a previous study conducted at Appalachian State University, endurance athletes ingesting large amounts of quercetin (1,000 mg/day for three weeks) experienced improved mental vigilance and reduced illness rates when subjected to stressful amounts of exercise. The primary purpose of this study is to determine if 500 or 1,000 mg quercetin per day compared to placebo during a 12-week period reduced inflammation, oxidative stress, illness, and blood lipids while improving mental function, cognition, and mood.

II. PROCEDURES

One thousand non-institutionalized males and females, 18-75 years of age, will be recruited through mass advertisement in the Boone, NC area. Female subjects must not be or expect to be pregnant or lactating during the study period, January to April, 2008 (and for the second group, September to December, 2008). You must agree to avoid any other supplements containing quercetin. No other restrictions will be placed on diet, supplement usage, or medications, but you will list all current use of supplements and medication in a questionnaire. Subjects with no known disease will randomized to one of three groups: Quercetin-500 (500 mg/day), quercetin-1000 (1000 mg/day), or placebo.

Subjects with known diseases (e.g., heart disease, cancer, type 2 diabetes, osteoporosis, arthritis) will be randomized into one of two groups: Quercetin-1000 or placebo. You will ingest two soft chew supplements twice daily: in the morning after waking, and then again between 2:00 pm and the last meal of the day. This will continue each day during a 12-week period.

You will come to the ASU Human Performance Laboratory (Holmes Convocation Center, Room 054, 111 Rivers Street, Boone, NC; phone 828-262-3142) for two appointments at the beginning and end of the 12-week period. In each of these sessions, you must come to the lab not having consumed food or beverage (other than water) for 9-12 hours, and then provide a blood sample (45 ml or 3 tablespoons). Your resting blood pressure will also be measured. Questionnaires will be administered in both sessions to provide basic demographic and lifestyle habits, and psychological status. The blood samples will be assayed for a wide variety of measures including blood lipids, inflammation indicators such as C-reactive protein (CRP) and cytokines, oxidative stress, and quercetin. These results will be shared with you free-of-charge after the study is completed.

You will start ingesting supplements immediately after the first blood sample and continue for 12 weeks. During the 12-week supplementation period, you will record illness symptoms each day using a validated questionnaire called the Wisconsin Upper Respiratory Symptom Survey. Every four weeks, you will record quality of life measures, gastrointestinal and other health symptoms.

III. RISKS

The amount of blood drawn during each of the two sampling appointments (~45 ml) does not have a negative influence on health. A small amount of bruising at the blood sample site on your arm may be experienced for several days.

Universal precautions will be used throughout all blood sample collections. This refers to a “mindset” or “attitude” taken by the researchers that assumes all blood or body tissues are potentially infectious.

In limited human studies using similar quantities of quercetin supplements, subjects did not experience any measurable adverse effects to their health.

IV. BENEFITS

You will receive results of all tests when they become available. Summaries of the study will be e-mailed and/or mailed to you. This study will help determine if quercetin compared to placebo supplements are effective in improving mental function, cognition and mood, lowering blood lipids, reducing inflammation, reducing oxidative stress, reducing illness, and reducing the incidence and duration or upper respiratory tract infections such as the common cold. You will also receive compensation as described in the compensation section of this consent form. This study is not designed to measure change in disease status for subjects with known disease. Should the experiments notice any changes in disease status, such changes will be shared with the involved subjects.

V. EXTENT OF ANONYMITY AND CONFIDENTIALITY

Your identity will not be disclosed in any published documents or shared with anyone but the experimenters without your express written permission. No mass e-mails

will be sent to subjects that display all recipients to everyone. Mass e-mails will be sent by placing the subjects' e-mail addressed in the BCC area. Additionally, the names of participants will not be publicly displayed.

VI. COMPENSATION

Subjects will receive $300 for completing all aspects of the study. If you drop out of the study for any reason, you will be compensated according to the percentage of study requirements completed. For example, if you complete half of the study requirements, you will receive $150.

You may at any time choose to discontinue participation in this study and will not be expected to continue against your will. If as a result of this research project, the investigator determines that you should seek counseling or medical treatment, a list of local services will be provided. In the event of physical injury resulting from the research procedures, immediate first-aid is provided free of charge. No funds have been set aside for medical treatment of any injury or illness resulting from this project.

VII. FREEDOM TO WITHDRAW

You are free to withdraw from this study at any time without penalty subject to the terms described under "compensation" above.

VIII. APPROVAL OF RESEARCH

This research project has been approved, as required, by the Institutional Review Board of Appalachian State University. The investigators have no financial interest in this research project.

IX. SUBJECTS RESPONSIBILITIES

I voluntarily agree to participate in this study. I have the following responsibilities:

1. SUPPLEMENTATION:

a. If you are subject *without known disease*, you agree to be randomized to one of three groups: Quercetin-500 (500 mg/day), quercetin-1000 (1000 mg/day), or placebo.

b. If you are a subject *with known disease*, you agree to be randomized to one of two groups: Quercetin-1000 (1000 mg/day), or placebo.

c. All subjects *agree to avoid any other supplements containing quercetin*. No other restrictions will be placed on diet, supplement usage, or medications, but you will list all current use of supplements and medication in a questionnaire.

d. You will ingest two soft chew supplements twice daily: in the morning after waking, and then again between 2:00pm and the last mean of the day. This will continue each day during a 12-week period.

2. TWO LABORATORY SESSIONS, ASU HUMAN PERFORMANCE LAB:

a. You agree to the ASU Human Performance Laboratory for two appointments at the beginning and end of the 12-week period.

b. In each of these sessions, you agree to come to the lab not having consumed food or beverage (other than water) for 9-12 hours, and then provide a blood sample. You also agree to have your blood pressure measured.
c. In each of these sessions, you agree to fill in questionnaires to provide basic demographic and lifestyle habits. You also agree to have your psychological status and cognition tested using a computerized software package.

3. MONITORING DURING THE 12-WEEK STUDY:

a. During the 12-week supplementation period, you agree to record illness symptoms each day using a validated questionnaire.
b. Every four weeks during the study, you agree to provide answers regarding quality of life measures, gastrointestinal and other healthy symptoms, and other questions brought to your attention by the investigators.

X. SUBJECT'S PERMISSION

I have read and understand the Informed Consent and conditions of this project. I have had all my questions answered. I hereby acknowledge the above and give my voluntary consent:

_____ Date

_____
Subject Signature

_____ Date

_____
Subject printed name

_____ Date

_____
Witness (optional except for certain classes of subjects)

Should I have any questions about this research or its conduct, I may contact:

David C. Nieman	828-262-6318	niemandc@appstate.edu
Investigator	Telephone	E-mail

Robert L. Johnson	828-262-2692	johnsonrl@appstate.edu
Administrator, IRB	Telephone	E-mail

Graduate Studies & Research
Appalachian State University, Boone, NC 26608

Retain a copy for your records.

Vitae

Jared Cook attended Northeast Guilford high school in Mcleansville, North Carolina. He graduated with a Bachelor of Arts Degree in English from the University of North Carolina at Greensboro in 2004 and a Bachelor of Arts Degree in Psychology from the same university in 2008. Jared presented a poster in Seattle at the 2009 conference for the International Society for Research in Child and Adolescent Psychopathology. He presented another poster in Chattanooga at the 2010 conference for the Southeastern Psychological Association, and he was first author for a poster presented at the 2010 Association for Behavioral and Cognitive Therapies conference in San Francisco.

In fulfillment of program requirements at Appalachian State University, Jared completed his internship at the Wake Forest Baptist Medical Center Neuropsychology Clinic, focusing on psychological assessments. He will pursue a PhD in clinical psychology.