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## Discriminating between putative orbitofrontal and dorsolateral-prefrontal profiles using the personality assessment inventory

Kevin Michael Harkins  
*Northeastern University*

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DISCRIMINATING BETWEEN PUTATIVE ORBITOFRONTAL AND  
DORSOLATERAL-PREFRONTAL PROFILES USING  
THE PERSONALITY ASSESSMENT INVENTORY

A dissertation presented

by

Kevin Michael Harkins

Submitted to

The Department of Counseling and Applied Educational Psychology

In partial fulfillment of the requirements for the degree of  
Doctor of Philosophy

In the field of

Counseling Psychology

Northeastern University  
Boston, Massachusetts  
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ABSTRACT OF DISSERTATION

Submitted in partial fulfillment of the requirements  
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## ABSTRACT

The integration of cognitive neuroscience with neuropsychology has been advocated (Stuss & Levine, 2002). Lichter and Cummings' (2001) description of "circuit specific behavioral syndromes" suggested that an "orbitofrontal (OF) syndrome" could be discriminated from a "dorsolateral-prefrontal (DLPF) syndrome," based on a theoretical model of frontal-subcortical circuits. Using Morey's (1991) Personality Assessment Inventory (PAI), a cluster variate of antisocial features, aggression, mania, and obsessive-compulsive behavior was selected to partition a diagnostically heterogeneous, archival sample of clinic-referred college students ( $N = 22$ ) using cluster analysis. A two-group cluster solution emerged from the results of combined hierarchical-agglomerative and iterative partitioning procedures, potentially corresponding to the putative OF and DLPF classifications. The "OF profile group" obtained significantly higher scores on self-report measures of antisocial features, aggression, mania/hypomania, and obsessive-compulsive behavior than the "DLPF profile group." External validation of the cluster solution employing univariate logistic regression analyses suggested the DLPF profile group performed more poorly than the OF profile group on measures of sustained attention and spatial working memory, and the OF profile group performed more poorly than the DLPF profile group on a measure of color naming. Utilizing the PAI in conjunction with neuropsychological tests to assist in identifying OF and DLPF neurobehavioral profiles is suggested. Implications for treatment and academic accommodations for clinic-referred college students are discussed.

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## Dedication

Dedicated to my wife, Karen. I simply could not have done it without her. Thank you!

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Discriminating Between Putative Orbitofrontal and Dorsolateral-Prefrontal Profiles  
Using the Personality Assessment Inventory

Neuropsychology is defined as “the understanding of brain-behavior relationships and the clinical use of this information” (Stuss & Levine, 2002, p. 403). Although it is a sub-discipline within the broader field of general psychology, neuropsychology also is a close cousin of the medical professions, including behavioral neurology, neuropsychiatry, and cognitive neuroscience. From a neuropsychological perspective, the central nervous system is the biological substrate which mediates all human behavior. Weintraub (2000) regards the methods of neuropsychological assessment as “firmly rooted in a model of behavioral neuroanatomy that links domains of complex mental activity to the large-scale neuroanatomical networks that subserve them” (p. 164). Suffice it to say, brain-behavior relationships are complicated:

The relationship between brain and behavior is exceedingly intricate and frequently puzzling. Our understanding of this fundamental relationship is still very limited.... Any given behavior is the product of a myriad of complex neurophysiological and biochemical interactions involving the whole brain. (Lezak, Howieson, & Loring, 2004, p. 40)

Although the localization of brain functions has a long and storied history (Benton, 2000), it has become increasingly clear that cognition, emotion, and behavior are mediated by the coordinated and integrated functioning of widely distributed neuroanatomical networks (Mesulam, 2000).

The neuropsychological evaluation of adults is complicated by the fact that performance on traditional neuropsychological measures is often correlated with educational level; that is, the more education an individual has, the more likely it

becomes that his or her test performance will be statistically “normal” in relation to the population from which the normative data was derived (see Heaton, Ryan, and Grant, 2009). Moreover, general intelligence level also has been shown to correlate with performance on many neuropsychological tests (e.g., Jung, Yeo, Chiulli, Sibbit, & Brooks, 2000). Therefore, the evaluation of highly educated adults (e.g., college students) presents a challenge to the neuropsychological examiner, because “most cognitively oriented tasks are influenced by a [person’s] education and baseline cognitive abilities” (Kramer & Quitania, 2007, p. 280).

Indeed, college students who present to the clinic with difficulty meeting the demands of post-secondary education, ostensibly due to attention problems and learning disabilities, pose a unique challenge for neuropsychological assessment and rehabilitation. The Americans with Disabilities Act of 1990 (ADA) acknowledges that attention-deficit/hyperactivity disorder (ADHD) and learning disorders are disabilities which may require accommodations in the educational environment or workplace. When a diagnosis has been well-documented as a developmentally-based disorder which continues to exert a negative impact on learning and achievement, the student requesting accommodations in a post-secondary setting may be granted certain privileges, to ensure fair competition with peers who do not share the limitations associated with the disability. If, however, there has never been a formal diagnosis of a neurodevelopmental or learning disorder, or there is insufficient documentation to ascertain or corroborate the existence of a disability, then the college student who is in academic dire straits may seek or be referred for a neuropsychological evaluation. This assessment may either refute or provide

supportive evidence of a cognitive, psychiatric, and/or learning disorder that is having a substantially limiting, negative impact on academic functioning. Due to the inherent complexities involved in the neuropsychological evaluation of college students, best practice remains an open question in need of further investigation (cf. Weyandt & DuPaul, 2006).

The challenge in the neuropsychological assessment of college students is to ascertain those factors that may be contributing to the presenting problem. By definition, this cohort has successfully graduated from high school and gained admission to college. What is happening now to interfere with their success in the post-secondary educational setting? A comprehensive neuropsychological assessment includes obtaining a detailed mental status and reviewing documentation; evaluating cognitive, affective, and behavioral functions in multiple domains; and assessing personality and the ecological context.

Academic difficulties in college may be a consequence of individual, situational, and contextual variables, operating independently or in conjunction with other factors, resulting in sub-optimal achievement. For example, is there any history of concussion or mild head trauma? Are there any significant socio-emotional, behavioral, or psychiatric concerns? What are the students' attitudes and behaviors concerning the use of alcohol and psychoactive substances? What are their current living situations? What kinds of schedules do they keep? How do they organize and manage their academic assignments and commitments? Are they motivated, or is something interfering with goal-directedness? The clinical interview seeks answers to

these and related questions, and this information is integrated into the case interpretation and diagnosis.

College students who are having difficulty managing their academic workloads in the post-secondary setting may be referred to the clinic by concerned parties (e.g., family, professor, academic dean), or they may be self-referred. Presenting complaints often revolve around difficulties organizing academic assignments and keeping up with the reading requirements of multiple classes. Difficulties sustaining attention in class or initiating study independently are frequently reported. Problems meeting advanced, college mathematics and writing requirements are common problems encountered in the clinic. Because there are multitudinous variables that may be implicated in these kinds of presenting problems, diagnostic interviewing and a thorough review of previous documentation often yields important data (e.g., past diagnoses, behavioral observations, grades) that are considered, weighted, and integrated into the case formulation.

Many college students present for neuropsychological evaluation of problems that are associated with ADHD and/or learning disorders. For example, on the basis of rating scales, Weyandt, Linterman, and Rice (1995) found that between 2% to 8% of the college student population reported being affected by ADHD symptomatology. Remarkably, however, “little information is available concerning the neuropsychological functioning of college students with ADHD” (Weyandt & DuPaul, 2006, p. 15).

A neuropsychological assessment conducted in the post-secondary setting necessarily must include an evaluation of attention, executive functions, memory,

learning, and academic achievement. Guidelines have been established for the adequate documentation of learning disabilities in adolescents and adults (AHEAD, 1997), but concerns have been raised that clinicians who conduct these assessments may disregard established criteria (e.g., APA, 2000) in making diagnoses (Gordon, Lewandowski, Murphy, & Dempsey, 2002). For example, “the criteria for ADHD clearly requires the manifestation of significant impairment prior to high school at the latest, and in the absence of brain injury” (Gordon et al., p. 362). Some students who present for an evaluation may be involved in college athletics, including high-impact contact sports, so interviewing for a history of concussion or other mild head injury is critical (e.g., see Collins et al., 1999). If there has been no reported impairment prior to high school, then *de novo* diagnoses of ADHD in adults may be viewed with suspicion. Moreover, learning disabilities must be explicitly identified, based on substantive findings, in the written documentation: “The neuropsychological or psycho-educational evaluation for the diagnosis of a specific learning disability must provide clear and specific evidence that a learning disability does or does not exist” (AHEAD, p. 2).

Thus, the neuropsychological assessment of college students is a complicated enterprise that requires clinical acumen, diagnostic rigor, and descriptive clarity. The consequences of each assessment can be far-reaching: academic accommodations may (or may not) be approved by the college’s disability resource center; emotional-behavioral disorders may be diagnosed, supporting the need for psychological or psychiatric services; accommodations for standardized testing may be granted (e.g., Graduate Record Examinations), to give only a few examples.

The neuropsychological assessment, by definition, includes an evaluation of personality, mood, and behavior (Lezak et al., 2004). The most commonly used, comprehensive self-report measure (the Minnesota Multiphasic Personality Assessment Inventory, 2<sup>nd</sup> edition, or MMPI-2) is time-intensive, typically requiring between one to two hours to complete (Strauss, Sherman, & Spreen, 2006). An alternative personality measure that is gaining more widespread use is the Personality Assessment Inventory (PAI; Morey, 1991) which only requires 40-50 minutes to complete (Strauss et al., 2006). Although the PAI recently was the subject of a special issue in the *Journal of Personality Assessment* (Kurtz & Blais, 2007), and the test has been used in multiple contexts with widely varied populations, including forensic (Duellman & Bowers, 2004), law enforcement (Weiss, Rostow, Davis, & DeCoster-Martin, 2004; Weiss, Zehner, Davis, Rostow, & DeCoster-Martin, 2005), traumatic brain injury (Demakis et al., 2007; Kurtz, Shealy, & Putnam, 2007), chronic pain (Karlin et al., 2005), schizophrenia (Klonsky, 2004), and post-traumatic stress disorder (Crawford, Calhoun, Braxton, & Beckham, 2007), “few studies have been published bearing on the utility of the PAI in the neuropsychological context” (Strauss et al., p. 1130). This study attempts to redress the paucity of research using the PAI in the context of outpatient neuropsychological practice, with an emphasis on the evaluation of college students. As noted by Strauss et al., “the PAI includes a number of features that may contribute information that is highly relevant to the neuropsychological context, such as indications about substance use, aggression, suicide potential, and attitudes toward treatment” (p. 1132). The utility of the PAI in comparison to the MMPI-2 and in the evaluation of college students (particularly

those with learning disorders and other diagnostic comorbidities) is not restricted to brevity alone (discussed further in Chapter 2).

Stuss and Levine (2002) have advocated for “an approach to clinical neuropsychology that is informed by recent findings from cognitive neuroscience” (p. 401). With this in mind, the present study is concerned with discriminating between two neurobehavioral “profiles” that have been described in the empirical literature, theoretically associated with frontal-subcortical dysfunction. The theory of frontal-subcortical circuits involved in neurobehavioral functioning was first articulated over 20 years ago (Alexander, DeLong, & Strick, 1986; cited in Lichter & Cummings, 2001). According to Chow and Cummings (2007), “Frontal-subcortical circuits (FSCs) incorporate complex input from the central nervous system to modulate the expression of cognition and emotion through behavior and movement” (p. 25). Each one of the FSCs is associated with the same brain structures, but the circuits are arranged in parallel, more-or-less segregated from one another. Each FSC loops from the prefrontal cortex to the caudate nucleus, to the globus pallidus, on to the thalamus, and back to the prefrontal cortex. In addition to the communal neuroanatomical structures, each FSC also employs the same neuropeptides and neurotransmitters, “although the distribution of neuroreceptor subtypes might mediate different activations for each circuit” (Chow & Cummings, p. 26).

Lichter and Cummings (2001) outlined “three principal frontal lobe behavioral symptom complexes” related to specific frontal-subcortical circuitry:

A DLPF [dorsolateral prefrontal syndrome] with neuropsychological deficits involving executive functions, including decreased verbal and design fluency, abnormal motor programming, impaired set shifting, reduced learning and memory retrieval, and poor problem-solving; an

OF [orbitofrontal] syndrome, with prominent disinhibition and irritability; and a medial frontal-AC [anterior cingulate] syndrome, with apathy and diminished initiative. (p. 13)

In this study, the first two “behavioral symptom complexes,” or neurobehavioral profiles, will be examined (i.e., DLPF and OF). As will be discussed in the next chapter, individuals with a putative OF profile would be expected to report a greater degree of behavioral disinhibition, sensation-seeking, and antisocial behavior, as well as higher levels of activity, irritability, and obsessive-compulsive behavior, compared to individuals with a putative DLPF profile. Higher ratings of externalizing pathology (e.g., verbal and physical aggression) would be expected among the “OF profile group,” and higher ratings of internalizing pathology (e.g., anxiety, depression) would be expected among the “DLPF profile group.” Individuals exhibiting a DLPF profile would be expected to perform more poorly on neuropsychological tests of attention, verbal fluency, visuoconstructional skills, memory, and executive functions compared to individuals exhibiting an OF profile.

Thus, the primary purpose of this study is to determine whether differences between these two circuit-specific behavioral syndromes can be discerned utilizing the PAI and neuropsychological tests. It is essential to discriminate between such disparate functional syndromes, because the choice of interventions and rehabilitation treatments will be predicated on the symptoms associated with the diagnostic profile. As Stuss and Levine (2002) have noted, “Truly understanding the individual cognitive and affective processes of the brain, and their disturbance in damage of various types and lesion locations, is a sine qua non for diagnosis and rehabilitation” (p. 406).

In the next chapter, diagnostic considerations relevant to an archival sample are discussed first, beginning with dyslexia, continuing to attention-deficit/hyperactivity disorder and cognitive disorder not otherwise specified, and concluding with “dyslexia-plus.” Second, the theory of frontal-subcortical circuits, specifically as they pertain to their functional presentations in clinical populations, is reviewed, focusing first on the DLPF profile, then on the OF profile. The foundation for discriminating between these profiles will be elaborated, using four clinical “indicators” which are expected to effectively distinguish individuals who exhibit an OF profile from those who display a DLPF profile: manic behavior, antisocial features, aggression, and obsessive-compulsive behavior. On the basis of the literature review, these indicators have been selected as the starting points for partitioning of the sample using cluster analysis.

The method of cluster analysis was developed to identify homogeneous groups within a population by maximizing between-groups differences and minimizing within-groups differences (Aldenderfer & Blashfield, 1984). The three major purposes of cluster analysis are exploration (“to explore a data set to produce a summary of its structure”), confirmation (“if prior knowledge or theory suggests a particular psychological classification, clustering might be used to test this classification”), and simplification (“cluster analysis might be fruitful in identifying patterns of problems that certain subgroups of clients might be experiencing”) (Borgen & Barnett, 1987, p. 461). Therefore, the primary goals of this study are: (1) to explore an archival data set from a group of college students presenting with attention and learning problems; (2) to seek confirmation of the theoretical

classification discriminating between putative OF and DLPF neurobehavioral profiles; and (3) to simplify the data in order to identify patterns of problems specific to these classifications.

The principal rationale for this study is to suggest a possible means for the classification of clients who present with a behavioral pattern similar to that which has been reported clinically in individuals with damage to the orbitofrontal cortex, which heretofore has been determined primarily through behavioral observations and history-gathering. There are relatively few instruments currently available to assist the clinician in the diagnosis of this particular type of neurobehavioral syndrome. This study is an attempt to use a well-validated instrument (the Personality Assessment Inventory) to assist in the diagnosis and classification of individuals who may belong to this clinical subgroup.

The specific aims of this study are (1) to explore whether “circuit-specific behavioral syndromes” (Lichter & Cummings, 2001, p. 13) can be discriminated from one another using an objective personality test (the Personality Assessment Inventory), utilizing an exploratory data reduction strategy (i.e., cluster analysis); and (2) to seek external validation of the hypothesized two-group cluster solution using the available neuropsychological measures that were administered to an archival sample. None of the participants in the archival sample (described in Chapter 3) had received structural or functional neuroimaging identifying brain damage or dysfunction that could be localized to any specific brain region. The use of the terms “DLPF profile group” and “OF profile group” throughout is intended only to identify individuals based on their clinical presentations, and does not imply damage to any

specific regions of the brain. Bearing this caveat in mind, the specific hypotheses of this exploratory study are:

- 1) One cluster of participants (“OF profile group”) will obtain significantly higher scores on two PAI clinical scales (Antisocial Behavior and Mania), one PAI treatment scale (Aggression), and one PAI clinical subscale (Obsessive-compulsive Features) compared to a second cluster of participants (“DLPF profile group”).
- 2) The DLPF profile group will obtain lower scores on computerized measures of reaction time, indicating poorer performance (i.e., slower reaction times) than the OF profile group.
- 3) The DLPF profile group will obtain higher scores on computerized measures of vigilance and sustained attention (Vigil omission and commission errors), indicating poorer performance than the OF profile group.
- 4) The DLPF profile group will obtain lower scores on measures of auditory attention (Digit Span-Forward) and working memory (Digit Span-Backward), indicating poorer performance than the OF profile group.
- 5) The DLPF profile group will obtain lower scores on measures of visual attention (Spatial Span-Forward) and working memory (Spatial Span-Backward), indicating poorer performance than the OF profile group.
- 6) The DLPF profile group will obtain lower scores on measures of verbal fluency (phonemic and semantic), indicating poorer performance than the OF profile group.

- 7) The DLPF profile group will obtain lower scores on measures of visual attention, sequencing, and divided attention (Trail Making Test, Parts A and B), indicating poorer performance than the OF profile group.
- 8) The DLPF profile group will obtain lower scores on measures of rapid naming and inhibition of competing responses (Stroop Test), indicating poorer performance than the OF profile group.
- 9) The DLPF profile group will obtain lower scores on a measure of visuoconstructional ability (Rey Osterrieth Complex Figure Test), indicating poorer performance than the OF profile group.
- 10) The DLPF profile group will obtain lower scores on measures of visual memory (Rey Osterrieth Complex Figure test, immediate and delayed recall conditions), indicating poorer performance than the OF profile group.
- 11) The OF profile group will obtain lower scores on the PAI Anxiety and Depression clinical scales than the DLPF profile group.
- 12) The OF profile group will obtain comparable scores to the DLPF profile group on all other clinical, treatment, and interpersonal scales of the Personality Assessment Inventory.

## Chapter 2

### Literature Review

The literature review will address diagnostic considerations relevant to an archival sample first, in order to describe the participants in a heterogeneous, clinic-referred group. Second, the theory of frontal-subcortical circuits will be outlined, including a review of the theoretical and empirical foundation for discriminating between OF and DLPF circuit-specific behavioral syndromes. Third, the Personality Assessment Inventory (PAI) will be contrasted with the Minnesota Multiphasic Personality Inventory, Second Edition (MMPI-2) in order to provide necessary background information on the instrument used to partition the archival data set.

#### *Diagnostic considerations*

The majority of individuals from the archival sample presented for a neuropsychological assessment due to the difficulties they were experiencing in the post-secondary academic setting. These students did not have adequate documentation of a learning disability or ADHD that would have enabled them to procure academic accommodations to address their reported deficits. In order to evaluate their neuropsychological functioning, a comprehensive test battery was administered, including (in the majority of cases) the PAI. On the basis of the evaluation, the clinical diagnoses in this heterogeneous sample included learning disabilities, ADHD, and cognitive disorder NOS, as well as various, comorbid Axis I disorders (e.g., anxiety and depressive disorders). A brief discussion of the principal neurocognitive disorders provides necessary background information for the consequent description of the archival clinical sample.

### *Dyslexia*

According to the American Psychological Association's official *APA Dictionary of Psychology*, dyslexia is “a neurologically based learning disability manifested as severe difficulties in reading, spelling, and writing words and sometimes in arithmetic” (2007, p. 307). Therefore, dyslexia, broadly defined, encompasses not only specific reading disability, but also difficulties in writing and mathematics (cf. Miles & Miles, 1992). From an epidemiological standpoint, Brown et al. (2001) stated, “Dyslexia affects 5 to 10% of school-aged children and can persist into adulthood” (p. 781).

Shaywitz and Shaywitz (2005) concluded from the “overwhelming evidence” that has accrued over the past two decades:

Dyslexia represents a disorder within the language system and more specifically within a particular subcomponent of that system, phonological processing. Recent advances in imaging technology and the development of tasks which sharply isolate the subcomponent processes of reading now provide for the first time, a neurobiological signature for dyslexia: a disruption of left hemisphere posterior brain systems in dyslexic readers while performing reading tasks. (p. 1307)

This core deficit in phonological processing may have a widespread effect on multiple areas of learning, including reading, writing, and mathematics. Other theories that attempt to explain dyslexia include the double-deficit hypothesis (reviewed in Vukovic & Siegel, 2006) and the cerebellar deficit hypothesis (e.g., Kibby & Hynd, 2008). Whichever the preferred theoretical explanation, a neurobiological basis for dyslexia, or specific reading disability, is presumed to underlie the individual's learning disorder. Probable neural substrates of dyslexia include the left occipito-temporal region (Shaywitz & Shaywitz, 2005) and the

primary visual cortex (Demb, Boynton, & Heeger, 1997). Brown et al. (2001) found widespread gray matter deficits in a small group of men with dyslexia compared to matched controls, not only in the left temporal lobe, but also in the cerebellum and caudate nucleus.

A Reading Disorder (RD) is diagnosed when “reading achievement, as measured by individually administered standardized tests of reading accuracy or comprehension, is substantially below that expected given the person’s chronological age, measured intelligence, and age-appropriate education,” and this “significantly interferes with academic achievement or activities of daily living that require reading skills” (American Psychiatric Association, [APA], 2000, p. 53). From the practitioner’s standpoint, the diagnosis of Reading Disorder (RD) corresponds most closely to the construct of dyslexia, though diagnoses of Mathematics Disorder (MD), Disorder of Written Expression (WD), and Learning Disorder NOS (not otherwise specified) also may apply: “Reading Disorder, alone or in combination with [MD] or [WD], account for approximately four of every five cases of Learning Disorder” (APA, p. 52).

Shaywitz and Shaywitz (2005) argue that “dyslexia fits a dimensional model” and “is a persistent, chronic condition,” as distinct from a “developmental lag” (p. 1301); in other words, reading ability and reading achievement are distributed normally, and individuals with dyslexia fall at the tail of a Gaussian distribution. Although reading skills may improve with remediation, a performance gap between the reading-impaired individual and the normal reader persists. Dyslexia is familial and heritable and often is preceded by specific language impairment (SLI), or

deficient oral language skills (Bishop & Snowling, 2004). Dyslexia is frequently accompanied by significant comorbidity in children, including internalizing and externalizing psychopathology, with regression models showing higher rates of disruptive behavior disorders in children with comorbid RD and ADHD (Willcutt & Pennington, 2000).

Adults who have successfully compensated for dyslexia (e.g., college students) may have transferred neurobiological responsibility for reading processes to alternate regions of the brain, principally in the right hemisphere:

The right hemisphere sites may represent the engagement of brain regions that allow the poor reader to use other perceptual processes to compensate for his or her poor phonologic skills. A number of studies of young adults with childhood histories of dyslexia indicate that although they may develop some accuracy in reading words, they remain slow, nonautomatic readers.... In dyslexic readers disruption of parieto-temporal and, in particular, occipito-temporal left hemisphere posterior reading systems underlies the failure of skilled reading to develop, while a shift to ancillary systems in left and right anterior regions and right posterior regions supports accurate, but not automatic, word reading. (Shaywitz & Shaywitz, 2005, p. 1307)

The nonautomaticity in reading single words naturally results in slower reading speed. Although decreased rate is not specifically diagnostic of Reading Disorder as defined in the DSM-IV-TR criteria set (APA, 2000), decreased reading accuracy likely covaries to a degree with speed. The compensated reader with dyslexia may draw on ancillary language processing systems that enable the decoding and comprehension of written texts (precipitated by left occipito-temporal dysfunction), but the process may lack fluency and automaticity, thereby reducing reading rate.

For descriptive purposes, the broad definition of dyslexia (American Psychological Association, 2007) was accepted in this study; in the archival sample,

clinical diagnoses of Reading Disorder, Mathematics Disorder, Disorder of Written Expression, and Learning Disorder NOS were subsumed under the category “dyslexia,” or learning disability (LD). College students, by definition, have compensated for their LD, but the increase in demand for fluent reading in post-secondary education poses an obstacle to their potential achievement.

*Attention deficit/Hyperactivity Disorder in adults*

Attention-deficit/hyperactivity disorder is a neurodevelopmental disability that persists into adulthood in between 8-66% of all childhood cases (Zametkin & Ernst, 1999), with an estimated prevalence of adult ADHD in approximately 3-5% of the population (Biederman, 2005; Kessler et al., 2006). Only in the last decade has ADHD “been largely reconceptualized as a lifespan disorder and not merely a condition of childhood” (McGough & Barkley, 2004, p. 1948), though adult ADHD as a distinct variant of the childhood disorder has been studied for more than a quarter century (Wender, 2000). For example, in a landmark paper on decreased glucose metabolism in adults with “histories of hyperactivity in childhood who continued to have symptoms” (Zametkin et al., 1990, p. 1361), large metabolic reductions were found in the premotor cortex and superior prefrontal cortex of adults with “residual” ADHD, as well as “reductions in glucose metabolism in left parietal, temporal, and rolandic..., in addition to subcortical structures...” (Zametkin et al., p. 1366).

While efforts to describe neuropsychological performance and discriminate between different subtypes of adult ADHD were undertaken in the late nineties (e.g., Downey, Stelson, Pomerleau, & Giordani, 1997; Gansler, et al., 1998), Barkley promulgated the theory that ADHD arises out of a core deficit in behavioral inhibition

(1997a, 1997b). Barkley spearheaded the International Consensus Statement on ADHD, which states that “psychological deficits in inhibition and attention have been found in numerous studies of identical and fraternal twins... to be primarily inherited” and argues on behalf of an 86-member consortium of international scientists that ADHD is “a valid disorder having varied and substantial adverse impact on those who may suffer from it through no fault of their own or their parents and teachers” (Barkley et al., 2002, pp. 90-91):

For those it afflicts, ADHD can cause devastating problems. Follow-up studies of clinical samples suggest that sufferers are far more likely than normal people to drop out of school (32-40%), to rarely complete college (5-10%), to have few or no friends (50-70%), to underperform at work (70-80%), to engage in antisocial activities (40-50%), and to use tobacco or illicit drugs more than normal. Moreover, children growing up with ADHD are more likely to experience teen pregnancy (40%) and sexually transmitted diseases (16%), to speed excessively and have multiple car accidents, to experience depression (20-30%) and personality disorders (18-25%) as adults, and in hundreds of other ways mismanage and endanger their lives. (Barkley et al., p. 90)

Thus, the International Consensus Statement explicitly states that ADHD is a heritable disorder with multiple negative outcomes, beginning in childhood and often persisting into adulthood. Although Barkley’s theory of behavioral inhibition has been criticized as overly reductive (e.g., Voeller, 2001), deficits in attention and inhibition at the least play a major role in the disorder.

Biederman (2005) offered a current definition of ADHD and summarized the state of the science:

[ADHD] is an early-onset, highly prevalent neurobehavioral disorder, with genetic, environmental, and biologic etiologies that persist into adolescence and adulthood in a sizeable majority of afflicted children of both genders. It is characterized by behavioral symptoms of inattention, hyperactivity, and impulsivity across the life cycle. Comorbidity is a distinct clinical feature of both childhood and adult

ADHD. Although its etiology remains unclear, emerging evidence documents its strong neurobiologic and genetic underpinnings. A pathophysiologic profile of ADHD has not been fully characterized, although structural and functional imaging studies consistently implicate dysfunction in the fronto-subcortical pathways and imbalances in the dopaminergic and noradrenergic systems in the core symptoms. (p. 1218)

Common comorbidities of ADHD include RD and other learning disorders, oppositional defiant disorder, conduct disorder, intermittent explosive disorder, anxiety disorders, and mood disorders (Biederman, 2005; Kessler et al., 2006), as well as substance use disorders (Wilens, Biederman, Spencer, & Frances, 1994; Wilens, 2006). Comorbidity is, then, a cardinal feature of ADHD and learning disorders, which further complicates differential diagnosis in the neuropsychological assessment of college students who present with complaints of inattention, distractibility, and disorganization.

Thus, ADHD is a *neurobehavioral developmental lifespan disorder* with significant diagnostic comorbidity that may result in multiple negative outcomes in adulthood, including difficulty finishing college, underperformance in the workplace, and self-endangering, stimulus-seeking behaviors (e.g., drug abuse, speeding). The prevalence of ADHD in childhood has been shown to vary significantly by age, gender, race, and ethnicity (Cuffe, Moore, & McKeown, 2005), and the same variability associated with demographic characteristics also has been demonstrated in adults (Kessler et al., 2006; McGough et al., 2005).

Despite the fact that assessment of multiple neurocognitive domains, including executive functioning, processing speed, and short- and long-term memory,

is recommended by AHEAD (1997) in the documentation of learning disabilities in adolescents and adults, it has been argued that

There are insufficient data to support the use of laboratory-based measures in the diagnosis of ADHD. ADHD remains a clinical diagnosis that is best determined through careful history taking, adherence to well-described clinical criteria, and training in the differential diagnosis of adult disorders. (McGough & Barkley, 2004, p. 1953)

However, Nigg (2005) recently provided a meta-analytic summary of neuropsychological studies of ADHD versus non-ADHD children, showing moderate-to-large effect sizes across studies on tasks involving spatial working memory, arousal, set-shifting, and response inhibition, pointing to the utility of neuropsychological tests for discriminating between groups. Neurocognitive research on adult ADHD has accumulated at a rapid clip since the millennium, with publication of two meta-analyses of neuropsychological test performances of individuals with ADHD (Frazier, Demaree, & Youngstrom, 2004; Hervey, Epstein, & Curry, 2004). Neuropsychological deficits on tasks of attention, behavioral inhibition, and memory were identified (i.e., moderate-to-large mean weighted effect sizes), although simple reaction time was normal (Hervey et al., 2004). Adults with ADHD showed moderate-to-strong decreases in intelligence, sustained attention, and academic achievement compared to normal controls (Frazier et al., 2004). In light of the meta-analytic evidence, the clinical utility of “laboratory-based” neuropsychological measures to identify learning disabilities and discriminate between adults with or without ADHD appears to be settled.

The DSM-IV-TR criteria set for ADHD includes symptoms of inattention, hyperactivity, impulsivity, and distractibility—all of which may be associated with

many psychiatric disorders, including posttraumatic stress disorder, other anxiety disorders, bipolar disorder, schizophrenia, depressive disorders, and dissociative disorders. Denckla (1993) noted, “Absence of childhood history convincingly characteristic of ADHD, the adult patient presents a difficult differential diagnosis, both because of the frequency with which a variety of psychiatric disorders are associated with impaired attention and because of the genuine comorbidity of ADHD with affective disorders, alcoholism, and conduct disorders” (p. 113). Moreover, there are numerous physiological conditions associated with inattention and disinhibition—behavioral *phenocopies*: “The list of phenocopies is very long and includes subclinical epilepsy; traumatic brain injury; a history of CNS infection; and basal ganglia disorders such as lupus erythematosus and Sydenham’s chorea” (Voeller, 2001, p. 357, see also Conners, 2006, Appendix B).

The differential diagnosis of adult ADHD is, then, a complicated task which requires adherence to interdisciplinary diagnostic standards (e.g., APA, 2000) and the recognition that diagnostic comorbidity is common (Kessler et al., 2006; McGough et al., 2005; Wilens, 2006). If there is a clear history of head injury, then the diagnosis of ADHD may be ruled out, depending on the temporal relationship between the trauma and the observed symptoms. Denckla (1993) observed that “head injury (very common as a complication of ADHD) is often the source of *frontal lobe* deficits” (p. 113). On the one hand, a diagnosis of ADHD may predispose an individual to engage in sensation-seeking behaviors that may result in head injury, while on the other hand, a head injury may precede onset of a behavioral syndrome similar to ADHD. If a medical condition is determined to be the cause of presenting symptoms of inattention

and impulsivity, the accurate diagnosis is instead cognitive disorder not otherwise specified.

*Cognitive Disorder NOS*

Cognitive Disorder NOS (CD-NOS) is a residual diagnostic category in the DSM-IV-TR, indicated when “cognitive dysfunction [is] presumed to be due to the direct physiological effect of a general medical condition” (APA, 2000, p. 179). Examples of CD-NOS include mild neurocognitive disorder (“impairment in cognitive functioning as evidenced by neuropsychological testing or quantified clinical assessment, accompanied by objective evidence of a systemic general medical condition or central nervous system dysfunction” [APA, p. 160]) and postconcussional disorder (“following a head trauma, impairment in memory or attention with associated symptoms” [APA, p. 160]). The proposed criteria sets for mild neurocognitive disorder and postconcussional disorder are published in Appendix B of the DSM-IV-TR. A mild neurocognitive disorder by definition states that a “systemic general medical condition or central nervous system dysfunction” is presumed to be the underlying basis for the cognitive disorder. According to the DSM-IV-TR research criteria:

Individuals with this condition have a new onset of deficits in at least two areas of cognitive functioning. These may include disturbances in memory (learning or recalling new information), executive functioning (e.g., planning, reasoning), attention or speed of information processing (e.g., concentration, rapidity of assimilating or analyzing information), perceptual motor abilities (e.g., integrating visual, tactile, or auditory information with motor activities), or language (e.g., word-finding difficulties, reduced fluency). The report of cognitive impairment must be corroborated by the results of neuropsychological testing or bedside standardized cognitive assessment techniques. (APA, p. 762).

Research criteria for postconcussional disorder include “a history of head trauma that has caused significant cerebral concussion,” together with “evidence from neuropsychological testing or quantified assessment of difficulty in attention (concentrating, shifting focus of attention, performing simultaneous cognitive tasks) or memory (learning or recalling information)” (APA, p. 761). Postconcussional disorder is characterized by fatigue, disordered sleep, and emotional-behavioral symptoms, including “irritability or aggression on little or no provocation” and “anxiety, depression, or affective lability” (APA, p. 761). Though mild neurocognitive disorder and postconcussional disorder are both subsumed under the diagnosis of CD-NOS, “postconcussional disorder can be differentiated from mild neurocognitive disorder by the specific pattern of cognitive, somatic, and behavioral symptoms and the presence of a specific etiology (i.e., closed head injury)” (APA, p. 761). The research criteria for each diagnosis require evidence on neuropsychological testing to substantiate the verisimilitude of the disorder.

In the archival sample to be examined in this study, CD-NOS was diagnosed when a verifiable medical condition or history of cerebral concussion was determined to be the most probable basis for problems with attention and executive functioning. When no clear medical condition could be established in cases of observed deficits on neuropsychological tests, and when emotional-behavioral factors were ruled out, a diagnosis of attention-deficit/hyperactivity disorder not otherwise specified (ADHD-NOS) was assigned. ADHD-NOS is a residual category in which individuals exhibit subthreshold symptomatology or do not meet DSM-IV-TR criteria for having symptoms prior to age 7. In this study, participants with a diagnosis of either ADHD

(irrespective of subtype) or CD-NOS were classified under a single category “neurobehavioral disorder” (NBD). Irrespective of the specific diagnosis, a behavioral pattern of inattention, disinhibition, and executive dysfunction was identified on neuropsychological assessment.

### *Dyslexia-Plus*

Denckla (1993) introduced the term “dyslexia-plus” to account for cases in which individuals diagnosed with dyslexia also showed signs of impaired attention: “Along the dimension implied by *dyslexia-plus*, i.e., that of *attentional impairment*, even if subjects are not overtly over the border into the category *ADHD*, electrophysiologic studies of adults implicate anterior brain regions classically associated with, not only attention, but also with much effortful processing” (p. 114). Therefore, the extent of attentional impairment involved in dyslexia-plus frequently may fall under the subthreshold, residual category (ADHD-NOS). Denckla further stated, “Executive dysfunction is the zone of overlap between ADHD and LD,” defining the construct bridging the two disorders as

A neuropsychologic weakness, hypothesized to originate from dysfunction of the frontal lobes or its interconnected regions, which results in impairments in a variety of abilities that can have both academic and interpersonal consequences. These problems involve the cognitive competencies of selective and sustained attention, inhibition of verbal and nonverbal responses, strategic memorization, organization, self-monitoring, planning and sequencing of complex behaviors and management of time and space. (p. 115)

A briefer definition states that “executive functioning globally refers to an individual’s ability to engage in goal-oriented behavior” (Kramer & Quitania, 2007, p. 280). In the present study, executive functions, or cognitive competencies, were assessed using well-known, valid, and reliable neuropsychological measures

(described in Chapter 3). For descriptive purposes, participants who were diagnosed with both LD and NBD were classified as dyslexia-plus (LD+), to discriminate them from the more “pure” LD and NBD classifications. In addition to these neurocognitive disorders, some individuals in the sample were diagnosed with comorbid Axis I disorders, and in a few cases, with principal Axis I disorders (when there was insufficient evidence for an LD or NBD, but with significant impairment in daily functioning).

#### *Frontal-subcortical circuits*

The theory of frontal-subcortical circuits in cognitive neuroscience is complex and continues to be developed and refined; a comprehensive review of the theory is beyond the scope of this study, but a selective overview is necessary in order to understand the basic structural and functional differences between dorsolateral-prefrontal and orbitofrontal neurobehavioral profiles. More comprehensive reviews of the theory are provided by Lichter and Cummings (2001) and Chow and Cummings (2007).

As noted previously, frontal-subcortical circuits (FSCs) share similar neuroanatomical structures and neurochemical messengers, but “no single neurotransmitter has one simple role in activating or inhibiting a given circuit” (Chow & Cummings, 2007, p. 27). The *activation* of a given FSC occurs through direct pathways between the prefrontal cortex and the thalamus, while the *inhibition* of an FSC occurs through indirect pathways:

The manifestations of direct or indirect pathway dominance allow a wide repertoire of adaptive responses to shifting internal priorities or external environmental stimuli. The manifestation of a particular

neuropsychiatric symptom can reflect a loss of the balancing mechanism within one or more FSCs. (Chow & Cummings, p. 25).

Although FSCs are arranged in parallel and are segregated from one another, they do share a degree of connectivity; each FSC has connections within its own direct and indirect pathways, corticocortical connections with other FSCs, and open connections to regions outside of the FSCs (Chow & Cummings, 2007). In essence, a balance between activation and inhibition of each circuit is necessary to integrated and healthy brain functioning; when there is a disruption within a particular FSC, neurocognitive and neurobehavioral symptoms may be exhibited:

The manifestation of a particular neuropsychiatric symptom reflects an imbalance of the direct and indirect pathways within a frontal-subcortical circuit. Events that can destabilize the normal state of equilibrium between these two pathways include cortical or subcortical structural lesions along the circuit, input from the limbic system or other open connections, and neurotransmitter effects on the striatal striosome matrix. (Chow & Cummings, 2007, p. 38)

From a functional perspective, three of the accepted five FSC's originate within the prefrontal cortex (Lichter & Cummings, 2001); excluding the anterior cingulate/superior medial frontal FSC, the two hypothetical FSCs with which this study shall be concerned are the dorsolateral-prefrontal (DLPF) and the orbitofrontal (OF) circuits. These circuits are functionally dissimilar in that the OF circuit is typically associated with emotional-behavioral processes and the DLPF circuit is typically associated with cognitive processes. As Mesulam (2000) noted, "Deficits of compartment are more frequently associated with lesions of orbitofrontal and adjacent medial frontal cortex whereas deficits of executive function and working memory are more frequently associated with damage to dorsolateral prefrontal cortex" (p. 89). Theoretically, this functional division between the affective profile

(OF) and the cognitive profile (DLPF) should be discriminable in clinical samples by using valid and reliable instruments which measure these domains.

*The dorsolateral-prefrontal cortex*

There is general agreement that the dorsolateral-prefrontal cortex (DLPFC) is comprised of Brodmann areas 9 and 46 (Chow & Cummings, 2007; Kaufer, 2007; MacDonald, Cohen, Stenger, & Carter, 2000; Ramnani & Owen, 2004). Activation of the DLPFC has consistently been implicated in the process of working memory and “higher-order” cognitive control (i.e., executive functioning). Working memory has been defined in various ways by different investigators. Curtis and D’Esposito (2003) state that working memory “refers to the temporary representation of information that was just experienced or just retrieved from long-term memory [and]...these active representations... can be subjected to various operations that manipulate the information in such a way that makes it useful for goal-directed behavior” (p. 415). A similar definition is provided by Courtney, Petit, Haxby, and Ungerleider (1998): “Working memory is the process of maintaining a limited amount of information in an active representation for a brief period of time so that it is available for use” (p. 1819). Therefore, working memory is a critical precursor component in higher-order executive functioning, because it holds information (representations) “on-line” while allowing additional cognitive operations to be performed before arriving at solutions to problems (i.e., goal-directed behavior).

Intact functioning of the DLPFC is necessary for the successful implementation of higher-order executive functions, including verbal fluency, inhibition of competing responses, and attentional control (Stuss & Levine, 2002).

When the functioning of the DLPFC is impaired, deficits in these areas may be shown on neuropsychological measures (e.g., Controlled Oral Word Association Test, Stroop Color-Word Interference Test, Trail Making Test, respectively). Lichter and Cummings (2001) summarized what they termed “the DLPF syndrome,” which is principally characterized by such executive function deficits:

Patients with restricted DLPF cortex lesions have difficulty focusing and sustaining attention, generating hypotheses, and maintaining or shifting sets in response to changing task demands.... Associated features include reduced verbal and design fluency, impairment of memory search strategies and of organizational and constructional strategies on learning and copying tasks, and motor programming disturbances. (p. 15)

Thus, dysfunction within the DLPFC, whether due to neuroanatomical abnormalities, neurotransmitter dysregulation, or cerebral hypoperfusion, may be reflected in a DLPF profile, in which individuals perform poorly on neuropsychological measures relative to the norm (i.e., the average performance of the normative sample to which the individual’s test performance is compared).

Individuals with a DLPF profile also might be expected to demonstrate internalizing behaviors (e.g., depression and anxiety). Galynker et al. (1998) found that “[regional cerebral blood flow] in the left dorsolateral prefrontal cortex and in the left anterior temporal cortex was positively correlated with depressive symptoms,” although their findings were “confounded by the patients’ medication use” (p. 611). Hooley, Gruber, Scott, Hiller, and Yurgelun-Todd (2005) found “decreased activation in DLPFC in response to being challenged by criticism” (p. 811) in a small sample of adults; compared to healthy controls, participants with a history of unipolar depression (i.e., remitted depression) “showed a greater increase in negative mood,

along with a significant failure to activate DLPFC” (p. 811) in response to critical remarks made by their mothers, with the former measured by a self-report instrument and the latter by magnetic resonance imaging. With respect to anxiety, Mathew et al. (2004) found that a measure of “neuronal viability” (i.e., N-acetylaspartate/creatine ratio) “was increased in the right dorsolateral prefrontal cortex in generalized anxiety disorder patients versus healthy comparison subjects” (p. 1120); approximately one-third of their small sample had a comorbid depressive disorder (i.e., dysthymic disorder). Thus, there is some empirical evidence implicating both right and left DLPFC in the expression and regulation of anxiety and depressive symptoms.

#### *The orbitofrontal cortex*

The orbitofrontal cortex (OFC) has been referred to interchangeably as the ventromedial cortex (e.g., Stuss & Levine, 2002). From a broad perspective, “the term ‘orbitofrontal cortex’ is used to designate the entire ventral surface of the frontal lobes” (Mesulam, 2000, p. 50). Although there is less consensus as to the specific neuroanatomical components of the OFC (MacPherson, Phillips, & Sala, 2002), the cytoarchitectonic regions most frequently cited include Brodmann areas 10, 11, 12, 13, 14, and 47 (Kringelbach & Rolls, 2004; Rolls, 2004; Rule, Shimamura, & Knight, 2002). The OFC is phylogenetically older than the DLPFC and has reciprocal connections with the limbic system, particularly the amygdala (Kringelbach & Rolls, 2004). The OFC is highly variable between individuals (Kringelbach & Rolls, 2004) and has recently been implicated in the evaluation of reward and punishment values (Berridge & Kringelbach, 2008; Kringelbach & Rolls, 2004; Rolls, 2000; Rolls, 2004).

From a functional perspective, dysfunction within the OFC most often has been associated with emotional-behavioral symptomatology; Lichten and Cummings (2001) summarized what they termed “the OF syndrome,” characterized by personality and emotional changes:

The OF cortex... is involved in the determination of the appropriate time, place, and strategy for environmentally elicited behavioral responses. Lesions in this area... [result] in behavioral disinhibition and prominent emotional lability.... Decreased impulse inhibition may be associated with improper sexual remarks or gestures and with other antisocial acts.... Patients may appear irritable, and trivial stimuli may result in outbursts of anger.... Inattention, distractibility, and increased motor activity may be seen, and hypomania or mania is not uncommon. (p. 14)

The description of the OF syndrome has its origins in the archetypal case of Phineas Gage (Harlow, 1848/1999; see Barker, 1995 for the historical context), who sustained a penetrating head injury when a 13-pound, three-foot long tamping iron was propelled through his skull, “resulting in severe injury to his left and, in all probability, his right prefrontal cortex” (Neylan, 1999, p. 280). Remarkably, Gage recovered from the injury, but he was no longer the man of “temperate habits” and “considerable energy of character” (Harlow, 1848/1999, p. 281) that he was before the accident. Instead, he had become “fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operation, which are no sooner arranged than they are abandoned in turn for others appearing more feasible” (Harlow, 1868; cited in Neylan, 1999, p. 280). Harlow’s description of Gage post-injury thus indicates the

behavioral disinhibition, emotional lability, irritability, and antisocial behavior characteristic of an OF syndrome. In short, “the change in Gage’s personality would be consistent with damage to the orbitofrontal cortex of the ventral aspect of his frontal lobe, affecting affect and emotion” (O’Driscoll & Leach, 1998, p. 1674). Damasio (1994) emphasized Gage’s poor judgment and decision-making after the injury, while also noting his emergent “collector’s behavior” (“strong attachment to objects and animals, which was new and somewhat out of the ordinary” [p. 9]). In contrast, Gage’s neurocognitive functioning was remarkable for “the apparent intactness of the several instruments of mind—attention, perception, memory, language, [and] intelligence” (Damasio, p. 11). However, there were no neuropsychological instruments available at the time to substantiate this contention.

Damasio (1994) described a contemporary case of an OF syndrome, in which his patient (“Elliot,” a.k.a., EVR) exhibited a profile similar to Gage’s after removal of an orbitofrontal meningioma that had caused bilateral damage to the ventromedial cortex. Contrary to expectation, Elliot performed in the normal range on traditional neuropsychological tests, but his personality and behavior had changed markedly after the surgery. Like Gage, he demonstrated deficient planning, poor judgment, and impaired decision-making, and he developed obsessive-compulsive behavior (hoarding). However, there were fewer indications of disinhibited mood, though Damasio noted that, “on the rare occasions when he [displayed anger], the outburst was swift” (p. 45), similar to the description provided by Lichter and Cummings (2001).

Mesulam (2000) briefly described the case of a 63-year-old woman who, following removal of an olfactory groove meningioma, “started to initiate intimate relations with total strangers, one of whom had just been released from jail” (p. 43). Yet, her performances on neuropsychological measures were all in the normal range. Her post-surgical disinhibition was associated with radiological findings which showed that “the major area of damage involved the orbitofrontal cortex and ... the dorsolateral prefrontal areas were relatively intact” (p. 43). In another case, collecting behavior (accumulation of pornography) and disinhibited sexualized behavior (“acquired pedophilia”) were observed in a 40-year-old man who developed a large right orbitofrontal tumor (Burns & Swerdlow, 2003). Kim and Lee (2002) reported the case of a 66-year-old man who suddenly developed obsessive-compulsive symptoms (checking rituals), secondary to “a single infarct confined to the medial portion of left orbitofrontal cortex” (p. 89); however, “on neuropsychological examination... no impairment was found in memory and executive function or in any other cognitive domains” (p. 89).

These clinical cases represent a degree of severity that would not be expected in a high-functioning population. However, the personality and behavioral characteristics of an OF profile nonetheless might be present in an attenuated form, depending on the degree of neuroanatomical irregularity or neurotransmitter dysregulation. In these milder forms of the syndrome, individuals would be expected to exhibit subthreshold symptoms of mania (e.g., disinhibition, sensation-seeking), antisocial features (e.g., irritability), aggression (e.g., anger, verbal outbursts), and

obsessive-compulsive behavior (e.g., hoarding, checking). All of these symptoms have been associated with orbitofrontal dysfunction in the empirical literature.

*Mania or hypomania*

As Lichter and Cummings (2001) noted, symptoms of mania or hypomania are frequently observed in individuals who display an OF profile. Manic and hypomanic behavior may include motor restlessness and sensation-seeking behaviors, which are associated with diagnoses of ADHD and bipolar disorders (APA, 2000). Berlin, Rolls, and Kischka (2004) noted that OF damage has been associated with socially inappropriate and disinhibited behavior; they found that OFC patients (i.e., individuals with lesions including or restricted to the orbitofrontal cortex) self-reported a greater degree of impulsive behavior and demonstrated more impulsivity on experimental measures than patients with lesions elsewhere in the prefrontal cortex (i.e., DLPFC) or normal controls. Rolls, Hornak, Wade, and McGrath (1994) studied patients with damage to the ventromedial portion of the frontal lobe and found impaired reversal learning relative to patients with damage elsewhere in the brain (nonventral); on a behavior questionnaire, the ventral group reported significantly greater disinhibited or socially inappropriate behavior, misinterpretation of other's moods, and impulsiveness. The investigators concluded that the difficulty shown by the ventral group in reversing stimulus-reinforcement associations was "at least partly responsible for their disinhibited and inappropriate behavior" (p. 1523). Blumberg et al. (1999) examined regional cerebral blood flow (rCBF) in a small group of individuals with bipolar I disorder and found decreased activity in bilateral orbitofrontal cortex when they were at rest, by more than 20 percent compared to

healthy controls. Thus, orbitofrontal dysfunction has been associated with self-reports of disinhibition, impaired reversal learning, and decreased rCBF bilaterally in the empirical literature.

*Antisocial behavior*

ADHD has been conceptualized as a disorder of frontal-subcortical circuitry (Voeller, 2001), and antisocial behavior has consistently been linked with ADHD in empirical studies (Barkley, Murphy, & Fischer, 2008). Voeller (2001) noted that “teenagers with ADHD are at substantially increased risk for antisocial/criminal behaviors and for drug and alcohol abuse, compared to peers who do not have ADHD” (p. 344). Moreover, “higher rates of antisocial behavior and substance use disorders emerge as consistent findings in virtually all studies of comorbidity and adult ADHD” (McGough et al., 2005, p. 1621).

Chow and Cummings (2007), following Middleton and Strick (2001), discriminated further between *lateral* OFC and *medial* OFC frontal-subcortical circuits, which nonetheless share corticocortical connections. On the whole, the two OF circuits are thought to mediate empathic and socially appropriate behavior, though the specific behavioral correlates differ:

The medial and lateral OFC circuits play distinct but complementary roles in affect and social behavior. Both the medial and lateral OFC circuits mediate the individual’s affect, impulse control, and recognition of reinforcing stimuli. Lesions in either OFC can result in emotional incontinence and disinhibition, but individuals with these lesions manifest impairments differently. A patient with an impaired medial OFC shows abnormal autonomic responses to socially meaningful stimuli and has difficulty extinguishing unreinforced behavior. These characteristics correlate with antisocial behavior....

In contrast to patients with a medial OFC circuit dysfunction, a patient with a lateral OFC lesion is more likely to show irritability, mood disorders, utilization behaviors, undue familiarity with strangers,

imitation behavior, and acquired obsessive-compulsive disorder....  
(Chow and Cummings, 2007, p. 31)

In sum, antisocial behavior has been associated with medial OFC dysfunction and a clinical diagnosis of ADHD, as well as comorbid substance use disorders (Dom, Sabbe, Hulstijn, & Van Den Brink, 2005). Perhaps not surprisingly, antisocial behavior also has been linked with aggressive behavior (Blair, 2001, 2004).

### *Aggression*

According to Blair (2001, 2004), aggressive behavior may be distinguished by its reactive and instrumental forms; individuals with orbitofrontal brain pathology (“acquired sociopathy”) are thought to exhibit exclusively reactive aggression (i.e., responding to frustration or threat), whereas individuals with so-called “developmental psychopathy” display primarily instrumental aggression (i.e., purposeful and goal-directed). Aggression may include verbal and physical expressions of behavior, but whether they are purposeful versus reactive may distinguish between a sociopath (i.e., someone with antisocial personality disorder) and a person with orbitofrontal dysfunction. In cases of reactive aggression, behavioral correlates would likely include impulsivity and difficulty inhibiting emotional responses (i.e., emotional incontinence).

Coccaro, McCloskey, Fitzgerald, and Phan (2007) studied a small group of individuals with intermittent explosive disorder (IED), none of whom met criteria for antisocial personality disorder. [IED is an impulse-control disorder whose essential feature is “the occurrence of discrete episodes of failure to resist aggressive impulses that result in serious assaultive acts or destruction of property” (APA, 2000, p. 663); although aggressive acts associated with IED are disproportionate to provocations or

precipitating stressors, the descriptive features associated with the disorder indicate that the aggression is reactive in nature: “Explosive episodes may be associated with affective symptoms (irritability or rage, increased energy, racing thoughts) during the aggressive impulses and acts, and rapid onset of depressed mood and fatigue after the acts” (APA, p. 664).] Compared to healthy controls, individuals with IED showed heightened activation in the amygdala in response to angry faces (but not to other types of facial expression), with concomitant decreased activation in the orbitofrontal cortex, which suggested reduced neuromodulatory activity in response to social threat; in addition, a positive correlation was found between amygdala reactivity to angry faces and the extent of prior aggressive behavior. The investigators averred that “OFC hypofunction may be a common mechanism underlying the pathophysiology of aggressive behavior in general” (Coccaro et al., 2007, p. 174).

The orbitofrontal cortex has been linked to aggressive behavior in healthy individuals, as well. Pietrini, Guazzelli, Basso, Jaffe, and Grafman (2000) analyzed rCBF in a small group of healthy participants using imaginal scripts, in which the subjects were asked to envision four different scenarios involving threat to their mothers. Physiological measures indicated that participants “experienced significantly greater anger, frustration, and anxiety during the aggressive conditions compared to the neutral condition” (p. 1773). Using positron emission tomography (PET), the investigators found “significant rCBF decreases in the medial orbitofrontal cortex compared to the neutral condition” (p. 1774). Moreover, the degree of functional deactivation of the OFC was greatest when participants were instructed to imagine expressing rather than inhibiting their aggressive behavior. The results suggested that

the OFC (and specifically, the medial OFC) plays a modulatory role in determining whether aggressive behavior is inhibited (increased activation) or expressed (decreased activation).

*Obsessive-compulsive behavior*

Obsessive-compulsive behaviors are thought to be associated with both genetic and environmental factors, with four major symptom dimensions identified in a recent, large meta-analysis: “1) forbidden thoughts, 2) obsessions with symmetry and exactness and related ordering and arranging rituals as well as counting and repeating rituals, 3) contamination obsessions and washing compulsions, and 4) hoarding obsessions and compulsions” (Leckman & Bloch, 2008, p. 1230). Like ADHD, obsessive-compulsive disorder (OCD) has been conceptualized as a disorder of frontal-subcortical circuitry, specifically involving the OFC: “Most neuroimaging studies (PET, SPECT, and fMRI) have identified abnormally high orbital paralimbic prefrontal cortex... and head of caudate nucleus... activity in subjects with OCD, compared to various control populations, when studied under ambient conditions” (Baxter, Clark, Iqbal, & Ackermann, 2001, p. 209). Effective treatment with selective serotonin reuptake inhibitors (SSRIs) and behavioral therapies is associated with decreased functional activity in the orbitofrontal cortex, caudate nucleus, and thalamus (Baxter et al., 2001). Whereas antisocial behavior and aggressive behavior have been associated with the medial OFC, “both primary and acquired OCD are highly related to the lateral OFC” (Chow & Cummings, 2007, p. 36).

Together with the primary symptom dimensions of OCD noted above, “obsessive compulsive spectrum disorders include pathological gambling,

kleptomania, risk-seeking behavior, and body dysmorphic disorder” (Chow & Cummings, 2007, p. 36). Gambling behavior, in particular, has been associated with dysfunction within the OFC, as described in studies by Bechara and colleagues using the Iowa Gambling Task (e.g., Bechara, 2003; Bechara, Damasio, & Damasio, 2000; Bechara, Damasio, Tranel, & Damasio, 1997; Bechara, Damasio, Tranel, & Anderson, 1998). Although a review of this work, much of which is oriented toward garnering empirical support for Damasio’s (1994) somatic marker hypothesis, is beyond the scope of this study, the gist of their findings indicates that individuals with OFC dysfunction demonstrate deficits in decision-making that are associated with diminished physiological arousal (i.e., skin conductance responses) to punishment and the persistent use of disadvantageous strategies when trying to maximize earnings on the gambling task (see Naqvi, Shiv, & Bechara, 2006 for a concise review of this literature; see Bechara & Damasio, 2005 for a comprehensive review; cf. Dunn, Dalgleish, & Lawrence, 2006; Maia & McClelland, 2004 for critiques of the Iowa Gambling Task and the somatic marker hypothesis).

Thus, obsessive-compulsive disorder is highly variable in its clinical presentation (Evans, Lewis, & Iobst, 2004; Leckman & Bloch, 2008), and obsessive-compulsive behaviors in general have consistently been associated with overactivation in the lateral OFC, caudate nucleus, and thalamus (Baxter et al., 2001; Evans et al., 2004). Clinical cases involving orbitofrontal damage frequently indicate the onset of obsessive-compulsive behaviors (i.e., acquired OCD), such as hoarding, collecting, and checking (Burns & Swerdlow, 2003; Damasio, 1994; Kim & Lee, 2002). Pathological gambling is a type of obsessive-compulsive spectrum disorder

which may be associated with impaired decision-making secondary to deficient anticipatory responses to stimuli that signal the potential for punishment (Bechara, Damasio, Tranel, & Damasio, 1997; Bechara, Damasio, Tranel, & Anderson, 1998).

*Differentiating between OF and DLPF profiles*

In the preceding sections, four indicators of putative orbitofrontal dysfunction have been explicated: mania (or hypomania), antisocial behavior, aggressive behavior, and obsessive-compulsive behavior. The presence of these personality and behavior correlates would be expected to discriminate individuals with an OF profile from individuals with a DLPF profile, based on a review of the empirical literature. Those with an OF profile presumably would perform normally on measures of executive function, as neurocognitive functioning is frequently intact in cases of ventromedial damage or dysfunction. Those with a DLPF profile would be expected to perform more poorly on neuropsychological measures, because deficient working memory is implicated in cases of dorsolateral-prefrontal damage or dysfunction. However, in relatively high-functioning samples (e.g., college students), impairment in working memory and executive functions may not be readily discerned on traditional neuropsychological tests, due to the influence of variables including intelligence and educational level on test performance; conceivably, this might hold true for all college students, irrespective of whether or not they exhibit a DLPF or OF profile. Conversely, the validity of self-reporting on personality and behavior measures may be enhanced in high-functioning individuals, as suggested by Glutting, Youngstrom, and Watkins (2005): “It is possible that college students might have more insight into their own symptoms than is typical for youths with externalizing

problems, by virtue of either their age or their above-average cognitive ability” (p. 53).

The impetus for the present study was the clinical observation that a subset of college students who presented to the clinic for neuropsychological assessment often performed normally on neurocognitive tests, but their self-reporting on an objective personality test frequently revealed significant elevations in antisocial and manic behavior. Another subset of college students demonstrated mild difficulties on various neurocognitive tests, but their self-reporting on the personality test did not include these elevations in antisocial and manic behavior. These observations appeared to be consistent with the emerging literature in cognitive neuroscience on frontal-subcortical circuits, and specifically the distinction between the DLPF profile and the OF profile. The objective personality test used in the clinic was Morey’s (1991) Personality Assessment Inventory (PAI), which had only been available for a decade at the time data for the first case in the archival sample was collected. The PAI has many advantages over the more popular MMPI-2, the most prominent of which are discussed below.

#### *The PAI versus the MMPI-2*

The PAI has several advantages over the MMPI-2, including its shorter length, lower reading level, gradation of responses, and enhanced discriminant validity (Strauss et al., 2006). With respect to length, the PAI has 344 items and the MMPI-2 has 567 items; consequently, the PAI requires 40-50 minutes to complete, while the MMPI-2 requires 1-2 hours to complete. In fact, Strauss et al. observed, “Within the context of the neuropsychological examination, many clinicians avoid

routine administration of the MMPI-2 because of its length and significant demands on attention and comprehension” (p. 1114). The PAI is less time-intensive and reduces demands on sustained attention—important factors to consider when evaluating individuals with disorders that affect arousal and attention.

Second, the PAI has a lower reading level compared to the MMPI-2; whereas items on the MMPI-2 require an estimated grade 6 reading level, items on the PAI require an estimated grade 4 reading level (Strauss et al., 2006). Although this might not be considered an issue in high-functioning populations, a lower reading level certainly helps to mitigate invalid responding related to misunderstanding of item content; moreover, in the evaluation of individuals whose presenting problems include reading difficulties (or outright learning disabilities), a lower reading level is desirable to ensure comprehension of item content.

Third, the PAI allows for a gradation of responses on a four-point scale (never, slightly true, mainly true, very true), whereas the MMPI-2 only allows dichotomous responses (true, false). Presumably, the gradation of responses reduces the number of omitted items secondary to a forced-choice paradigm in which participants must make a determination whether the experiences and perceptions embodied by the items are either “always” true or false.

Fourth, the PAI is constructed of nonoverlapping scales, so each item contributes to only one scale. In contrast, any single item on the MMPI-2 may contribute to more than one scale. The PAI’s nonoverlapping item content thus enhances discriminant validity, because each construct measured by the instrument is composed of responses exclusive to that construct.

Similar to the MMPI-2, the PAI has several validity scales which allow the clinician to determine whether an individual has produced a valid protocol for interpretation. Recent research has shown that the PAI validity scales perform comparably (or better) than the MMPI-2 validity scales; for example, among veterans, the PAI produced fewer invalid profiles than the MMPI-2 in both in-patients and out-patients (Braxton, Calhoun, Williams, & Boggs, 2007).

Most significantly for the present study, the PAI clinical scales provide for relatively straightforward measurement of the proposed indicators of an orbitofrontal neurobehavioral profile. Two of the indicators (mania, antisocial features) are measured by clinical scales (MAN, ANT, respectively), one indicator (obsessive-compulsive behavior) is measured by a subscale within the broader construct of anxiety-related disorders (ARD-OCD), and the remaining indicator (aggression) is measured by one of the treatment scales (AGG). This study predicts that a putative OF profile will be discriminated from a putative DLPF profile using these four variables for partitioning into homogeneous groups of college students, employing hierarchical cluster analysis to establish start values for a *k*-means cluster analysis (Aldenderfer & Blashfield, 1984; Beauchaine & Beauchaine, 2002; Borgen & Barnett, 1987; Hair, Anderson, Tatham, & Black, 1998), with the expectation of a two-group solution.

## Chapter 3

### Method

#### *Participants*

The sample was drawn from an archival database of 31 neuropsychology referrals in which the doctoral candidate directly administered and scored the personality, intelligence, neuropsychological, and academic achievement measures. The participants were non-consecutive referrals to either a university disability resource center or a private out-patient clinic. These individuals were assessed within a three-year period between 2001-2004, under the supervision of two board-certified neuropsychologists who contributed to the case formulations and verified the clinical diagnoses. A majority of the cases were post-secondary students (80.6%), comprised of undergraduates ( $n = 17$ ), graduate students ( $n = 5$ ), and continuing education students ( $n = 3$ ). Students either were referred from a person or department within the university, or self-referred, because of their difficulty meeting the academic demands of post-secondary education. The remaining cases were composed of adults referred by their employer and/or a state-funded agency due to vocational problems, secondary to attention and organizational difficulties ( $n = 6$ ). Participants provided verbal and/or written consent to use their non-identifying (anonymous) test data in group research. The research was approved by Northeastern University's Institutional Review Board.

To be considered for inclusion in the final sample, the following criteria had to be met. First, because test results on the Personality Assessment Inventory (PAI) were to be used in selecting the indicator variables for performing the proposed

cluster analyses, cases in which the PAI was not administered were excluded from the study ( $n = 2$ ). Second, only those cases in which a valid, interpretable PAI was obtained were included; the four PAI validity scales and the criteria for invalidation are described in a subsequent section. Invalid PAI profiles comprised 6.9 percent of the 29 protocols ( $n = 2$ ). Third, because the focus of the study was on post-secondary students, enrollment in college-level coursework (undergraduate, post-secondary, or continuing education) at the time of the request for a neuropsychological assessment was required for inclusion; of the cases remaining after invalid PAI exclusions, 11.5 percent ( $n = 3$ ) were excluded due to this criterion. Fourth, minimum full-scale intelligence and verbal intelligence quotients of 85 were required; one participant was excluded due to this criterion. Upon examination of the demographic data following exclusions, one additional case was excluded because the age of the participant deviated markedly from the age range of the rest of the sample. After all exclusions, the sample included 22 cases; demographic data and clinical characteristics are described below.

With respect to demographics, participants ranged in age from 18-28 years old ( $M = 21.95$ ,  $SD = 3.11$ ). The sample was predominantly Caucasian (77.3%), with the remaining participants either African-American (13.6%) or Hispanic (9.1%). Women comprised 54.5% percent of the sample. Handedness was coded as a dichotomous variable, according to self-report; participants who reported ambidexterity were classified based on their preferred writing hand. The majority of participants were right-handed (77.3%). Data for birth weight was available for 18 participants, provided by verbal report in pounds and ounces; these estimates were converted to

standard measurement units, with imputation of the mean for the remaining 4 cases ( $M = 2885.71$  grams,  $SD = 604.38$  grams). Demographic data for education, intelligence, and academic achievement are provided in Table 1.

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Table 1

*Education, intelligence, and academic achievement demographic data for the archival sample ( $N = 22$ )*

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	Mean	Median	<i>SD</i>	Range
Education (years)	14.36	14.00	2.08	12–19
Full Scale IQ	110.78	109.50	8.98	92–129
Verbal IQ	108.05	108.00	7.59	91–121
Performance IQ	110.29	109.64	9.66	94–129
Vocabulary	53.57	52.29	7.44	41–67
Similarities	56.43	57.00	4.45	48–65
Block Design	56.09	55.50	8.14	43–69
Matrix Reasoning	58.09	57.00	6.33	41–67
WRAT-3 Reading	51.00	52.00	5.49	33–59
WRAT-3 Spelling	51.27	52.50	8.92	33–65
WRAT-3 Arithmetic	51.59	52.50	8.40	38–69
NDRT Reading Speed	37.36	34.00	8.92	27–61
NDRT Reading Comp.	43.91	44.50	9.21	27–73

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*Note.* Intelligence data were obtained using the Wechsler Abbreviated Scale of Intelligence for the majority of cases ( $n = 18$ ) (see Instruments section for additional details). IQ scores are reported as standard scores ( $M = 100$ ,  $SD = 15$ ). All other scores are reported as T-scores ( $M = 50$ ,  $SD = 10$ ). IQ = Intelligence quotient. WRAT-3 = Wide Range Achievement Test, Third Edition. NDRT = Nelson-Denny Reading Test, Form G. Comp. = Comprehension.

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Table 2

*Clinical characteristics of the archival sample (N = 22)*

	LD	LD+	NBD	Axis I
<i>n</i>	2	11	6	3
%	9.1	50	27.3	13.6

In terms of clinical characteristics, the heterogeneous sample included cases in which the principal diagnosis was learning disorder (LD), neurobehavioral disorder (NBD), or dyslexia-plus (LD+), as described in Chapter 2 (see Table 2). Among the 19 cases assigned to one of these three categories, a comorbid, Axis I psychiatric disorder was diagnosed in 15.8 percent of the cases ( $n = 3$ ). For the remaining 3 cases, a principal, Axis I psychiatric diagnosis was rendered. Of the six participants assigned an Axis I psychiatric diagnosis, the diagnoses were either Depressive Disorder NOS ( $n = 3, 50\%$ ) or Anxiety Disorder NOS ( $n = 3, 50\%$ ).

Table 3

*Breakdown of 18 learning disorder diagnoses in subset of archival sample (n = 13)*

	RD	WD	MD	LD-NOS
<i>n</i>	10	5	2	1
%	55.5	27.8	11.1	5.6

*Note.* RD = Reading Disorder. WD = Disorder of Written Expression. MD = Mathematics Disorder. LD-NOS = Learning Disorder not otherwise specified.

Table 4

*Breakdown of neurobehavioral disorder diagnoses in subset of archival sample (n = 17)*

	CD-NOS	ADHD-NOS	ADHD-I	ADHD-C
<i>n</i>	10	4	2	1
<i>%</i>	58.8	23.5	11.8	5.9

*Note.* CD-NOS = Cognitive Disorder not otherwise specified. ADHD-NOS = Attention-deficit/Hyperactivity Disorder not otherwise specified. ADHD-I = Attention-deficit/Hyperactivity Disorder, Predominantly Inattentive Type. ADHD-C = Attention-deficit/Hyperactivity Disorder, Combined Type.

Among the LD diagnoses, five of 13 participants were diagnosed with two learning disorders. The breakdown of the 18 LD diagnoses are shown in Table 3. The breakdown of the 17 NBD diagnoses are shown in Table 4. Approximately one-third of the sample ( $n = 5$ , 31.8%) reported having sustained at least one concussion at some point in their lives; a history of (self-reported) concussion was coded dichotomously (concussed, not concussed).

### *Setting*

Among the 22 cases in the final sample, 77.3 percent were assessed in the disability resource center of an urban university in the greater Boston area. The remaining 5 cases were assessed at a private, out-patient practice in the greater Boston area. Participants were typically evaluated within two or three sessions, with the PAI administered in a single session at the beginning of the evaluation process. Paper-and-pencil tests were administered in a quiet room with minimal distractions.

Computerized testing (a continuous performance test) was administered in a separate room, also quiet and relatively free from distractions.

### *Instruments*

All participants were administered a standard but flexible neuropsychological protocol, including tests of personality, intelligence, academic achievement, attention, executive functions, learning, and memory. The majority of the measures used in this study are reviewed in at least one of the three major neuropsychology compendiums (Lezak et al., 2004; Mitrushina, Boone, Razani, & D'Elia, 2005; Strauss et al., 2006), to which the reader is referred for more detail.

### *Personality Assessment Inventory*

The Personality Assessment Inventory is a 344-item self-report measure of personality (Morey, 1991). The PAI contains four sets of nonoverlapping scales, including four validity scales, 11 clinical scales, five treatment scales, and two interpersonal scales (see Strauss et al., 2006, p. 1127). The four PAI validity scales are inconsistency (ICN), infrequency (INF), negative impression management (NIM), and positive impression management (PIM). All except two of the clinical scales are subdivided into three or four component subscales of the superordinate construct (e.g., Antisocial scale: Antisocial Behavior, Egocentricity, and Stimulus-seeking subscales); the exceptions are Alcohol Problems (ALC) and Drug Problems (DRG), which are unitary in design. The interpersonal scales assess dominance versus submission (Dominance, DOM) and interest in supportive relationships (Warmth, WRM).

The PAI normative standardization sample consists of 1000 community-dwelling adults selected from an initial sample of 1462 adults living in the United States, with an age range from 18-89. The standardization sample had a mean educational level of 13.7 years, with roughly equal numbers of men (48%) and women (52%). Race and ethnic background of the sample was consistent with 1995 U.S. Census data. According to Morey (1991), there is minimal variability in the internal consistency of the PAI as a function of race, gender, or age. The PAI utilizes linear T-scores ( $T$ ) for all of its scales and subscales ( $M = 50$ ,  $SD = 10$ ), so approximately 84% of the standardization sample yielded T-scores less than 60 (one standard deviation above the mean) and 98% of the sample yielded T-scores less than 70 (two standard deviations above the mean).

*PAI validity scales*

The PAI validity scales include two measures which assess the care with which the test was completed (ICN and INF). The internal consistency of these measures is somewhat low ( $< .60$ ) compared to that of the clinical scales. The ICN scale consists of 10 pairs of highly correlated items which are designed to detect careless or random responding; the INF scale consists of eight items that were infrequently endorsed in both normal and clinical samples, with endorsement indicating careless or idiosyncratic responding (Morey, 1991). In the present study, participants were excluded if their PAI protocols were invalidated due to inconsistent, careless, or random responding (ICN  $T \geq 72$ ; INF  $T \geq 74$ ); these cutoff scores have been employed in recent research using the PAI (e.g., Braxton et al., 2007).

The other two PAI validity scales assess impression management; that is, whether the participants attempted to portray themselves in an overly positive light (PIM) or in an unusually negative light (NIM). The PIM and NIM scales each contain nine items and have adequate internal consistency (.72 and .71, respectively; Morey, 1991). Morey (1991) originally suggested that “faking good” and “faking bad” could be determined using cutoff scores (PIM  $T \geq 57$ , NIM  $T \geq 73$ ), and recent research indicates that these cutoffs are efficient for detecting impression management in a psychiatric sample (Baity, Siefert, Chambers, & Blais, 2007). However, a recent meta-analysis (Hawes & Boccaccini, 2009) indicates that a NIM cutoff score of  $\geq 81$  is optimal for discriminating between honest responding and over-reporting of pathology, so this criterion was used to determine whether a given protocol was invalidated by “faking bad.”

#### *PAI clinical scales*

The PAI has eleven clinical scales which cover major categories of psychopathology: Somatic Concerns (SOM); Anxiety (ANX); Anxiety-Related Disorders (ARD); Depression (DEP); Mania (MAN); Paranoia (PAR); Schizophrenia (SCZ); Borderline Features (BOR); Antisocial Features (ANT); Alcohol Problems (ALC); and Drug Problems (DRG). Internal consistency of the clinical scales is adequate (alpha reliabilities ranging between .74 and .90) and test-retest reliability is moderate-to-high (test-retest reliabilities ranging between .85 and .94); internal consistency of the clinical subscales ranges between .42 and .89 (Morey, 1991). Comparable reliability and internal consistency estimates have been found in samples of psychiatric in-patients (Boone, 1998) and chronic pain patients (Karlin et al.,

2005). As previously described in Chapter 2, two clinical scales (ANT and MAN) and one clinical sub-scale (ARD-OCD) will be used as indicator variables of the putative orbitofrontal profile in a cluster analysis.

The PAI Mania scale consists of 24 items and has good internal consistency (.82) and test-retest reliability (.85). The MAN scale is comprised of three subscales tapping affective, cognitive, and behavioral features of mania and hypomania: Activity Level, Grandiosity, and Irritability. The PAI Antisocial Features scale also consists of 24 items, with good internal consistency (.84) and high test-retest reliability (.90). The ANT scale is comprised of three subscales, related to a history of antisocial acts, lack of empathy, and excitement-seeking: Antisocial Behaviors, Egocentricity, and Stimulus-seeking. The PAI Anxiety-Related Disorders (ARD) scale has 24 items; it has lower internal consistency (.76) than most of the clinical scales, perhaps due to the diversity of symptoms subsumed by the construct, as represented by its three subscales: Obsessive-Compulsive, Phobias, and Traumatic Stress; however, test-retest reliability of the ARD scale is comparable to the other clinical scales (.85).

#### *PAI treatment scales*

The PAI contains five treatment scales, four of which are unitary in design: Suicidal Ideation (SUI), Stress (STR), Nonsupport (NON), and Treatment Rejection (RXR). The remaining treatment scale (Aggression, AGG) will be utilized as one of the four indicators of the putative orbitofrontal profile. Internal consistency of the treatment scales is adequate (ranging between .72 and .85), as are test-retest reliabilities (ranging between .71 and .88). The AGG scale consists of 18 items that

tap characteristics related to anger, hostility, and aggression; internal consistency (.85) and test-retest reliability (.85) are adequate. Like the majority of the clinical scales, the AGG scale is subdivided into three subscales: Aggressive Attitude, Verbal Aggression, and Physical Aggression.

### *Intelligence*

A full-scale intelligence quotient (FSIQ) was derived from all four subtests comprising the Wechsler Abbreviated Scale of Intelligence (WASI) to assess general cognitive ability in the majority of the sample (Psychological Corporation, 1999). In a subset of cases ( $n = 3$ ), the FSIQ was derived from the Wechsler Adult Intelligence Scale—3<sup>rd</sup> edition (WAIS-III) (Psychological Corporation, 1997). Both the WASI FSIQ and the WAIS-III FSIQ have strong test-retest reliability (.92 for the WASI and .95–.97 for the WAIS-III); the FSIQs on the two instruments are highly correlated (.92). In one case, an estimate of general intelligence (WAIS-R FSIQ) was derived from the Shipley Institute of Living Scale—Revised (see Lezak et al., pp. 669-670). Both the WASI and the WAIS-III also provide a verbal intelligence quotient (VIQ) and a performance intelligence quotient (PIQ). For one case, VIQ and PIQ data were not available, so the mean values for the final sample were imputed. The three IQ scores for both instruments are represented by standard scores ( $M = 100$ ,  $SD = 15$ ). The WASI consists of four subtests, two of which are verbal (Vocabulary and Similarities) and two nonverbal (Block Design and Matrix Reasoning); the WAIS-III contains different versions of the same four subtests. For one case, T-scores on the Vocabulary, Similarities, and Block Design subtests were not available, so the mean values for the final sample were imputed.

Normative data for the WASI and the WAIS-III are provided for 13 age groups in their respective manuals, but there are no other demographic corrections. Whereas the WASI converts raw subtest scores into T-scores, the WAIS-III utilizes scaled scores ( $M = 10$ ,  $SD = 3$ ). In order to maintain a common metric, WAIS-III subtest scores were transformed into T-scores using a standard conversion table (see Strauss et al. [2006], pp. 279-310 for further discussion and additional psychometric properties of these instruments).

#### *Academic achievement*

Two well-known, standardized tests of academic achievement were administered: the Wide Range Achievement Test—3<sup>rd</sup> edition (WRAT-3) and the Nelson-Denny Reading Test (NDRT). The WRAT-3 (Wilkinson, 1993) consists of three subtests assessing orthography (Spelling), single word decoding (Reading), and mathematics skills (Arithmetic). The WRAT-3 manual provides normative data by age groups, though “the normative sample is not well-described, and the lack of information on education is a major omission” (Strauss et al., 2006, p. 389). The WRAT-3 manual provides standard scores for each of the three subtests, which were converted to T-scores. The NDRT (Brown, Fishco, & Hanna, 1993) includes measures of reading rate and comprehension. The measure of reading rate is obtained while the examinee reads the first of seven stories; each story is followed by multiple-choice questions tapping literal and interpretive reading comprehension. The NDRT manual provides normative data by educational level for fall and spring administrations (percentile ranks), which were converted to  $z$ -scores before linear transformation to T-scores.

### *Neuropsychological*

The neuropsychological tests used in evaluating participants in the archival sample are shown in Table 5. A test is designated “neuropsychological” if it has been used clinically or experimentally to evaluate one or more neurocognitive functions, including (but not limited to): arousal/activation; focused, sustained, and divided attention; inhibition; language; and learning and memory. Each neuropsychological test, along with its respective dependent measures and examples of cognitive functions assessed, is listed. Scores on the 20 neuropsychological dependent measures were converted to a standard metric (T-scores,  $M = 50$ ,  $SD = 10$ ), in order to facilitate comparison across tests (Glass & Hopkins, 1996). A maximum  $z$ -score of  $\pm 3$  was applied, to minimize the effect of outliers on distributions (T range = 20-80).

#### *Vigil-W continuous performance test*

Continuous performance tests (CPTs) have for a long time been a staple of neuropsychological assessment and are used “to examine the ability to sustain and focus attention in itself” (Lezak et al., 2004, p. 350). Computerized CPTs typically assess arousal, vigilance, impulsivity, and sustained attention. The Vigil-W CPT (Cegalis & Bowlin, 1991) employs the classic paradigm in which letters are presented on a computer screen one at a time, and the participant must respond (by pressing a spacebar) whenever a specified target (the letter K) appears. In the second part of the task (“priming”), the participant must again respond to the specified letter, but only when it is preceded by a different, cue letter (A). Each trial (K and AK) is eight minutes in duration with an interstimulus interval of 900 milliseconds. This task was administered on an IBM-compatible computer, using the standardized instructions

Table 5

*Neuropsychological measures used for external validation of cluster solution*

Neuropsychological Instrument With Indented Dependent Measures	Example of Neurocognitive Abilities Measured
Vigil-W Continuous Performance Test	Arousal, attention, impulsivity
Reaction Time-K	Processing speed
Reaction Time-AK	Processing speed
Omissions-K	Activation/attention
Omissions-AK	Activation/attention
Commissions-K	Attention/impulsivity
Commissions-AK	Attention/impulsivity
Digit Span—Forward	Immediate auditory attention
Digit Span—Backward	Auditory attention/working memory
Spatial Span—Forward	Immediate visual attention
Spatial Span—Backward	Visual attention/working memory
Controlled Oral Word Association Test	Verbal fluency and generativity
CFL or FAS	Phonemic word fluency
Animals	Semantic word fluency
Trail Making Test—Part A	Visual attention/tracking/sequencing
Trail Making Test—Part B	Divided attention/cognitive flexibility
Stroop Color-Word Interference Test	Processing speed and inhibition
Color Naming	Processing speed
Word Reading	Processing speed
Color-Word Interference	Inhibition of pre-potent response
Rey-Osterrieth Complex Figure Test	Visuoconstruction and visual memor
Copy	Visuoconstructive ability
Immediate Recall	Short-delay visual memory
Delayed Recall	Long-delay visual memory

provided in the manual. Dependent measures include reaction time, omission errors, and commission errors for each trial. Normative data is provided for seven age groups in the manual (6-8, 9-10, 11-14, 15-19, 20-49, 50-64, and 65-90), with separate norms for each gender. Therefore, raw scores were demographically corrected for age and gender before conversion to  $z$ -scores and linear transformation to T-scores.

#### *Digit Span and Spatial Span*

Two tests of attention span and working memory were administered, one in the auditory modality (Digit Span; Psychological Corporation, 1997) and one in the visual modality (Spatial Span; Psychological Corporation, 1997). Both span tests include a measure of immediate attention to stimuli (i.e., forward span), in which the examinee either repeats the numbers spoken aloud by the examiner or duplicates the order in which a sequence of blocks is tapped. Both span tests also include a measure of working memory (i.e., backward span), in which the examinee must cognitively manipulate the numbers (or sequence of blocks) in order to provide the stimuli in the reverse order of the examiner's. Because forward and backward conditions tap different cognitive functions (Lezak et al., 2004), scaled scores for the two conditions combined were not utilized. For Digit Span, the WAIS-III manual provides normative data for 13 age groups based on the highest level attained (means and standard deviations for forward and backward conditions). Therefore, raw scores (highest span) were corrected for age before conversion to  $z$ -scores and linear transformation to T-scores. For Spatial Span, the WMS-III manual provides supplemental normative data for 13 age groups, based on the raw scores obtained for both forward and backward conditions. Raw scores for each condition are converted to scaled scores.

Therefore, spatial span raw scores on each condition were corrected for age before obtaining scaled scores and transforming to T-scores.

#### *Controlled Oral Word Association Test*

The Controlled Oral Word Association Test (COWAT), also known as the verbal fluency test, used in this research included tests of both phonemic fluency and semantic fluency. Verbal fluency tests also have a long history in neuropsychological assessment, as reviewed in Mitrushina et al. (2005); verbal fluency tests evaluate “the spontaneous production of words under strict search conditions” (Strauss et al., 2006, p. 499).

Phonemic fluency is typically assessed by requiring the examinee to name as many words as possible that start with a given letter within a specified time frame, with certain restrictions of content. In this study, phonemic fluency was assessed using two different letter sets: CFL and FAS. For each letter in a set, participants were instructed to provide as many words as possible beginning with that letter, excluding numbers and proper names of people and places, given one minute per letter. For participants who were administered the CFL set, raw scores (i.e., the sum of correct words across all three letters) were compared to normative data corrected for gender and level of education (Ruff et al., 1996; cited in Strauss et al., 2006, p. 507). For participants who were administered the FAS set, raw scores were compared to normative data corrected for age and level of education (Tombaugh et al., 1999; cited in Strauss et al., p. 507). Both sets of norms provide means and standard deviations for converting raw scores to *z*-scores, before linear transformation to T-scores.

Semantic fluency is usually assessed by requiring the examinee to name as many items as possible that belong to a given category, within a specified time frame. In this study, participants were asked to name as many animals as possible within one minute. Raw scores were compared to normative data corrected for age and level of education (Tombaugh et al., 1999; cited in Strauss et al., 2006, p. 510). This set of norms provides means and standard deviations for converting raw scores to  $z$ -scores, which were transformed to T-scores.

#### *Trail Making Test*

The original Trail Making Test (TMT) was part of the Army Individual Test Battery (1944) (cited in Lezak et al., 2004) and consists of two parts. In Part A, the numbers 1-25 are pseudo-randomly arrayed on a page, and the examinee is instructed to connect the numbers in sequential order as quickly as possible, without making mistakes; the task assesses visual attention, scanning/tracking, and information processing speed. Part B has both numbers (1-13) and letters (A-L) pseudo-randomly arrayed on a page; the examinee is instructed to draw lines connecting numbers and letters in alternating order (1-A, 2-B, etc.), as fast as possible without error. Part B is a test of executive functioning; in addition to the cognitive skills required to complete Part A, the task requires ‘on-line’ maintenance of two sets of information simultaneously (i.e., working memory and divided attention), while accurately and quickly switching between sets (i.e., cognitive flexibility). Scores for TMT performance were obtained from normative data corrected for age (Tombaugh, 2004); this set of norms provides means and standard deviations for speed of completion on both trials, for conversion to  $z$ -scores before transformation to T-scores. For several

participants ( $n = 3$ ), the original TMT was not administered; instead, the Trail Making Test from the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001) was completed. In these cases, the scaled scores obtained on Condition 2 (an analog for TMT, Part A) and on Condition 4 (an analog for TMT, Part B) were substituted, with age-corrected scaled scores (provided in the manual) transformed to T-scores.

#### *Stroop Color-Word Interference Test*

This test is “among the oldest in experimental psychology,” but “there is no one recognized standard version of the Stroop Test” (Mitrushina et al., 2005, pp. 109-110). The test is named after the experimenter who described the general procedure in 1935 (Stroop, 1935/1992), wherein “color of the print was to be the controlling stimulus and not the name of the color spelled by the word... to be known as the ‘Naming color of word test where the color of the word and the print are different’” (p. 17). In other words, the examinee must inhibit the natural (prepotent) tendency to read a word (e.g., red) that is printed in an incongruous color (e.g., green), and name the ink color instead. This ‘interference’ portion of the test is preceded by rapid naming tasks in which the examinee reads words (e.g., red, blue) or identifies colors by name. The Stroop test is considered a measure of executive functioning that assesses “selective attention and cognitive flexibility” (Strauss et al., 2006, p. 477), although Lezak et al. (2004) describe it as “a measure of concentration effectiveness” (p. 365). In this study, the Kaplan modification was utilized, in which the color naming trial is administered first, followed by the word reading trial, and concluding with the interference trial. The specific materials and procedure are described in

Mitrushina et al. (p. 111). Three sets of normative data, obtained using Kaplan's procedure, were used, summarized in Mitrushina et al. (pp. 669-670); all norms provide means and standard deviations for speed of completion on the three trials, which were converted to  $z$ -scores after corrections for age and (when possible) ethnicity, before transformation to T-scores. For several participants ( $n = 4$ ), the traditional Kaplan version was not administered; instead, the Color-Word Interference Test from the Delis-Kaplan Executive Function System (D-KEFS; Delis et al., 2001) was completed. However, the same order of administration (i.e., color naming, word reading, interference) is employed on the D-KEFS. In these cases, the scores obtained on Conditions 1, 2, and 3 were substituted, with age-corrected scaled scores transformed to T-scores.

#### *Rey-Osterrieth Complex Figure Test*

The Rey-Osterrieth Complex Figure Test (ROCF) is a measure of "visual-spatial constructional ability and visual memory" (Strauss et al., 2006, p. 811) which, again, has a long history in clinical neuropsychology, first developed by André Rey in 1941 (Gallagher & Burke, 2007). The ROCF is reproduced in Lezak et al. (2004, p. 537). The usual procedure requires the examinee to copy the figure on a blank page of paper, during which the examiner records organizational strategies (or lack thereof) employed during the task; hence, the copy condition also serves to assess executive functioning (e.g., planning, organization, task monitoring). After completion of the copy trial, the stimulus is removed from sight and the examinee is asked to reproduce the figure from memory (immediate recall trial). After a longer delay (typically filled with verbal tasks), the examinee is again asked to reproduce the figure (delayed recall

trial). Administration procedures in this study included a copy trial without specific time limits, an immediate recall trial administered within 30 seconds, and a delayed recall trial administered within 30 minutes of completing the immediate recall trial. Denman's (1984) scoring procedures and normative data were utilized, which entails assigning a value between 0-3 points for 24 separate elements of the design (range = 0-72). Age-corrected normative data are provided for eight age groups (13-15, 16-18, 19-21, 22-29, 30-39, 40-49, 50-59, and 60-69). Scaled score equivalents for raw scores on the three trials are provided in the manual, which were corrected for age before linear transformation to T-scores. For two cases, the ROCF was not administered, so imputation of the mean was used to replace missing data on the copy, immediate recall, and delayed recall trials.

#### *Design and Data Analysis*

The sample was analyzed using cluster analysis to determine whether the putative orbitofrontal (OF) profile could be discriminated from an ostensibly dorsolateral-prefrontal (DLPF) profile using the cluster variate specified in Chapter 2. Cluster analysis is an umbrella term for an exploratory data reduction strategy that employs "a group of multivariate techniques whose primary purpose is to group objects based on the characteristics they possess" (Hair et al., 1998, p. 473). A cluster variate is the specific set of variables used to compare objects (or cases) in the cluster analysis (Hair et al.). According to Aldenderfer and Blashfield (1984), "the choice of variables to be used with cluster analysis is one of the most critical steps in the research process... variables should be chosen within the context of an explicitly stated theory that is used to support the classification" (pp. 19-20). In the present

study, the cluster variate consists of the Personality Assessment Inventory's Mania scale (MAN), Antisocial Features scale (ANT), Aggression scale (AGG), and Obsessive-Compulsive subscale (ARD-OCD), in which the inclusion of each variable is predicated on both theory and empirical research relevant to circuit-specific behavioral syndromes, as explicated in Chapter 2.

Cluster analysis may employ either hierarchical or iterative partitioning methodologies, or a combination of the two approaches. Hierarchical procedures may involve agglomerative or divisive methods for recovering clusters, using a variety of linkage methods designed to discern either the similarity or dissimilarity of cases based on the cluster variate (see Aldenderfer & Blashfield, 1984; Borgen & Barnett, 1987). In this research, a combination of the two approaches was utilized, with an initial hierarchical cluster analysis performed in order to establish "seeds" for a subsequent *k*-means non-hierarchical procedure, as recommended by Hair et al. (1998):

First, a hierarchical technique can establish the number of clusters, profile the cluster centers, and identify any obvious outliers. After outliers are eliminated, the remaining clusters can then be clustered by a nonhierarchical method with the cluster centers from the hierarchical results as the initial seed points. In this way the advantages of the hierarchical methods are complemented by the ability of the nonhierarchical methods to 'fine-tune' the results by allowing the switching of cluster membership. (p. 498).

An agglomerative hierarchical method was employed, utilizing squared Euclidean distance ( $d^2$ ) as the proximity measure and Ward's minimum variance method to merge groups, given that "comparative studies now suggest that Ward's method is one of the more effective methods for recovering underlying structure" (Borgen & Barnett, 1987, p. 465). The squared Euclidean distance is obtained by calculating the

proximity between each pair of cases for a given variable by finding the difference between scores, squaring the difference, and summing the values of the squared distances over the profile (Borgen & Barnett). When applied to a proximity matrix of Euclidean distances, Ward's method merges single cases, or groups of cases, which results in the minimum increase in the within-groups (error) sum of squares (Borgen & Barnett). Hierarchical methods produce a clustering tree, or dendrogram, which assists the researcher in determining the optimal cluster solution; the results for two, three, and four clusters were examined. The cluster centroids (i.e., the mean values of the observations on the variables comprising the cluster variate) obtained in the hierarchical procedure were then utilized as seed points for iterative partitioning.

The use of *k*-means partitioning is optimized when start values (i.e., seeds) from a hierarchical-agglomerative procedure are utilized (reviewed in Beauchaine & Beauchaine, 2002). Iterative partitioning provides the advantage of reallocating cases upon each successive iteration, or pass, through the data, whereas hierarchical-agglomerative methods do not allow for reallocation of cases to a cluster once it has been fixed earlier in the agglomeration schedule (therefore, "the later grouping may not be completely optimal, as defined by the clustering algorithm at a given step" [Borgen & Barnett, 1987, p. 464]). In the *k*-means procedure, "the method calculates centroids for a set of trial clusters, places each object in the cluster with the nearest centroid, and then recalculates the centroids and reallocates the objects. This process iterates until there is no change in cluster membership" (Borgen & Barnett, p. 465). Using this combined approach, cluster recovery was optimized, with an expectation that a two-group solution would best define the data set. For strictly descriptive

purposes, the significance and relative contribution of each variable in the cluster variate toward discriminating between groups was examined using analysis of variance.

Once a cluster solution has been identified, external validation and profiling of the solution are necessary. According to Aldenderfer and Blashfield (1984), “basically, the procedure is to perform significance tests that compare the clusters on variables *not* used to generate the cluster solution” (p. 66). As a form of criterion or predictive validity,

The processes of validation and profiling are critical due to the exploratory and often atheoretical basis for the cluster analysis. It is essential that the researcher perform all possible tests to confirm the validity of the cluster solution while also ensuring the cluster solution has practical significance. (Hair et al., 1998, p. 512)

Discriminant function analysis may be used in tandem with cluster analysis to validate a cluster solution, but the assumptions underlying this statistical procedure are stringent (e.g., multivariate normality and equal variance-covariance matrices across groups). Because the size of the clusters was expected to be modest ( $n's \leq 15$ ), decreasing the likelihood of meeting the normality assumption, binary logistic regression was utilized instead; according to Hair et al. (1998), “logistic regression is equivalent to two-group discriminant analysis and may be more suitable in many situations,” in part because “logistic regression does not face these strict assumptions and is much more robust when these assumptions are not met” (p. 276). Logistic regression is a method of maximum likelihood estimation in which a predictor variable (or variables) is regressed onto a dichotomous criterion, in “an attempt to predict the probability that a case will be classified into one as opposed to the other of

the two categories of the dependent variable” (Menard, 2002, p. 12). In planning to use binary logistic regression to validate the cluster solution, it was predicted that two groups (i.e., OF profile and DLPF profile) would best describe the data set (see Chapter 1, hypothesis #1).

In the first stage of the external validation procedures, each of the neuropsychological measures (i.e., 20 separate variables) was entered as a univariate predictor of membership in the OF profile group, with an expectation that the DLPF profile group would have poorer scores than the OF profile group on all measures (see Chapter 1, hypotheses #2-10), consistent with theoretical and empirical work differentiating between these profiles, reviewed in Chapter 2. The logistic coefficients for each neuropsychological measure were calculated, to test the hypothesis that significant coefficients would be found for all neuropsychological measures, utilizing the Wald statistic, with subsequent interpretation of the odds ratios (i.e., the odds of being classified in the OF group) (Hair et al., 1998; Menard, 2002; Pampel, 2000).

Second, the remaining PAI clinical, treatment, and interpersonal scales (i.e., those not used in the cluster variate) were entered as univariate predictors of membership in the OF group. Because the ARD-OCD subscale was part of the cluster variate, the full ARD scale was not utilized as a predictor, but the other two subscales comprising the ARD scale (ARD-Traumatic Stress [TRM] and ARD-Phobias [PHO]) were entered as predictors of group membership in this stage of the external validation process. The DLPF profile group was expected to have higher scores on measures of internalizing behavior—specifically, the anxiety (ANX) and depression (DEP) scales (Galynker et al., 1998; Hooley et al., 2005; Mathew et al., 2004).

Therefore, higher scores on these scales were expected to decrease the odds of being in the OF profile group (see Chapter 1, hypothesis #11) Logistic coefficients for these clinical scales were calculated, to test the hypothesis that significant coefficients would be found, using the Wald statistic, with interpretation of the odds ratios. For all other PAI scales (and the two specified subscales) not used in the cluster variate, no significant differences were hypothesized (i.e., an expectation of null results; see Chapter 1, hypothesis #12).

Following the external validation procedures, the cluster solution was profiled using demographic characteristics (i.e., age, education, intelligence, academic achievement, gender, ethnicity, concussion history, and birth weight). As in external validation, only variables that were not used in forming the cluster variate are examined in profiling: “In short, the profile analysis focuses on describing not what directly determines the clusters but the characteristics of the clusters after they have been identified” (Hair et al., 1998, p. 501). One-way analysis of variance (for continuously distributed variables) and chi-square analysis (for categorical variables) were utilized to determine if groups differed on any of the specified demographic characteristics.

For the univariate logistic regression analyses, a  $p$ -value of .10 was selected *a priori* for determining the level of significance. Due to the small sample size, a multivariable logistic regression could not be conducted because of the likelihood of overfitting (Babyak, 2004). According to Bagley, White, and Golomb (2001), “For a given set of data, introducing more variables will generally produce a model better fit to the data; with excessive numbers of variables, idiosyncrasies of the particular data

set unduly influence the coefficients in the model, which is said to be ‘overfit’” (p. 980). In choosing logistic regression as a method for externally validating the predicted two-group solution, the goals were (1) to test hypotheses that the putative DLPF profile group would score more poorly than the putative OF profile group on the neuropsychological measures, and (2) to identify those variables that might be important for inclusion in multivariable logistic regression modeling in future studies with larger samples. By this reasoning, the purposeful selection of variables for a multivariable logistic regression entails setting a less stringent  $p$ -value than is usual in significance testing; Bursac, Gauss, Williams, and Hosmer (2008) suggest that the purposeful selection of variables to include in a multivariable logistic regression analysis begins with a univariate analysis of each variable, with a significance test of the Wald statistic using a  $p$ -value cut-off of .25. Due to the expected number of univariate comparisons (i.e., 20 for the neuropsychological variables and 15 for the personality variables), a  $p$ -value between the conventional significance level of .05 and the .25 level was selected for determining statistical significance. Because this study is descriptive and exploratory by design, and the size of the archival sample was small, the selection of a  $p$ -value of .10 acknowledges the increased probability of making type-I errors (i.e., finding significant differences from null where there are none), but a decreased risk of making type-II errors (i.e., failing to identify significant differences when they are present).

For demographic profiling of the cluster solution, the traditional  $p$ -value of .05 was selected for determining the level of significance. Given the expectation of making multiple comparisons without correction (e.g., the Bonferroni adjustment),

this  $p$ -value represents a liberal criterion for determining whether differences between groups were significant. Again, because this study is exploratory in nature, the consequent increased likelihood of type-1 errors, offset by the decreased likelihood of type-II errors, is acknowledged (cf. Glass & Hopkins, 1996; see also Perneger, who argues that “adjusting statistical significance for the number of tests that have been performed on study data—the Bonferroni method—creates more problems than it solves” [1998, p. 1236]).

### *Materials*

Materials specific to the tests used in evaluating participants are described in several widely available texts (Lezak et al., 2004; Mitrushina et al., 2005; Strauss et al., 2006). The data was analyzed using the *SPSS Graduate Pack 16.0 for Windows* (SPSS Inc., 2007) statistical software.

Chapter 4  
Results

The results of the hierarchical cluster analysis are described first, followed by results employing the *k*-means clustering procedure. Results for the two stages of the external validation procedures (neuropsychological and personality) are then described, followed by profiling of the clusters using demographic data, including intelligence and academic achievement data.

*Hierarchical cluster analysis*

The hierarchical cluster analysis using squared Euclidean distance as the proximity measure and Ward’s method to merge groups was selected for two, three, and four cluster solutions. As shown in the dendrogram of the results (see Figure 1), a

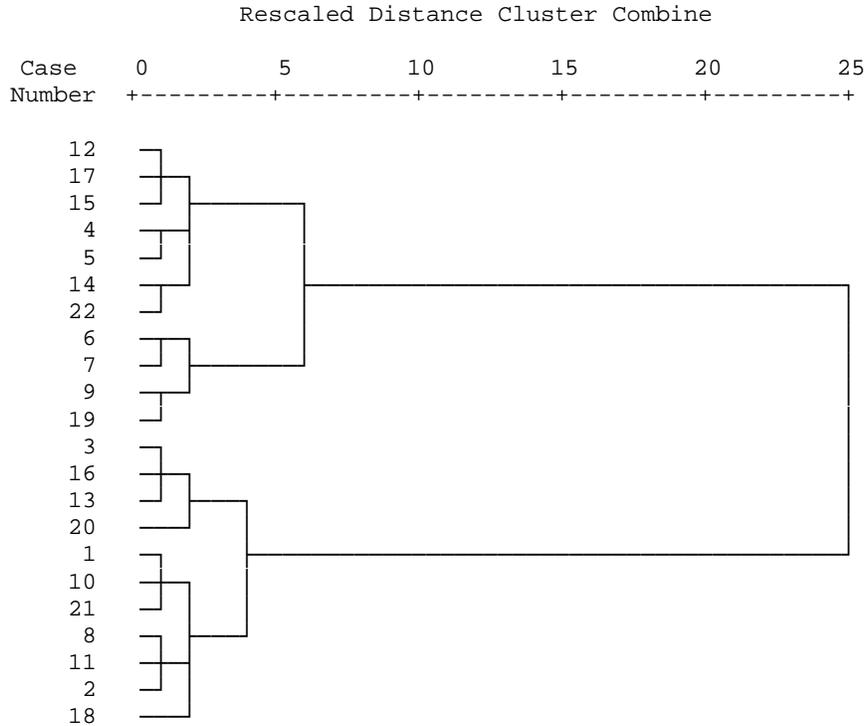


Figure 1. Dendrogram using Ward’s Method revealing two-group cluster solution.

two-group solution emerged from the data. Although there are no definitive criteria for determining an optimal cluster solution (Aldenderfer & Blashfield, 1984), a two-group solution appeared to be the best fit, as represented by the ‘jump’ in distance (i.e., a large increase in the agglomeration coefficient, or within-groups sum of squares) when the two groups were combined (see Table 6; cf. Hair et al., 1998).

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Table 6

*Analysis of agglomeration coefficient for hierarchical cluster analysis*

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Number of Clusters	Agglomeration Coefficient	Percentage Change in Coefficient to Next Level
5	2505.1	17.5
4	2943.4	23.6
3	3638.3	33.5
2	4856.7	108.4
1	10119.5	—

---

As a preliminary check of the external validity of the two-group solution, hierarchical analyses for the same cluster variate were performed using alternative clustering methods (between-groups linkage and median clustering), again utilizing squared Euclidean distance as the proximity measure. In each case, the two-group solution remained consistent with the primary analysis, with no change in group classification of any of the 22 cases. The two groups were comprised of 11 cases each, confirming the hypothesis that a two-group cluster solution, potentially corresponding to the putative OF and DLPF classifications, would optimally describe the data set.

Consequently, the cluster centers obtained in the hierarchical analysis were used as seed points for iterative partitioning of the sample.

*K-means cluster analysis and external validation*

The *k*-means clustering procedure produced identical classifications, with no change in group membership for any of the 22 cases. The initial cluster centers obtained in the hierarchical analysis and the final cluster centers following iterative partitioning are shown in Table 7. The results of a purely descriptive analysis of variance appear in Table 8. All four variables in the cluster variate significantly discriminated between groups, in the expected direction (i.e., mean values were higher in the OF profile group compared to the DLPF profile group on measures of antisocial features, aggression, mania, and obsessive-compulsive behavior).

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Table 7

*Initial and final cluster centers represented by T-scores in k-means clustering*

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Variable	Initial Cluster Centers		Final Cluster Centers	
	DLPF	OF	DLPF	OF
PAI-ANT	45	77	50.36	69.27
PAI-AGG	32	67	43.36	60.73
PAI-MAN	42	72	47.73	61.73
ARD-OCD	33	70	48.00	58.09

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Table 8

*Analysis of variance for the cluster variate in predicting group membership*

Cluster		Error		F	<i>p</i> -value	
Cluster	Mean Square	df	Mean Square			df
PAI-ANT	1966.545	1	46.236	20	42.532	.000
PAI-AGG	1658.227	1	57.436	20	28.871	.000
PAI-MAN	1078.000	1	65.518	20	16.453	.001
ARD-OCD	560.045	1	73.645	20	7.605	.012

*Note.* The F tests are for descriptive purposes only, because the clusters have been chosen to maximize the differences among cases in different clusters. The observed significance levels are not corrected for this and thus cannot be interpreted as tests of the hypothesis that the cluster means are equal. df = degrees of freedom.

In order to further explore the relationships among the 4 variables comprising the cluster variate, the 6, bivariate, Pearson correlations were calculated. As depicted in Table 9, the 4 variables in the cluster variate showed significant, bivariate, moderate, positive correlations (i.e.,  $r$ 's = .5966,  $p$ 's  $\leq$  .002), with a single exception. Specifically, antisocial features (ANT) did not correlate with obsessive-compulsive behavior (ARD-OCD), providing indirect, supportive evidence of the theoretical distinction between lateral and medial orbitofrontal-subcortical presentations, associated with predominantly obsessive-compulsive and antisocial behavioral features, respectively.

Table 9

*Pearson correlation matrix for the cluster variate (N = 22)*


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	AGG	MAN	ARD-OCD
ANT	.64*	.59**	.24
AGG	–	.59**	.59**
MAN		–	.66*

---

\*  $p \leq .001$ . \*\*  $p = .002$ .

With the identification of two distinct clusters potentially corresponding to the putative DLPF and OF classifications, an attempt to validate the cluster solution was undertaken. Due to the limiting sample size ( $n = 11$ ), which precluded performing multivariable logistic regression (see Babyak, 2004), each variable used in the external validation procedures was entered as a single predictor in a series of univariate logistic regression analyses. Because of the exploratory nature of this study, the alpha level for determining significance was set at  $p < .10$ .

As shown in Table 10, the two clusters were discriminated from one another on 5 of the 20 neuropsychological variables that were entered as univariate predictors of group membership. Consistent with the hypothesized direction, the DLPF profile group had significantly poorer scores than the OF profile group on three measures of sustained attention, assessed by computerized continuous performance testing.

Table 10

*Descriptive data on neuropsychological measures by putative profile group*

	DLPF profile group			OF profile group		
	<i>M</i>	<i>SD</i>	<i>SE</i>	<i>M</i>	<i>SD</i>	<i>SE</i>
Vigil-W Reaction Time-K	50.4	10.7	3.2	45.5	12.9	3.9
Vigil-W Reaction Time-AK	48.3	11.5	3.5	43.4	9.8	3.0
Vigil-W Omissions-K	62.4	17.6	5.3	48.5	3.8	1.1
Vigil-W Commissions-K	52.7	12.1	3.6	43.6	3.2	1.0
Vigil-W Omissions-AK	58.2	13.0	3.9	51.7	7.9	2.4
Vigil-W Commissions-AK	50.5	6.0	1.8	45.7	4.3	1.3
Digit Span- Forward	50.2	11.6	3.5	53.5	6.3	1.9
Digit Span-Backward	51.2	11.0	3.3	52.5	5.6	1.7
Spatial Span-Forward	50.0	12.0	3.6	53.1	8.4	2.5
Spatial Span-Backward	48.9	9.5	2.9	57.2	7.4	2.2
Phonemic Fluency	49.9	9.7	2.9	47.5	6.1	1.8
Semantic Fluency	50.1	12.7	3.8	49.5	11.2	3.4
Trail Making Test-A	45.1	12.0	3.6	48.1	9.2	2.8
Trail Making Test-B	49.4	15.4	4.7	43.9	13.6	4.1
Stroop—Color Naming	48.8	12.2	3.7	32.7	9.7	2.9
Stroop—Word Reading	45.8	17.7	5.3	35.4	15.5	4.7
Stroop—Interference	47.7	14.4	4.4	38.5	12.2	3.7
ROCF—Copy	37.0	11.8	3.6	39.4	13.5	4.1
ROCF—Immediate	38.9	10.9	3.3	42.2	14.9	4.5
ROCF—Delayed	39.4	12.0	3.6	42.9	13.2	4.0

*Note.* T-scores on Vigil-W error measures (i.e., omissions and commissions) are reverse-scored, with higher values representing poorer performance. ROCF = Rey-Osterrieth Complex Figure.

Table 11

*Significant neuropsychological variables in univariate logistic regression analyses*

Variable	$\beta$	SE	Wald	p-value	OR
Vigil-W Omissions-K	-.095	.050	3.690	.055	.909
Vigil-W Commissions-K	-.229	.128	3.221	.073	.795
Vigil-W Commissions-AK	-.188	.102	3.365	.067	.829
Spatial Span-Backward	.119	.061	3.824	.052	1.126
Stroop-Color Naming	-.123	.050	6.041	.014	.885

*Note.* Degrees of freedom = 1 for all variables. OR = Odds ratio.

Specifically, on the simple K condition of the Vigil-W, the DLPF profile group had a higher frequency of omission errors ( $M = 62.4$ ,  $SD = 17.6$ ) than the OF profile group ( $M = 48.5$ ,  $SD = 3.8$ ), though there was significantly greater variability of performance within the DLPF profile group compared to the OF profile group (i.e., unequal variances). The DLPF profile group also had a higher frequency of commission errors on the K condition of Vigil-W ( $M = 58.2$ ,  $SD = 13.0$ ) compared to the OF profile group ( $M = 51.7$ ,  $SD = 7.9$ ). On the cued, AK condition of Vigil-W, the DLPF profile and OF profile groups did not differ in their frequency of omission errors, but the DLPF profile group had a higher frequency of commission errors ( $M = 50.5$ ,  $SD = 6.0$ ) than the OF profile group ( $M = 45.7$ ,  $SD = 4.3$ ). The odds of being in the OF profile group decreased by 9.1% for every unit increase in Omissions-K, by

20.5% for every unit increase in Commissions-K, and by 17.1% for every unit increase in Commissions-AK.

Also as predicted, on a measure of visual attention and working memory (Spatial Span-Backward), the DLPF profile group obtained poorer scores ( $M = 48.9$ ,  $SD = 9.5$ ) than the OF profile group ( $M = 57.2$ ,  $SD = 7.4$ ). The odds of being in the OF profile group increased by 12.6% for every unit increase in the Spatial Span-Backward score.

Contrary to the hypothesized direction, the OF profile group performed more poorly on the Color Naming condition of the Stroop Test ( $M = 32.7$ ,  $SD = 9.7$ ) than the DLPF profile group ( $M = 48.8$ ,  $SD = 12.2$ ). The odds of being in the OF group increased by 11.5% for every unit decrease in the Stroop-Color Naming score. On the remaining 15 neuropsychological measures, the DLPF profile group and the OF profile group obtained comparable results (see Table 10).

In the second stage of the external validation procedure, each of 15 PAI personality measures were entered as predictors of group membership (7 clinical scales, 2 clinical subscales, 4 treatment scales, and 2 interpersonal scales) in a series of univariate logistic regression analyses. Descriptive data for the PAI variables appear in Table 12. Significant results, with alpha set at  $p < .10$ , appear in Table 13.

Against expectation, the DLPF and OF profile groups did not differ on measures of anxiety (ANX) or depression (DEP). Both groups reported mildly elevated levels of anxiety (DLPF:  $M = 61.9$ ,  $SD = 10.8$ ; OF:  $M = 64.2$ ,  $SD = 12.7$ ), with mean scores above the 84<sup>th</sup> percentile, and depressive symptoms (DLPF:  $M = 57.8$ ,  $SD = 9.6$ ; OF:  $M = 58.1$ ,  $SD = 10.1$ ) that fell within normal limits.

Table 12

*Descriptive data on Personality Assessment Inventory scales by putative profile group*

	DLPF profile group			OF profile group		
	<i>M</i>	<i>SD</i>	<i>SE</i>	<i>M</i>	<i>SD</i>	<i>SE</i>
Anxiety-Related Disorders (ARD)						
Phobias	55.9	12.6	3.8	54.6	6.8	2.0
Traumatic Stress	48.4	6.9	2.1	58.4	6.5	2.0
Somatic Complaints (SOM)	50.6	6.1	1.8	55.6	7.9	2.4
Anxiety (ANX)	61.9	10.8	3.2	64.2	12.7	3.8
Depression (DEP)	57.8	9.6	2.9	58.1	10.1	3.0
Schizophrenia (SCZ)	58.3	9.3	2.8	63.3	10.7	3.3
Borderline Features (BOR)	57.5	10.0	3.0	65.5	10.1	3.0
Alcohol Problems (ALC)	48.5	8.0	2.4	53.8	9.4	2.8
Drug Problems (DRG)	47.8	7.3	2.2	51.6	9.6	2.9
Suicidal Ideation (SUI)	52.9	9.4	2.8	48.1	6.4	1.9
Stress (STR)	51.1	10.2	3.1	60.6	8.4	2.5
Nonsupport (NON)	58.0	13.0	3.9	55.2	7.3	2.2
Treatment Rejection (TXR)	45.6	10.8	3.2	45.4	7.2	2.2
Dominance (DOM)	45.9	10.5	3.2	51.2	9.1	2.7
Warmth (WRM)	44.8	9.0	2.7	49.5	8.2	2.5

Although null results were expected on the remaining personality measures, scores on several measures increased the odds of membership in the OF profile group. First, the OF profile group reported higher levels of traumatic stress ( $M = 58.4$ ,  $SD = 6.5$ ) compared to the DLPF profile group ( $M = 48.4$ ,  $SD = 6.9$ ). The odds of being in the

Table 13

*Significant personality variables in univariate logistic regression analyses*

Variable	$\beta$	<i>SE</i>	Wald	<i>p</i> -value	OR
ARD-TRM	.219	.091	5.785	.016	1.245
PAI-BOR	.082	.048	2.983	.084	1.086
PAI-STR	.114	.057	4.031	.045	1.121

*Note.* Degrees of freedom = 1 for all variables. OR = Odds ratio. ARD = Anxiety-Related Disorders. TRM = Traumatic Stress. PAI = Personality Assessment Inventory. BOR = Borderline Features. STR = Stress.

OF profile group increased by 24.5% for every unit increase in the ARD-TRM score. Second, the OF profile group reported a higher frequency of borderline personality features ( $M = 65.5$ ,  $SD = 10.1$ ) compared to the DLPF profile group ( $M = 57.5$ ,  $SD = 9.9$ ). The odds of being in the OF profile group increased by 8.6% for every unit increase in the PAI-BOR score. Third, the OF profile group reported a greater level of perceived stress ( $M = 60.6$ ,  $SD = 8.4$ ) than the DLPF profile group ( $M = 51.1$ ,  $SD = 10.2$ ). The odds of being in the OF profile group increased by 12.1% for every unit increase in the PAI-STR score.

Following the external validation procedures, profiling of the cluster solution was undertaken, in an attempt to identify demographic differences associated with the OF and DLPF classifications. First, a series of descriptive, one-way analyses of variance were conducted to determine differences between groups on continuously distributed variables (age, education, birth weight, FSIQ, VIQ, PIQ, Vocabulary,

Similarities, Block Design, Matrix Reasoning, and the academic achievement measures). Alpha was set at  $p < .05$  for the demographic comparisons. Descriptive data on the intelligence measures are shown in Table 14 and descriptive data on the academic achievement measures are shown in Table 15.

Table 14  
*Descriptive data on intelligence measures by putative profile group*

	DLPF profile group			OF profile group		
	<i>M</i>	<i>SD</i>	<i>SE</i>	<i>M</i>	<i>SD</i>	<i>SE</i>
Full Scale IQ	111.7	9.4	2.8	109.8	8.9	2.7
Verbal IQ	110.7	5.9	1.8	105.4	8.4	2.5
Performance IQ	109.5	10.9	3.3	111.0	8.7	2.6
Vocabulary	56.5	5.6	1.7	50.7	8.2	2.5
Similarities	57.1	4.7	1.4	55.8	4.3	1.3
Block Design	55.6	9.3	2.8	56.6	7.2	2.2
Matrix Reasoning	56.8	7.0	2.1	59.4	5.6	1.7

*Note.* IQ scores are reported as standard scores ( $M = 100, SD = 15$ ). All other scores are reported as T-scores ( $M = 50, SD = 10$ ). IQ = Intelligence quotient.

Among the intelligence variables, there was a trend for the OF profile group to score more poorly on Vocabulary than the DLPF profile group,  $F(1, 20) = 3.74, p = .067$ , though mean scores for both groups were in the average range (DLPF:  $M = 56.5, SD = 5.6$ ; OF:  $M = 50.7, SD = 8.2$ ). Similarly, there was a trend for the OF profile group to score more poorly on overall verbal intelligence,  $F(1, 20) = 3.01, p =$

Table 15

*Descriptive data on academic achievement measures by putative profile group*

	DLPF profile group			OF profile group		
	<i>M</i>	<i>SD</i>	<i>SE</i>	<i>M</i>	<i>SD</i>	<i>SE</i>
WRAT-3 Reading	51.2	7.4	2.2	50.8	3.0	0.9
WRAT-3 Spelling	53.9	9.4	2.8	48.6	7.9	2.4
WRAT-3 Arithmetic	52.5	9.9	3.0	50.6	6.9	2.1
NDRT-Reading Speed	39.0	10.3	3.1	35.7	7.4	2.2
NDRT-Reading Comprehension	44.5	11.1	3.3	43.4	7.4	2.2

*Note.* WRAT-3 = Wide Range Achievement Test, 3<sup>rd</sup> edition. NDRT = Nelson-Denny Reading Test.

.098, but mean scores for both groups were, again, in the average range (DLPF:  $M = 110.7$ ,  $SD = 5.9$ ; OF:  $M = 105.4$ ,  $SD = 8.4$ ). There were no significant differences between groups in age, education, birth weight, FSIQ, PIQ, Similarities, Block Design, Matrix Reasoning, or the five academic achievement measures (all  $p$ 's > .10).

Second, a series of descriptive, chi-square analyses were conducted to determine differences between groups on categorical variables (gender, ethnicity, handedness, and concussion history). There was a trend for males to be over-represented in the OF profile group and females to be over-represented in the DLPF profile group, Pearson  $\chi^2(1, N = 22) = 2.93$ ,  $p = .087$ . There were no significant differences between observed and expected values for ethnicity, handedness, or concussion history.

## Chapter 5

## Discussion

This study represents a first attempt at utilizing an objective self-report personality measure (Morey's [1991] Personality Assessment Inventory) to discriminate between distinct neurocognitive profiles that have been described in the cognitive neuroscience literature. The prediction that an orbitofrontal (OF) profile, characterized primarily by antisocial features, mania/hypomania, aggressive behavior, and obsessive-compulsive behavior, could be discriminated from a dorsolateral-prefrontal (DLPF) profile, characterized primarily by cognitive deficits on neuropsychological measures, appeared to be confirmed by the results obtained in a small clinical sample of highly educated adults using the exploratory data reduction strategy of cluster analysis. A two-group cluster solution was identified by using combined hierarchical and *k*-means clustering procedures to discriminate between clusters on the basis of self-reported antisocial, aggressive, manic, and obsessive-compulsive behavioral features. Moreover, this solution remained consistent when alternative clustering methods were utilized. The two clusters, potentially corresponding to the putative OF and DLPF classifications, were further discriminated from one another via external validation procedures, in which the odds of membership in the OF profile group were increased by better performance on neuropsychological measures of sustained attention and spatial working memory compared to the DLPF profile group, as determined through a series of univariate logistic regression analyses. However, contrary to the hypothesized direction, the OF profile group performed more poorly than the DLPF profile group on a timed test of

color naming, on which poorer scores significantly increased the odds of an OF classification. This serendipitous finding was particularly surprising, in light of prior research that found reduced speed on color naming to be associated with left DLPFC dysfunction (reviewed in Stuss & Levine, 2002).

In addition to the four personality variables comprising the cluster variate, three additional personality measures predicted an increased odds of an OF classification, where null results were expected. The odds of membership in the OF profile group were significantly increased by self-reported traumatic stress, general stress, and borderline personality features. Upon demographic profiling, the OF profile group was somewhat more likely to have poorer verbal intelligence and vocabulary scores than the DLPF profile group. Male gender was somewhat more likely to be observed in the OF profile group and female gender in the DLPF profile group. In sum, attempts to externally validate the two-group cluster solution were minimally successful, given that the DLPF and OF profile groups performed comparably on 75 percent of the neuropsychological measures entered as univariate predictors of membership in the OF profile group. The results of the external validation and profiling procedures must be viewed as tentative and exploratory, due to the small sample size and large number of comparisons, which increased the probability of type-I errors.

The OF and DLPF profile groups reported comparable levels of depression and anxiety, although it was hypothesized that the DLPF profile group would self-report higher levels compared to the OF profile group on the basis of prior research implicating DLPFC involvement in these emotional-behavioral manifestations

(Galynker et al., 1998; Hooley, et al., 2005; Mathew et al., 2004). Lesser and Chung (2007) stated, “Multiple lines of evidence... lead to the postulate that major depression is associated with frontal lobe/frontal circuit dysfunction” (p. 644), but “the diversity of symptoms present in depression argues against a single etiology....” (p. 637). Similarly with anxiety, it has been noted that “the neurobiological bases of generalized anxiety disorder are poorly characterized” (Mathew et al., 2004, p. 1119). This study found no evidence to support the hypothesis that individuals who have an ostensibly DLPF profile differ from those with an ostensibly OF profile on global self-report measures of anxiety and depression.

As noted by Hair et al. (1998), it is necessary not only to externally validate a cluster solution, but also to explain the practical significance of the clusters. Because the sample under study was comprised of college students who presented to the clinic for neuropsychological assessment secondary to difficulties meeting the requirements of post-secondary education, a discussion of the practical significance of the cluster solution is oriented toward this population.

The college students who were classified as having an OF profile were differentiated from those classified as having a DLPF profile by their significantly higher levels of antisocial features, aggression, (hypo)mania, and obsessive-compulsive behavior. Students with this profile would be expected to have difficulty negotiating the interpersonal aspects of higher education (e.g., interaction with professors, group activities) due to their apparent difficulties with emotional-behavioral regulation. For example, students with an OF profile would be more likely to demonstrate egocentricity, irritability, aggressive attitudes, and impulsivity, leading

to interpersonal conflicts with professors and peers, which might then contribute to higher levels of stress and poorer academic outcomes. A tendency to demonstrate obsessive-compulsive behaviors could interfere with the organization and timely completion of academic assignments, further contributing to sub-optimal academic performance. Therefore, if college students with an OF profile could be reliably identified via their self-reporting on the PAI, then recommended treatments and accommodations could be tailored to their needs. For example, recommendations for students with an OF profile might include anger management, relaxation training, and social skills training. Assistance with organizing assignments and schedules also might be recommended.

Conversely, college students with an ostensibly DLPF profile would not be expected to display the emotional-behavioral dysregulation observed in students with an OF profile. However, as suggested by the external validation procedure, the DLPF group appeared to be discriminated from the OF group by poorer performance on measures of sustained visual attention (i.e., increased frequencies of both omission and commission errors) and spatial working memory. Therefore, if college students with a DLPF profile could be identified through a combination of their self-reporting on the PAI and neuropsychological test results on measures of sustained attention and spatial working memory, then recommended treatments and accommodations could be tailored to their unique needs. For example, recommendations for students with a DLPF profile might include (a) a psychopharmacological consultation to determine if a psychostimulant or norepinephrine reuptake inhibitor would be helpful in facilitating attention in class, (b) testing in a quiet room away from distractions, and

(c) assistance with organizing assignments and schedules.

Because students with an OF profile appear less likely to perform poorly on neurocognitive tests, it is possible that their significant difficulties in the affective and behavioral realm of functioning might be overlooked, whereas students with more clear-cut cognitive challenges, as determined by neuropsychological tests, may be more likely to receive accommodations and services. The emotional-behavioral dysregulation associated with an OF profile additionally may have an alienating effect on those individuals who are responsible for evaluating their disability status and determining whether or not a disability requiring accommodations exists. Therefore, it becomes all-the-more essential that a comprehensive personality assessment be conducted as part of the neuropsychological assessment of college students, lest these individuals be deemed ineligible for services in the face of 'normal' performance on neurocognitive tests.

It is notable that the OF profile group performed more poorly than the DLPF profile group on a single neurocognitive measure (Stroop Color Naming) that requires rapid color processing and naming. Zeki and Marini (1998) suggested that the processing of normal color (such as the red, blue, and green stimuli presented in the Stroop paradigm) which does not require judgment or decision-making is mediated by ventromedial frontal cortex. Furthermore, it has been suggested that individuals with ADHD may exhibit decreased color naming speed (specifically, for the colors blue and yellow), which hypothetically is associated with deficient retinal and central dopamine (Tannock, Banaschewski, & Gold, 2006). Therefore, this study provides preliminary evidence that orbitofrontal dysfunction in adults may be linked to

decreased color naming speed, which could be helpful to clinicians when making a determination whether or not an individual might be classified in the putative OF profile group.

The OF profile group also was discriminated from the DLPF profile group by higher self-report ratings of traumatic stress, general stress, and borderline personality features. Notably, emotional-behavioral dysregulation is associated with both post-traumatic stress disorder (PTSD) and borderline personality disorder, and recent neuroimaging research indicates that bilateral orbitofrontal cortex is strongly activated during recall of traumatic autobiographical information (Driessen et al., 2004). Given that traumatic stress was the strongest personality or psychological predictor of OF profile group membership (i.e., outside of the cluster variate), consideration might be given to adding this variable to the cluster variate in future studies that attempt to replicate the putative OF-DLPF cluster solution. The PAI Trauma subscale is subsumed under the PAI Anxiety-Related Disorders clinical scale, together with the Obsessive-Compulsive and Phobias subscales, so another option for modifying the cluster variate might be to replace the ARD-OCD subscale with the full PAI-ARD clinical scale in future studies (although the Phobias subscale did not discriminate between the putative OF and DLPF classifications).

An examination of the correlation matrix for the cluster variate showed significant, positive, bivariate correlations of moderate strength among the four variables, with the single exception of antisocial features and obsessive-compulsive behavior, which shared no significant association. These results indirectly supported the distinction between lateral and medial OFC frontal-subcortical profiles described

by Chow and Cummings (2007), with a medial profile corresponding to antisocial features and a lateral presentation corresponding to obsessive-compulsive behavior. An examination of whether an individual with a putative OF profile has a primarily lateral versus a primarily medial presentation could be helpful in determining the appropriate treatment approach (e.g., treatment with a selective serotonin reuptake inhibitor in cases with a more lateral presentation [see Baxter et al., 2001]).

Despite the suggestion of a two-group cluster solution that potentially corresponds to the OF and DLPF “syndromes” described in theoretical work (e.g., Lichter & Cummings, 2001), the use of these terms to describe the groups, as noted in the introduction, obviously does not suggest that the participants in this study had specific damage or dysfunction isolated to either orbitofrontal or dorsolateral-prefrontal brain regions. As the theory of frontal-subcortical circuits explicated by Chow and Cummings (2007) emphasizes, damage, dysfunction, or dysregulation in multiple brain regions, through open pathways within and between circuits, may be responsible for the cognitive, emotional, and behavioral outcomes observed in the circuit-specific behavioral syndromes. Moreover, it is not possible to state with any degree of certitude that an individual has brain damage or dysfunction without the corroborative evidence of structural or functional neuroimaging results. In fact, such corroboration would be an important next step in future research, whereby correlation of the OF-DLPF classification scheme obtained from objective personality results on the PAI and neuropsychological tests with radiological data might provide further evidence for the verisimilitude of these circuit-specific behavioral syndromes. However, as cautioned by Kringelbach and Rolls (2004), “We should remember...

that functional neuroimaging has limitations in that there are many sometimes quite small populations of neurons with different responses to different types of stimulus or event in the orbitofrontal cortex and other brain regions which may not all be revealed by neuroimaging....” (p. 342). Therefore, identification of circuit-specific behavioral syndromes using other methodologies (e.g., neuropsychological assessment, including personality assessment using objective self-report instruments) would appear to have continued relevance, despite its shortcomings in definitively identifying the specific brain regions responsible for a given cognitive, emotional, and behavioral presentation.

A significant drawback of this study is the fact that the cluster variate was specifically chosen in an attempt to positively identify the OF profile group, while the assignment of participants to the DLPF profile group essentially was predicated on exclusion (i.e., if not OF, then DLPF). A modicum of support for the DLPF profile was obtained via external validation procedures, wherein this group had poorer performance on measures of sustained attention and spatial working memory compared to the OF profile group. However, univariate logistic regression analyses were not corrected for multiple comparisons, inflating the probability of type-I errors. It must be reiterated that the labeling of participants according to OF and DLPF classifications does not imply that putative brain dysfunction is isolated to specific regions of cerebral cortex. Although the labels themselves are associated with specific areas of the cortex, the functional profiles encompassed by the terms are based on a theory that is quintessentially predicated on frontal-subcortical circuitry. As stated at the outset, brain-behavior relationships are complicated, and the coordinated

functioning of widely distributed neuroanatomical networks extending throughout the brain (cortical and subcortical, cerebral and cerebellar) mediates human behavior in all its complexity. One might suggest that what is known about the brain and its functioning is vastly exceeded by what remains unknown. This study does not claim to have definitely identified OF and DLPF profiles using the PAI in conjunction with neuropsychological instruments; rather, it merely points in the direction that Stuss and Levine (2002) advocated, by attempting to approach clinical neuropsychology from a perspective informed by cognitive neuroscience.

Although the sample of convenience in this study included approximately equal numbers of males and females, with representation of three ethnic groups, its limitations include its small size, restricted age range, and diagnostic heterogeneity. In addition, the sample was comprised of highly educated young adults who were enrolled in post-secondary education at the time they were evaluated, limiting the generalizability of the two-group cluster solution. It will be necessary to replicate the putative OF-DLPF classification scheme in different populations, including older adults and individuals with fewer years of formal education. The identification of an OF syndrome using the PAI also might have utility in forensic populations, where antisocial behavior, disinhibition, and aggression would be expected to an even greater degree, and therefore might be helpful in the prediction of recidivism.

Because of the limitation in sample size, it was not possible to perform a multivariable logistic regression analysis without producing spurious results (i.e., overfitting; see Babyak, 2004). Therefore, future replication of the putative OF-DLPF cluster solution should be conducted with larger samples, which would allow for

model-building that might provide improved predictive accuracy in discriminating between these profiles. This study has identified several neuropsychological measures that would be viable candidates for inclusion in multivariable logistic regression, including tests of sustained visual attention (CPTs), spatial attention and working memory (WMS-III Spatial Span), and color naming (Stroop tests). Additional neuropsychological measures for consideration in multivariable logistic regression might include tests of decision-making (e.g., the Iowa Gambling Task, which is now commercially available through Personality Assessment Resources, Inc.) and olfactory discrimination (e.g., the University of Pennsylvania's Smell Identification Test), deficits on which might be associated with orbitofrontal dysfunction (Bechara, Damasio, & Damasio, 2000; Kringelbach, 2004).

The critical importance of objective personality assessment in a thorough neuropsychological evaluation has been underscored by this study. It has been argued that the Personality Assessment Inventory (Morey, 1991) has many advantages over the MMPI-2, particularly when evaluating individuals with significant comorbidity including learning disorders. However, this need not rule out using the MMPI-2 to identify the putative OF-DLPF classifications; if the same variables included in the cluster variate in this study could be extracted from a combination of the MMPI-2's clinical, content, and/or supplementary scales, then convergent validity of the cluster solution might be obtained.

Given the strong emphasis on the measurement of cognitive skills and abilities in neuropsychology, it is notable that Aleksandr Luria, one of the founding fathers of modern neuropsychology, writing in 1965, opined:

Psychology has yet to become a science that is capable of dealing with the really vital aspects of human personality. It has yet to learn to depict the nature of personality in such a way that the functions of each individual trait could be seen in its relation to the total personality structure....

The development of such a psychology is a job for the future. And at present it is difficult to say how many decades it will be before we achieve it. For the progress that must be made if we are to have a scientific psychology of personality entails numerous turns off the main line of study, many areas of inquiry that will prove difficult to approach. But there is no doubt that research into the way an imbalance of individual aspects of development affect the formation of personality structure, a description of the process through which a personality “syndrome” is created, will constitute one important method in the approaches used. (1968, pp. 159-160)

Nearly 45 years later, psychology (including neuropsychology) continues to struggle with understanding “the really vital aspects of human personality.” This study represents a contribution toward understanding and conceptualizing personality through the lens of neuropsychology and cognitive neuroscience. That personality is conditioned and created not only by environmental circumstances, but also by the underlying neurobiology and neurochemistry that mediates all human experience cannot be denied. The identification of orbitofrontal and dorsolateral-prefrontal profiles through objective measurement, using a combination of an individual’s self-report and neuropsychological tests, appears to be a potentially fruitful avenue for developing treatments and rehabilitation strategies that target the specific needs inherent to these classifications. College students are only one population who may benefit from the identification of orbitofrontal and dorsolateral-prefrontal profiles. The future task remains to identify these groups within other populations, to aid in the development and application of rehabilitation strategies that selectively target the neurophysiological and biochemical underpinnings of human personality.

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