

Identifying Subtypes of Neurocognition using Latent Profile Analysis in Adults: A Precision Medicine
Approach

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Dissertation submitted to the faculty of the Virginia Polytechnic Institute and State University in partial
fulfillment of the requirements for the degree of

Doctor of Philosophy

in

Psychology

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May 7th 2025

Blacksburg, VA

Keywords: Neurocognition; MCI; LPA

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ABSTRACT

As the United States (US) population ages, the prevalence and societal cost of neurocognitive disorders such as dementia will continue to increase. Therefore, there is a pressing need to thoroughly elucidate these disorders' characteristics and progression. Despite existing research efforts, the exploration of neurocognitive subtypes remains limited, particularly given heterogeneity within and between the clinical manifestation of neurocognitive disorders. Conceptualizing these conditions as relatively homogenous can potentially impede patient care, delay timely interventions, and hinder advancements in treatment development. Enhancing our understanding of these conditions and how other psychosocial factors may affect them can lead to more targeted and effective interventions, potentially improving patient outcomes and reducing the burden of disease. Accordingly, the purpose of this study was to identify subgroups of neurocognition using latent profile analysis (LPA) to empirically distinguish neurocognitive profiles, determine the effects of profile membership on known risk factors for dementia including depression, anxiety, personality, sleep difficulties and chronic pain. Results of this study supported a 5-profile solution varying in degrees of cognitive strengths and weaknesses and profiles were significantly differentiated based on years of education, negative impression management, inconsistent response styles and schizophrenia related concerns. These findings add to the body of research regarding the heterogeneity within neurocognitive diagnoses and provide support for a more nuanced approach to diagnosing and treatment of neurocognitive concerns.

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GENERAL AUDIENCE ABSTRACT

As more people in the United States grow older, neurocognitive disorders are becoming more common and place increasing demands on individuals, families, and healthcare systems. While research has advanced our understanding of these disorders, many studies still treat neurocognitive impairment as a single, uniform condition. When, in reality, people experience cognitive decline in different ways, and this variation can impact diagnosis, treatment, and outcomes. This study aimed to identify subgroups of individuals with distinct patterns of cognitive functioning using a latent profile analysis. Five unique cognitive profiles were identified, ranging from broad impairments to areas of preserved or strong functioning. These profiles also differed based on several factors, including years of education, personality characteristics, sleep difficulties. The findings support the idea that cognitive concerns do not follow a one-size-fits-all pattern and highlight the value of tailoring assessment and intervention strategies to individuals' specific cognitive and psychosocial profiles.

Acknowledgements

To my family, who have always supported me. To my mother, María, for your dedication to education and for instilling in me a lifelong curiosity for knowledge. To my father, Germán, for teaching me perseverance and steadfast resolve to do anything I put my mind to.

(Gracias a mi familia por su apoyo incondicional. A mi mamá, María, por su dedicación a la educación y por inculcarme una curiosidad por el conocimiento que me acompañará toda la vida. A mi papá, Germán, por enseñarme perseverancia y la determinación para lograr lo que me propongo.)

To my siblings—what a privilege to have coincided with all of you in this life. From letting me practice cognitive tests on you to sitting through my presentations, your unwavering support has been a pillar throughout this journey.

(A mis hermanes: qué privilegio haber coincidido con ustedes en esta vida. Desde permitirme practicar con ustedes hasta escuchar mis presentaciones, su apoyo incondicional ha sido un pilar durante todo este proceso.)

To my grandparents, who have been my cheerleaders, I will be forever grateful for your love and encouragement. My grandfather hoped to witness this milestone, and though he could not, I carry him with me at this moment.

(A mis abuelos, quienes han sido mis “cheerleaders”, siempre estaré agradecida por su amor y ánimo. Mi abuelo anhelaba presenciar este logro, y aunque no pudo, lo llevo conmigo en este momento.)

I would like to acknowledge my dissertation committee, Dr. John A. Richey, Dr. Ann Sollinger, Dr. Heather Davis, Dr. Meagan Brem, and Dr. Rosanna Breaux, for their time, feedback, and guidance throughout this process. I am also deeply thankful for the mentors and supervisors who have shaped my development as both a clinician and researcher. Dr. Adriene Means-Christensen, Dr. Ann Sollinger, Dr. Lee Cooper, Dr. Rosanna Breaux, Dr. Sagar Lad, Dr. Shawn Mordhorst, and Dr. Justin Gray—thank you

for your guidance, generosity, and commitment to my growth. Your mentorship has left a lasting impact on my training and professional identity.

(Quisiera agradecer a mi comité de disertación Dr. John A. Richey, Dra. Ann Sollinger, Dra. Heather Davis, Dra. Meagan Brem y Dra. Rosanna Breaux, por su tiempo y orientación durante este proceso. Estoy profundamente agradecida con los mentores y supervisores que han guiado mi desarrollo como psicóloga e investigadora. Dra. Adriene Means-Christensen, Dra. Ann Sollinger, Dr. Lee Cooper, Dra. Rosanna Breaux, Dr. Sagar Lad, Dr. Shawn Mordhorst y Dr. Justin Gray, gracias por su guía, generosidad y compromiso con mi crecimiento. Su mentoría ha dejado una huella duradera en mi formación y en mi identidad profesional.)

Thank you for making this challenging path one full of laughter, support, and meaning. I'm deeply grateful in ways words cannot fully express.

(A mis amistades de la escuela graduada: gracias por llenar este camino de risas y apoyo. Les estoy profundamente agradecida, más de lo que puedo expresar con palabras.)

To Nick—thank you for being my anchor throughout this journey. Your unwavering support and belief in me carried me through every part of this experience.

(A Nick—gracias por ser mi ancla durante esta travesía. Tu apoyo incondicional y tu fe en mí me sostuvieron en cada etapa de esta experiencia.)

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List of Abbreviations

Activities of Daily Living.....	ADL
Akaike Information Criterion	AIC
Alzheimer’s Disease	AD
Animal Naming Test	ANT
Beck Anxiety Inventory.....	BAI
Beck Depression Inventory	BDI-II
California Verbal Learning Test – Second Edition	CVLT-II
Controlled Oral Word Association Test.....	COWA
Delis-Kaplan Executive Function System: Verbal Fluency	DKEFS:VF
Diagnostic and Statistical Manual of Mental Disorders	DSM-5
Digits Backward	DB
Digits Forward.....	DF
Frontotemporal Dementia	FTD
Generalized Anxiety Disorder – 7	GAD-7
Geriatric Depression Scale – Short Form	GDS-15
Hopkins Verbal Learning Test – Revised	HVLT-R
Instrumental Activities of Daily Living.....	IADL
Latent Class Analysis	LCA
Latent Profile Analysis.....	LPA
Lewy Body Dementia	LBD
Lo-Mendell-Rubin Test	LMR
Mild Cognitive Impairment	MCI
Neurocognitive Disorders.....	ND
Patient Health Questionnaire – 9.....	PHQ-9
Personality Assessment Inventory	PAI
Primary Progressive Aphasia	PPA
Repeatable Battery for the Assessment of Neuropsychological Status	RBANS
Rey Auditory Verbal Learning Test	RAVLT
Size-Adjusted Bayesian Information Criterion	SABIC
Trail Making Test A	TMT-A
Trail Making Test B.....	TMT-B
Vascular Dementia	VD
Wisconsin Card Sorting Test.....	WCST

Introduction

The United States population is becoming increasingly skewed, with older generations consistently making up the bulk of the total US population (Ortman et al., 2014). This trend is accompanied by an increase in costs associated with the care of older adults, specifically related to neurocognitive disorders, particularly dementia (Aranda et al., 2021; Cantarero-Prieto et al., 2020; Chen et al., 2023; Jutkowitz et al., 2017; World Health Organization (WHO), 2023). Dementia is one of the leading concerns for older populations; Alzheimer's disease is the seventh leading cause of death and often leads to increased societal costs due to disability and dependency (Centers for Disease Control and Prevention (CDCP), 2021; Prince et al., 2015). Furthermore, the WHO (2023) reported that dementia¹ costs an estimated \$1.3 trillion globally in 2019, and these costs are projected to increase to \$2 trillion by 2030 (Prince et al., 2015). Therefore, elucidating the nature and course of neurocognitive disorders is important to proactively and effectively intervene. Despite this need, research evaluating subtypes of neurocognition is limited and constitutes a gap in our understanding of the heterogeneity in the clinical presentation of neurocognitive disorders. Addressing this gap may improve our current one-size-fits-all approach, which potentially hinders patient care, is a barrier to early intervention, and delays research progress in understanding disease presentation and treatment development. Accordingly, the purpose of this study is to use latent profile analysis (LPA) to empirically identify neurocognitive profiles among an adult patient population with cognitive concerns, potentially offering a more precise classification of these disorders than is currently available using traditional statistical methods.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) classifies Neurocognitive Disorders (ND) based on cognitive and functional changes (e.g., instrumental activities of daily living (IADLs) or basic activities of daily living (ADLs; APA, 2013). However, research regarding subtypes of neurocognition is limited and does not specifically assess the inherent heterogeneity in the clinical presentation of these disorders (Cohen-Mansfield, 2000; Mayeux et al., 1985). Further, our understanding of subtle variations in cognitive functioning (e.g., attention, memory, language) both within individual neurocognitive profiles and across

¹ Dementia and Neurocognitive disorders are used interchangeably in the field.

different neurocognitive disorders is limited. Extant research underscores the importance of early and accurate diagnosis to optimize the effectiveness of timely interventions that limit disease progression, such as medication (i.e., acetylcholine inhibitors), which are most effective in maintaining function when prescribed early into the disorder's progression (Dubois et al., 2016; Prince et al., 2015; Robinson et al., 2015; Shah et al., 2016; WHO, 2017). Notably, not only does the DSM-5 classify these disorders, but there are also workgroups specific to the 'diagnostic concerns' etiology that have worked on elucidating the characteristics of each concern. Elucidating this heterogeneity in disease presentation, functional abilities, and cognitive profiles may enhance our understanding of neurocognitive disorders, inform timely interventions, and potentially guide the development of new treatments. However, the persistent knowledge gap regarding the specific neurocognitive factors contributing to disease progression continues to hamper patient care, intervention efforts, and the identification of underlying mechanisms associated with each disorder.

Diagnostic criteria for Neurocognitive Concerns and Disorders

Neurocognitive disorders include broad classes of neurological impairments and can vary widely in their expression but are generally classified into categories of Mild Neurocognitive Disorders (Mild ND) and Major Neurocognitive Disorders (Major ND; APA, 2013). These neurocognitive disorders are clinically defined in terms of mild to severe changes to cognition and the independent function of an individual. Changes in cognition are defined as cognitive changes usually above 1.5 standard deviations from age- and education-adjusted norms (Petersen et al., 1999; Petersen et al., 2001). Functional changes are defined as changes to activities of daily living (ADLs; e.g., ambulating, feeding, dressing, personal hygiene, continence, and toileting; Katz, 1983) and instrumental activities of daily living (IADLs, e.g., cleaning, managing money, managing medications, preparing meals, grocery shopping, and transportation; Cahn-Weiner et al., 2002). As such, neurocognitive disorders are defined by the level of cognitive and functional impairment.

Mild ND, also known as Mild Cognitive Impairment (MCI) in the literature, is related to cognitive performance that falls 1-2 standard deviations (SD; Luck et al., 2017) from age-, sex-, education-specific norms accompanied by minimal functional changes in ability to perform ADL/IADLs (e.g., ambulating, feeding, managing finances, or meal preparation [APA, 2013; Petersen et al., 2001; Petersen, 2004; Winblad et al., 2004]).

Conversely, major ND is related to significant changes in cognition (≥ 2 SD; Luck et al., 2017) and inability to independently perform ADL/IADLs (APA, 2013). The severity of these changes is captured with severity specifiers: Mild (e.g., requiring assistance with IADLs, such as managing medications), Moderate (e.g., difficulties with ADLs, feeding, or bathing), and Severe (e.g., fully dependent on IADLs and ADLs; APA, 2013). Moreover, Major ND can also be associated with behavioral changes such as apathy and mood disturbances. The research underscores the significance of defining clear cut-off points in standard deviations (SDs) to delineate cognitive decline. However, it is important to acknowledge that current diagnostic guidelines do not specify these cut-offs or levels of cognitive decline necessary for each diagnosis. While this flexibility allows providers to assess cognitive and functional changes concurrently, it can also lead to varying thresholds for diagnosing these concerns among practitioners.

Mild ND increases the risk of an individual developing Major ND (Bruscoli & Lovestone, 2004; Morris et al., 2001; Petersen et al., 2001; Winblad et al., 2004). Mild ND is typically categorized into two main categories: amnesic or non-amnesic and single or multiple domains (Petersen, 2003; Petersen, 2004). Amnesic refers to primarily having memory issues, while non-amnesic refers to a lack thereof (Petersen, 2003; Petersen, 2004). Still, in non-amnesic cases, one or more cognitive abilities may be impaired (e.g., language, visuospatial abilities, executive functioning). Meanwhile, the additional terminology of “single” or “multiple” impaired domains refers to whether an individual has impairments in one area of cognition (e.g., executive functioning, memory, language) or more (Petersen, 2003; Petersen, 2004). Within these complex presentations, there are a variety of combinations within which cognitive concerns can be present. For example, an individual can be both amnesic and have multiple impaired domains. Conversely, individuals can solely present with memory concerns and perform intact in other domains. Additionally, neurocognitive concerns are also clinically categorized based on neurological etiology (e.g., Alzheimer’s disease, vascular dementia, Lewy body disease). This data provides insight into the current subgrouping efforts within Mild ND, which represents a commonly assessed transitional stage between normal aging and more severe neurocognitive decline. Moreover, the increased risk of individuals with Mild ND progressing to Major (ND), as highlighted in the subsequent discussion, underscores the clinical

relevance of understanding and identifying Mild ND/MCI within the broader context of neurocognitive disorders.

Mild and Major Neurocognitive Disorders in Neuropsychological Testing

Aside from differences in core diagnostic criteria, these impairments and disorders are grouped according to etiology. The most diagnosed etiologies include Alzheimer's Disease, Vascular disease, Frontotemporal degeneration, Lewy bodies, and mixed etiologic dementias (Bhogal et al., 2013). There are other less common etiologies, such as neurocognitive disorders due to Prion's disease, Human Immunodeficiency Virus, Huntington's disease, and Parkinson's disease. These concerns are identified based on the combination of neuroimaging and the results of a neuropsychological evaluation assessing attention, memory, language, visuospatial, and executive functioning. While these concerns are associated with specific presentations in neuropsychological testing, heterogeneity in cognitive presentation is common and can deviate from the neurocognitive patterns presented below (Cohen-Mansfield, 2000; Mayeux et al., 1985).

Alzheimer's Disease

The current data on Alzheimer's Disease (AD) highlights cognitive changes related to brain shrinkage and an abnormal level of amyloid plaques (Coupé et al., 2019; Long & Holtzman, 2019). The neurocognitive profile of AD is characterized by memory impairment, particularly in episodic or declarative memory (e.g., facts or events; Salmon & Cermak, 2000; Weintraub et al., 2012). These impairments are further compounded by difficulty with free recall and recognition across auditory and visual learning (Salmon & Cermak, 2000). Moreover, individuals with AD have an increased likelihood of committing intrusion errors, possibly due to difficulty with inhibitory processes and an inability to use semantic information to encode new information (Delis et al., 1991; Martin et al., 1985; Dallabarba & Wong, 1995; Dallabarba and Goldblum, 1996). Additionally, AD is associated with changes or impairments to attention and psychomotor abilities (i.e., sustained, divided, and selective; Berardi et al., 2005; Bublak et al., 2011; Chau et al., 2015; McGuinness et al., 2010; Perry & Hodges, 2000; van Kan et al., 2017). Regarding Language, AD can lead to several language-related difficulties in confrontational naming and semantic (e.g., naming words based on a category) and phonemic fluency (e.g., naming words beginning with a specific letter; Henry et al., 2004; Taler & Phillips,

2008). AD can also lead to impairments in executive function as the disease progresses. Specifically, individuals with AD can often have difficulty with executive function inhibitory, attentional, and visuospatial aspects (Allain et al., 2013; Amieva et al., 2004; Bondi et al., 2002; Perry & Hodges, 2000). Difficulties with visuospatial abilities can also arise early into the disease due to changes in the parietal lobe, which can be uniquely affected by AD (Harciaiek & Jodzio, 2005; Quental et al., 2013). In summation, AD is primarily characterized by memory impairments that do not benefit from cuing and can be associated with impairments across neurocognitive domains (i.e., attention, language, and executive functioning).

Vascular Dementia

Vascular Dementia (VD) can be caused by reduced blood flow to the brain or cerebral vascular injury (e.g., white matter disease, brain infarcts, or strokes). The location of these strokes can vary widely, and therefore, VD presents variably in neuropsychological testing, as the cognitive deficits are highly variable, asymmetrically distributed, and dependent on where the vascular injury occurred (Jellinger, 2013). However, VD is often associated with difficulties in executive function, which encompass a wide variety of cognitive skills such as planning, working memory, problem-solving, inhibition, and task switching. (Gorelick et al., 2011). These difficulties with executive functioning can lead to difficulties in other domains, such as attention, language, and visuospatial ability (Heyanka et al., 2010; McGuinness et al., 2010; Ying et al., 2016). Attention and psychomotor slowing can be additional impaired domains within this population (McGuinness et al., 2010; van Kan et al., 2017). Regarding language, individuals with VD can also have difficulties with verbal fluency tasks (Yuspeh et al., 2002), possibly due to difficulties implementing effective retrieval strategies (Heyanka et al., 2010). Visuospatial abilities can also be affected; however, these are largely dependent on the location of the infarct and can be more indicative of executive dysfunction due to difficulty planning rather than visuospatial impairments (Ying et al., 2016). Patients with VD can also exhibit difficulties with memory retrieval; however, they tend to benefit from cuing and can recognize information better than patients with AD (Suades-González et al., 2009). Overall, the neurocognitive profile of VD is dependent on the location of the stroke, which underscores the inherent variability within this diagnosis. However, even with this variability, VD is heavily associated with difficulties in executive function.

Frontotemporal Dementia

Frontotemporal dementia (FTD) refers to a type of dementia that results in frontal and temporal lobar atrophy. FTD is characterized primarily by progressive changes in behavior and personality (e.g., inappropriate statements or actions), along with changes to language and cognition (Hou et al., 2004; Yeaworth & Burke, 2000). Frontotemporal dementias can be further subtyped into behavior and language variants. Behavioral aphasia is related to personality changes, apathy, impulsivity, and increased inappropriate social behavior and judgment (Piguet & Hodges, 2013). The language variants are further classified into non-fluent primary progressive aphasia (PPA), semantic progressive aphasia, and logopenic progressive aphasia (Gorno-Tempini et al., 2011).

In neuropsychological testing, individuals with FTD can present with memory concerns, associated with impulsive responding or a failure to monitor performance rather than an inability to learn new information (Hou et al., 2004). This tendency is observable during testing, as performance typically improves with cues (Hou et al., 2004). Executive functioning difficulties (e.g., poor planning, problem-solving difficulties, set-shifting) also arise for people with FTD (Carlin et al., 2000; Duara et al., 1999; Hou et al., 2004; Miller et al., 2003; Perry & Hodges, 2000; Rahman et al., 1999). Attention can also be affected and often results in stimulus boundness (i.e., attention becomes fixated on the most compelling stimulus; Attix & Welsh-Bohmer, 2006; Heilman & Valenstein, 2003; Sieroff et al., 2004). Visuospatial abilities can be relatively spared in patients with FTD; however, these can appear to be affected if how they are tested involves executive functioning skills. Moreover, these concerns are associated with nuanced difficulties with language as thoroughly posed, most recently by Gorno-Tempini and colleagues (2011). More specifically, a clinical diagnosis of non-fluent PPA necessitates at least one of these two criteria: (a) agrammatism in language production (e.g., problems with grammatical morphemes, short sentence length, difficulties with sentence construction; Almagro et al., 2005), (b) speech apraxia (e.g., halting speech, sound errors or distortions). The diagnosis also requires at least two out of the three following criteria: (a) reduced comprehension of complex sentences, (b) intact single-word comprehension, and (c) intact object knowledge. A clinical diagnosis of semantic PPA involves impaired confrontation naming *and* impaired single word comprehension. Additionally, at least three of the following criteria must be present: (a)

impaired object knowledge, (b) dyslexia or dysgraphia, (c) intact repetition, and (d) intact speech production. Lastly, a clinical diagnosis of logogenic PPA involves difficulties in sentence and phrase repetitions and single-word retrieval for naming and spontaneous speech. It also involves three out of four the following criteria: (a) errors in spontaneous speech and naming, (b) intact single-word comprehension and object knowledge, (c) intact motor production of speech, and (d) absence of agrammatism in language production. Due to these difficulties with language, FTD is also associated with difficulties with verbal fluency (Hodges et al., 1999; Pasquier et al., 1995; Rosen et al., 2004; Wicklund et al., 2007). While neuropsychological testing is important, the assessment of FTD can also benefit from observational data. For example, individuals with non-fluent aphasia may exhibit visible difficulties with language production as it relates to the motor component of speech. In essence, FTD is primarily characterized by reduced language and executive functioning abilities and can be accompanied by changes in attention, whereas visuospatial abilities can be relatively unaffected.

Lewy Body Dementia

The core features of Lewy Body Dementia (LBD) are fluctuations in cognition, recurrent visual hallucinations, and motor parkinsonism (e.g., rigidity, bradykinesia, resting tremors, loss of postural reflexes; Gelb et al., 1999; Outeiro et al., 2019). LBD can also be characterized by REM sleep behaviors (McKeith et al., 2017). The available neuropsychological data suggests that individuals with LBD can present with difficulties within several cognitive domains. LBD can result in impairments in attention, which results in one of the core aspects of LBD, which is fluctuations in cognition and attention (Ballard et al., 2001; Hansen et al., 1990; Walker et al., 2000).

Furthermore, notable alterations in visuospatial and constructional tasks are often present and warrant vigilant monitoring, as they may signify the potential development of hallucinations (Oda et al., 2009). Specifically, the perception of visual stimuli and visual organization may be impaired (Oda et al., 2009). Individuals with LBD do not always present with memory difficulties, but when they do, it is commonly visual or semantic (Lambon Ralph et al., 2001; Oda et al., 2009). Executive functioning can also be impaired, specifically deficits in working memory, inhibitory control, cognitive flexibility, and set-shifting (Johns et al., 2009). Regarding language, confrontational naming and verbal fluency can be impaired, likely as a result of

difficulty processing visual stimuli and the inability to employ the executive functioning skills needed to perform verbal fluency tasks (Metzler-Baddeley, 2007; Williams et al., 2007). LBD is mainly associated with marked impairments in attention, executive functioning, and visuospatial abilities. Impairments in other areas can occur but these are usually secondary to these deficits.

Healthy Aging

In contrast to the cognitive disorders discussed previously, healthy aging is characterized by relatively preserved and stable performance, particularly in crystallized intelligence tasks which tend to remain stable into adulthood (Schaie & Willis, 1993). While aging is associated with mild declines in processing speed, working memory, and some aspects of executive function, these changes tend to be subtle in nature, occur gradually, and do not interfere with daily functioning (Bopp & Verhaeghen 2009; Eckert et al., 2010). Research is mixed regarding language fluency, as some suggests that semantic fluency tends to remain stable while phonemic fluency has minor declines (Foldi et al., 2003; Kemper & Sumner, 2001; Troyer et al., 1997; Troyer 2000), and other research suggests phonemic fluency is stable while semantic fluency demonstrates minor declines (Loonstra et al., 2001; Rodriguez-Aranda & Martinussen, 2006). Both of these findings are believed to be at least partially due to a reduced both processing speed abilities (Bryan et al., 1997). Additionally, while attentional abilities are generally maintained, there is evidence that individuals experience more difficulties with divided attention and sustained attention as they age (Craik & Rose, 2012). Lastly, healthy adults often show preserved memory performance as they age. Particularly, when tasks provide environmental support or involve meaningful, well-learned content (Craik & Rose, 2012; Prince et al., 2024).

Prior Work Evaluating Heterogeneity in Neurocognitive Disorders

Heterogeneity in the ND field is a long standing and widely recognized concern (Cohen-Mansfield, 2000; Mayeux et al., 1985). The heterogeneity within dementia is believed to result from several different sources: genetic, biological, medical, psychosocial, and environmental (Cohen-Mansfield, 2000). These factors are further compounded by predisposing factors, lifetime events, and current functioning and are believed to result in the cognitive, behavioral, and functional manifestation of NDs (Cohen-Mansfield, 2000). The lack of research into the variability within and between types of dementia presentations has led to several problems

identified by experts in the field. Verdi and colleagues (2021) reported that the inability to incorporate heterogeneity into the statistical models used to analyze dementia populations may have affected our ability to fully understand the mechanism of etiology and, further, may have slowed the development of effective treatments. Moreover, Ramirez-Gomez et al. (2017) highlighted the importance of understanding and parsing out the heterogeneity at an individual level as it has important repercussions from a prognosis perspective (e.g., VD has a higher rate of morbidity and mortality and is associated with increased healthcare costs; Levine & Langa, 2011). It has also been recognized that without identifying the phenotypic heterogenic presentation of dementia, we will continue to be unable to detect key traits that vary by subgroup and can further inform etiology, treatment, progression, and mortality (Cohen-Mansfield, 2000; Perrault et al., 2000).

Prior work has sought to understand the heterogeneity in ND from a neuroimaging perspective, including work focusing on within-subgroup variability. Some have proposed that structural or neuroanatomical variability could be used to assess the heterogeneity in dementia (Verdi et al., 2021). In contrast, others have analyzed the heterogeneity in dementia by analyzing cognitive subgroups in MCI, AD/VD, or non-demented populations, which can more directly attune to the difficulties experienced by dementia patients on a day-to-day basis (Boots et al., 2020; Delano-Wood et al., 2009; Eppig et al., 2017; Lamar et al., 2021; Liew et al., 2018; Thomas et al., 2023). Delano-Wood and colleagues (2009) examined subgroups in a sample of individuals with MCI via Ward's minimum variance cluster analysis and further evaluated the relationship between group membership and white matter lesion (WML) burden. The results revealed three distinct subgroups named after the areas in which they experienced a relative weakness in: (a) memory/language, (b) executive/ processing speed (and visuoconstruction), and (c) pure memory. The groups also had a significant relationship with WML burden. Eppig et al. (2017) examined subgroups using LPA in an MCI sample and found three distinct profiles: mixed impairment MCI, amnesic MCI, and a normal class. Researchers also evaluated cerebrospinal fluid (CSF) biomarkers, genotype, and longitudinal outcomes by profile. Results highlighted that individuals in the mixed and amnesic classes were more likely to have AD alleles and have worse CSF bio markers. There were no significant differences in outcome by profile membership; however, the mixed MCI class progressed to AD more quickly. Thomas et al. (2023) utilized a cluster analysis to examine heterogeneity in early AD and its relationship

to progression in a non-demented population. Researchers identified five subgroups (a) average, (b) low executive, (c) low visuospatial issues, (d) low memory/language, and (e) low on all domains. Individuals with subtle difficulties in memory/language, executive, and visuospatial all declined faster than the average group. Additionally, Libon et al. (2014) conducted a Latent Class Analysis (LCA) in an AD and VD sample and uncovered four subgroups: moderate/mixed dementia, mild/mixed dementia, dysexecutive, and amnesic. Notably, these groups had differing difficulties. Specifically, moderate/mixed dementia had increased difficulties with confrontational naming, verbal fluency, and memory; mild/mixed had lesser difficulties with memory but had notable difficulties with declarative memory. Lastly, the dysexecutive group was notably impaired in executive function measures and mild impairment in other domains.

More broadly, Liew and colleagues (2018) conducted a latent class analysis for individuals with neuropsychiatric symptoms or mild neurocognitive impairment to increase its specificity and predictive ability for neurocognitive disorders. Their results revealed four distinct subtypes: (a) individuals with no significant deficits or neuropsychiatric symptoms, (b) individuals with only neuropsychiatric symptoms, (c) individuals with only cognitive deficits, and (d) individuals with both neuropsychiatric symptoms and cognitive deficits. Each subtype also had different risk levels of progressing to a Mild ND; subtypes a and b had the lowest risk, subtype c had moderate risk, while subtype 4 had the highest progression risk.

Additional research has explored subgroup distinction within a non-demented population and their association with lifestyle factors (Boots et al., 2020; Lamar et al., 2021). These classifications are based on six distinct cognitive metrics encompassing language proficiency, memory retention, working memory capacity, and executive functioning. Through a comprehensive analysis employing LCA and LPA, the research identified four discernible subgroups: high-average cognition, average cognition, decreased memory, and decreased executive functioning. Boots and colleagues (2020) assessed the effects of dietary habits and physical activity on subgroup allocation. Notably, adherence to a Mediterranean diet emerged as a significant determinant of profile membership, with individuals in the high-average cognition group demonstrating increased adherence to this dietary regimen. Conversely, the study found no significant relationship between sedentary behavior or

physical activity levels and subgroup classification. Lamar et al. (2021) expanded on this research and uncovered a relationship between the lower executive function subgroup and elevated glucose and A1C levels.

Moreover, depression, anxiety, personality, and other factors, such as sleep and pain, could contribute to the heterogeneity seen within this population. Previous research in mental health and neurocognition highlights ways in which depression and anxiety can differentially affect cognition (Kriesche et al., 2023). Acute depressive symptoms can contribute to deficits in attention, executive function, and learning/memory (Kriesche et al., 2023; Rock et al., 2014; Snyder 2013). These deficits are often present, although less pronounced, even once the person has entered remission from their depressive symptoms, along with deficits in working memory (Kriesche et al., 2023). Similarly, research regarding the effect of anxiety on neurocognitive performance has found it is also related to deficits in verbal memory, attention, and aspects of executive functioning (i.e., working memory; Dorenkamp & Vik, 2018). Limited research has evaluated the relationship between personality and neurocognitive performance past trait-based personality scales (e.g., Big Five Personality Inventory, Five-factor model; Chapman et al., 2017; Sutin et al., 2019). Aikman and Souheaver (2008) assessed the relationship between the Personality Assessment Inventory (PAI) and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), revealing a negative correlation between the Somatic Complaints scales of the PAI and the memory scales of the RBANS. Moreover, lower scores on the somatic complaints, depression, and borderline features scales were significantly associated with improved performance on an attention task. Conversely, Rosselli and colleagues (2001) evaluated the associations between personality profiles and neuropsychological performance in a psychological sample and found no significant associations.

Regarding other physical factors such as pain and sleep, research has found that chronic pain significantly affects neurocognition. Specifically, the experience of chronic pain can result in marked impairment or deficits in the following areas: memory and attention (Berryman et al., 2014; Moriarty et al., 2011). Chronic pain can also result in deficits in measures of executive functioning (i.e., working memory, executive control, mental flexibility, and set shifting; Berryman et al., 2014). However, the research regarding these effects is mixed (Higgins et al., 2018). Sleep difficulties can also affect neurocognition depending on the individual's sleep needs (Alhola & Polo-Kantola, 2007). Generally, inadequate sleep can result in deficits in attention and working

memory, an area of executive function (Lim & Dinges 2010; Killgore 2010; Lowe et al., 2017). Sleep difficulties can also contribute to long-term verbal memory difficulties, and individuals often have impaired free recall with generally intact recognition (Drummond et al., 2000). The effects of these factors on cognition are widely accepted. However, the data remains unclear on the extent of the effects these factors can have on cognition.

Prior work has robustly acknowledged the heterogeneity within neurocognitive disorders and has focused on identifying subgroups within specific populations, such as MCI, AD, VD, and non-demented groups. To date, no research has comprehensively and systematically evaluated heterogeneity in a neuropsychological sample with a broader mix of neurocognitive concerns and diagnoses. Accordingly, the research proposed here seeks to critically evaluate heterogeneity within and between neurocognitive profiles using quantitative methods aimed at creating subgroups of ND based on cognitive profiles. The long-term goal of this research program is to further clarify the heterogeneity within neurocognitive concerns in clinical populations, potentially leading to more targeted diagnostic and treatment approaches for individuals with differing cognitive profiles. Our central objective in the current project, which is a first step in pursuit of this goal, is to use latent profile analysis (LPA) to identify the cognitive profiles associated with neurocognitive disorders, aiming to pinpoint characteristics that are *most discriminative* in diagnosing specific conditions such as vascular dementia and Alzheimer's disease. The overall working hypothesis that drives the work outlined in this proposal is that mild ND and major ND can be distinguished based on neurocognitive domains such as attention, memory, executive function, and language.

The over-arching aim of the research outlined in this proposal is to use LPA to identify distinct cognitive profiles in a clinical population with neurocognitive concerns. LPA is a data-driven approach used to identify subgroups of individuals based on common factors among quantitatively distinct subgroups. The current study seeks to employ LPA to characterize the similarities within and differences between groups based on several neurocognitive domains (i.e., memory, attention, language, executive functioning, and visuospatial abilities). It is expected that there will be distinct cognitive profiles within the clinical population characterized by significant performance differences across neuropsychological domains. For example, a primarily amnesic profile similar to what is expected with AD or a profile with language and executive function impairments reminiscent of FTD. Additionally, we will determine the relationship of depression, anxiety, personality scales (i.e., somatic

complaints, anxiety, depression, mania, paranoia, schizophrenia, borderline features, antisocial features, alcohol problems), and other nonspecific factors (i.e., pain and sleep) on cognitive profile membership. We hypothesize that the clinical scales will be significantly associated with cognitive profile membership. Specifically, higher scores on measures of depression, anxiety, specific personality scales (e.g., Somatic Complaints, Anxiety, Depression, and Borderline Features), and the presence of sleep difficulties and chronic pain will be associated with membership in cognitive profiles characterized by greater cognitive impairment. Lastly, the clinical diagnostic distribution of all profiles generated by the LPA will be evaluated. By identifying distinct cognitive profiles that differentiate between various neurocognitive impairments, the study will allow neuropsychologists to improve their understanding of neurocognitive impairment presentations. Ultimately, outcomes of this work may lead to improvements in the quality of life for individuals with these conditions by implementing more tailored interventions and earlier diagnoses. These objectives and hypotheses are summarized here as the following three specific AIMS:

AIM 1: Identify distinct cognitive profiles in a clinical population with neurocognitive concerns using latent profile analysis (LPA) based on a comprehensive battery of neuropsychological tests, including attention, executive functioning, memory, and language.

Hypothesis 1: We hypothesize that LPA will reveal the presence of distinct cognitive profiles within the clinical population, characterized by significant differences in performance across the neuropsychological domains (i.e., attention, executive functioning, memory, and language).

AIM 2: Determine whether profile membership is differentially associated with psychological (i.e., depression, anxiety, and personality) and physical factors (i.e., sleep difficulties and chronic pain).

Hypothesis 2: We hypothesize that higher scores on measures of depression, anxiety, and personality scales (e.g., Somatic Complaints, Anxiety, Depression, and Borderline Features) and reports of sleep difficulties and chronic pain will be associated with membership in cognitive profiles characterized by marked cognitive impairment.

EXPLORATORY AIM: Assess the diagnostic distribution of the cognitive profile generated by the LPA.

Method

Procedures and Participants

The Neuropsychology Department at the Carilion Clinic received IRB approval to develop a data repository of prospective and previous patients. An additional IRB specific to this study and its aim was also submitted and approved. The IRB provided a waiver of consent for patients assessed within the following dates: 01/01/2018 until 2/1/2024. Conversely, patients assessed after 2/1/2024 provided informed consent to be included in the data repository. The repository of assessment data included all data collected as part of routine clinical care for a neuropsychological evaluation. This included data obtained at the neuropsychological consult and all testing data. The data collected included several measures of IQ, performance validity, motor skills, visuospatial skills, language functioning, learning and memory, executive functioning, mood, behavior, psychological functioning, and final diagnoses. These measures raw and standardized scores were collected. The collected data also included clinical information available in the neuropsychological report, such as reports of chronic pain, sleep concerns, and final diagnoses.

Participants were 421 adults 60.6 % of which identified as female. The racial sample included 92.8% participants who identified as White, 5.7% who identified as Black, 1.2% who identified as Asian, and 0.2% who identified as biracial. Regarding ethnic breakdown, 98.6% the sample did not identify as Hispanic or Latine whereas 1.2% identified as Hispanic or Latine and .2% identified as Caribbean. The average age of the sample was 51.97 (SD = 11.17) and the average years of education were 14.10 (SD = 2.64). Lastly, 67.2% of the sample endorsed experiencing sleep difficulties and 38.4% endorsed experiencing chronic pain. See Table 1 for a summary of sample demographics.

Measures

The proposed study assessed four cognitive areas: attention, memory, executive functioning, language and all variables were entered individually. See Independent Variables: Cognitive Measures section for a list of measures included in the LPA. **All variables were converted to z-scores for consistency within the LPA.** The third step of the LPA included psychological measures of depression, anxiety, personality, and physical factors

that can affect cognition (e.g., sleep and pain). See the Dependent Variables: Psychological and Physical Measures section. Refer to Table 2 for a visual aid of these measures. Refer to Table 3 for a detailed overview of each measure, along with the corresponding number of participants who completed the measure.

Independent Variables: Cognitive Measures

Attention

Trail Making Test A (TMT-A; Reitan & Wolfson, 1986). The TMT-A is a test measure of complex attention in which participants draw lines on a page connecting numbers 1 through 25 in sequential order. This test is primarily used to measure attention, although it also involves components of numerical sequencing, visuomotor speed, and visual search. The test is scored for time, which includes any corrections the examiner must make. The number of errors is also recorded. This test can be administered to individuals ages 18 to 89 years. Raw scores are converted into t-scores using Halstead-Reitan Battery (HRB) norms.

Digits Forward (DF; Weschler, 2008). Digits forward is a portion of the Digit Span test on the Wechsler Adult Intelligence Scale-IV (WAIS-IV). DF requires participants to repeat an increasingly longer series of digits in the order they are presented. DF measures simple attention and auditory processing (Groth-Marnat, 2009; Sattler & Ryan, 2009). Raw scores are converted into scaled scores using Weschler norms.

Executive Functioning

Trail Making Test B (TMT-B; Reitan & Wolfson, 1986). TMT-B is a timed test for individuals aged 18 through 89 in which participants connect numbers and letters on a page in alternating sequential order (e.g., 1-A-2-B-3-C). TMT-B assesses aspects of executive function, including executive control, mental flexibility, and set shifting (Arbuthnott & Frank, 2000; Ciolek & Lee, 2020). Individuals are scored based on time, which includes any corrections, and total number of errors are recorded. T-scores are calculated using HRB Norms based on the time required to complete the task.

Digits Backward (DB; Weschler, 2008). DB is the second portion of the Digit Span subtest on the WAIS-IV. This task requires participants to repeat back increasingly longer strings of numbers in backward order. This test measures aspects of executive functioning such as mental flexibility, and the ability to form and

maintain mental images based on an auditory stimulus (Lezak, 1995; Wielkiewicz, 1990). For this task, raw scores are converted to scaled scores using Weschler norms.

Wisconsin Card Sorting Test (WCST; Heaton et al., 1993). The WCST is a test in which participants are asked to match a response card to one of four stimulus cards. Both the response and stimulus cards vary in color, shape, and number. The sorting rule (i.e., color, shape, or number) changes after every 10 correct responses and the tests ends once all cards have been sorted. The variable utilized for this test was perseverative errors (WCST-PE) as it measures cognitive flexibility, an important aspect of executive functioning. The raw scores are converted to t-scores using WCST Norms.

Memory

Memory was assessed by measuring performance on a word list and included variables for immediate recall and delayed recall. Individuals were given different word list tasks based on their demographics.

California Verbal Learning Test – Second edition (CVLT-II; Delis et al., 1987). The CVLT-II is a verbal learning and memory task for individuals aged 16-89. CVLT-II consists of 16 words learned over five trials. These words can be clustered into semantic areas of vegetables, furniture, transportation, and animals. Immediate recall is assessed by totaling the number of words recalled across five trials and converting this score to a z-score. This test contains a second semantically related list, administered once and recalled immediately. After a 20-minute delay, individuals are asked to recall the word list, and this score reflects their delayed recall abilities. The test also includes a recognition portion in which individuals are given related and unrelated words and prompted to answer yes/no if they were on the list they learned. All raw scores are input into the CVLT-II comprehensive scoring system and converted into z-scores.

Hopkins Verbal Learning Test – Revised (HVLT-R; Benedict et al., 1998). HVLT-R is a 12-word verbal learning and memory task for individuals 16-80+ years old. The words are learned over three trials and are semantically related in three categories: animals, gems, and human dwellings. Immediate recall scores are produced by adding recall over the initial three trials. After a 20–25-minute period, individuals are asked to recall the words, and this score is used to assess delayed recall. Recognition is assessed by presenting the participant

with 24 words (12 targets and 12 distractors) and prompting them to answer yes or no if the word was on the list. All scores are converted into demographically corrected t-scores using HVLT norms.

Rey Auditory Verbal Learning Test (RAVLT; Rey 1958). RAVLT is a test involving memory and learning of a sequence of 15 semantically unrelated words across five separate trials for individuals ages 7-89. The scores for the five trials are summed into a total recall score, which produces an immediate memory score. After the five trials, individuals are given a second list, and free recall is assessed. After a 30-minute delay, delayed recall of the original list is assessed by prompting individuals to recall the word list. Afterward, individuals are presented with 24 words and asked whether it was on the list. All raw scores are converted to scaled scores using Ivnik et al., (1990) norms.

Language

Controlled Oral Word Association Test (COWA; Benton et al., 1983; Lezak et al., 2004). COWA is a verbal fluency test designed to assess phonemic fluency. During the phonemic fluency task, individuals are assigned three different letters (F-A-S) and tasked with producing as many words as possible in 60 seconds. Phonemic fluency scores are calculated by adding words produced across the three trials and excluding errors or repetitions. Phonemic fluency scores are calculated by converting the raw score into a t-score using HRB norms.

Animal Naming Test (ANT; Lezak et al., 2004). ANT is a verbal fluency test designed to assess semantic fluency. In 60 seconds, individuals are assigned to produce as many words as possible that fit in specific category (e.g., animals). Scores include the total of correct words produced and exclude any errors or repetitions. This score is converted into a T-score using HRB norms.

Delis-Kaplan Executive Function System (DKEFS: VF): Verbal Fluency (Delis, Kaplan, & Kramer, 2001). The Verbal Fluency task of the DKEFS measures phonemic and semantic fluency. The phonemic fluency task consists of three trials requiring participants to produce words beginning with a different letter. Scores from the three trials are added and converted into scaled scores using DKEFS norms. The semantic fluency task requires participants to produce words across two trials with distinct categories. Scores across both trials are summed up and converted into scaled scores using DKEFS norms. For this study, scores for FAS and Animals were re-normed using the HRB platform.

Dependent Variables: Psychological and Physical Measures

Psychological measures included measures assessing depression, anxiety, and personality. The physical measures included reports of sleep difficulty and chronic pain. See Table 4 for sample means, SD and frequency of endorsement.

Depression

To aid with comparison across measures, scores were categorized into severity ranges following established cutoffs for each measure (i.e., 0 = minimal, 1 = mild, 2 = moderate, and 3 = severe).

Geriatric Depression Scale- Short Form (GDS-15; Sheikh & Yesavage, 1986). The GDS is a 15-item self-report measure used to assess the presence of depression over the past week in adults over 65 years old. The items assess several aspects of depression, such as life satisfaction, feelings of boredom, happiness, helplessness, worthlessness, energy, and hopelessness. These items are rated in a yes or no format. Raw scores are categorized into ranges of minimal/normal (0-4), mild (5-8), moderate (9-11), and severe (12-15).

Beck Depression Inventory (BDI-II; Beck, Steer & Brown, 1996). The BDI-II is a self-report scale assessing depression in the past two weeks with 21 group statements. These items assess a general theme, such as sadness, loss of pleasure, loss of interest, suicidal thoughts or wishes, and loss of energy. The items contain statements that are scored from 0-3. For example, in the sadness theme, answers range from I do not feel sad (0), I feel sad much of the time (1), I am sad all the time (2), I am so sad or unhappy that I can't stand it (3). Raw scores are categorized into ranges of minimal (0-13), mild (14-19), moderate (20-28), and severe (29-63).

Patient Health Questionnaire – 9 (PHQ-9; Kroenke et al., 1999). The PHQ-9 is a self-report measure assessing the presence of depression in the past two weeks with 9 items. The items assess different aspects of depression such as anhedonia, feelings of sadness, difficulty with sleep, fatigue, appetite changes, etc. The items are rated on a 0 (not at all) to 3 (nearly every day) evaluating how often they are bothered by the symptoms. The final item asks the participant to rate (not difficult at all to extremely difficult) how difficult these problems have made it for them to work, complete tasks at home, and engage with others.

Anxiety

Generalized Anxiety Disorder – 7 (GAD-7; Spitzer et al., 2006). The GAD-7 is a self-report 7-item scale used to assess generalized anxiety symptoms in the past two weeks. The items assess how often participants have been bothered by the symptoms in the last two weeks using a 4-point scale ranging from 0 (not at all) to 3 (nearly every day). Raw scores are categorized into minimal anxiety (0-4 points), mild anxiety (5-9 points), moderate anxiety (10-14 points), and severe anxiety (15-21 points).

Beck Anxiety Inventory (BAI; Beck et al., 1988). The BAI is a 21-item self-report evaluating the presence of anxiety and its severity. The items assess physiological (e.g., dizzy/lightheaded, shaky/unsteady, indigestion) and emotional symptoms (e.g., fear of the worst happening, fear of losing control) of anxiety. Items are rated on a 4-point Likert scale ranging from 0 (not at all) to 3 (severely – it bothered me a lot), assessing how much the participant has been bothered by the symptoms in the past month.

Personality

Personality Assessment Inventory (PAI; Morey, 2004). The PAI is a self-report personality test containing 344 items assessing validity, clinical, treatment, and interpersonal domains. Items are rated on a 4-point scale ranging from false (1) to very true (4). For this study, we focused on the validity, clinical, and interpersonal domains. The validity scales of the PAI are inconsistency (i.e., assesses if respondents answer similar questions in different ways), infrequency (i.e., evaluates if respondents endorse rare or unusual statements as true), negative impression management (i.e., assesses if participants describe themselves as overly negative), and positive impression (i.e., evaluate if participants describe themselves in an overly positive or favorable light). The clinical scales of the PAI are somatic concerns, anxiety (i.e., measures general feelings of worry, tension, and nervousness), depression, mania, paranoia, schizophrenia, borderline features, antisocial features. Lastly, interpersonal scales measure two factors: dominance and warmth.

Sleep and Chronic Pain

Experiences of sleep concerns and chronic pain. As part of the interview process in neuropsychological assessment, participants are asked if they experience any sleep or pain problems. As such, the presence of sleep difficulties or chronic pain was coded. Participants were coded as having sleep difficulties

if they had a current insomnia diagnosis, slept under 4 hours a day, slept 5-6 hours or over 8 hours a day and noted fatigue or falling asleep mid tasks, needed sleeping aids (e.g., melatonin or trazadone), or endorsed interrupted sleep with accompanying fatigue. Regarding chronic pain, individuals were coded as having chronic pain if they reported experiencing pain regularly due to a medical health condition (e.g., fibromyalgia), reported being on disability due to pain associated with some sort of injury, reported being on medication for pain control, endorsed chronic pain that interrupted sleep, or had diagnoses of chronic pain syndrome/ chronic back pain. Individuals were coded as 0 (no sleep concerns) or 1 (endorsed sleep difficulties) regarding any sleep concerns. Similarly, individuals were coded as 0 (no chronic pain experience) or 1 (endorsed chronic pain).

Covariates

Demographics. As part of the analysis for Aim 2, the effects of several demographic variables were considered. Specifically, the effects of age, sex, and education were evaluated.

Test type. Coded variables were created to indicate what test each patient received for variables with different measures (i.e., memory, depression, and anxiety). For verbal memory, the word lists were coded accordingly: 1 = CVLT, 2 = HVL, and 3 = RAVLT. This variables was utilized in the second step of the LPA to assess whether they were a significant covariate in determining profile membership. For depression, the measures were coded as 1 = BDI-II, 2 = GDS-15, and 3 = PHQ-9. For anxiety, 1 = BAI and 2 = GAD-7 and were included in the analysis to assess if they were a significant covariate should depression and anxiety arise as significant.

Results

Data Analysis

Latent Profile Analysis

Before conducting three-step LPA (Vermunt, 2010), all variables used in the LPA were assessed for skewness, kurtosis, and multicollinearity, and all values were within the appropriate ranges to conduct an LPA (i.e., skewness > 3, kurtosis > 10, or VIF > 10 values are considered extreme and may distort estimates; Byrne, 2012; Kline, 2011; see Table 5 for values). Additionally, the data available for each variable and covariates were reported in Table 3.

Vermunt's three-step approach involved: (1) developing a latent profile model using the response variables, (2) assigning individuals to profiles based on their posterior membership probabilities, and (3) analyzing the relationship between profile membership and external variables while accounting for classification uncertainty utilizing R3STEP. In this third step, auxiliary variables were entered using the AUXILIARY = varlist (R3STEP) command in Mplus. This method reduces potential bias and preserves the integrity of the profile solution, avoiding the limitations associated with traditional one-step models (Asparouhov & Muthén, 2014a, 2014b; Berlin, Williams, & Parra, 2014; Vermunt, 2010).

Several iterations of the 3-step LPA, differing by the number of profiles, were run to identify the ideal number of profiles within this sample (Lubke & Muthén, 2005; Muthén & Muthén, 1998; Pastor et al., 2007). These models were subsequently evaluated by considering group composition, previous theory and research, profile prevalence and interpretability, and goodness of fit indices. The goodness of fit indices included sample size-adjusted Bayesian Information Criterion (SABIC), Akaike Information Criterion (AIC), Entropy, and Lo-Mendell-Rubin test (LMR) (see Table 6; Akaike, 1987; Celeux & Soromenho, 1996; Sclove, 1987).

The SABIC and AIC are valuable criteria to evaluate the goodness of model fit by considering both log-likelihood and parameter count. The SABIC adjusts for smaller sample sizes (<500) while the AIC does not consider sample size (Akaike, 1987; Henson et al., 2007; Morgan, 2015; Nylund, 2007; Sclove, 1987). Generally, lower SABIC and AIC values indicate a better model fit. The SABIC and AIC values consistently decreased as the number of profiles increased. Additionally, entropy assessed the model's ability to generate heterogeneous profiles and the accuracy of profile membership assignments, with higher entropy values suggesting a more accurate model. Research suggests entropy values at or above 0.76 are related to a 90% correct assignment (Wang et al., 2017) and that models with too high entropy can indicate an over-fit model (Sinha et al., 2022). Entropy values began and ended at 0.83 for the 2-profile solution and the 6-profile solution. Notably, values decreased in the 3- and 4-profile solutions to 0.81 and 0.78, respectively, and increased back to 0.82 with the 5-profile solution. The LMR test assesses whether adding a profile improves model fit. The LMR test was significant for the 2- ($p = 0.00$), 3- ($p = 0.04$), and 5-profile ($p = 0.02$) solutions, indicating that adding a second, third, and fifth profile improved model fit. The 4-profile solution (see Table 7 for profile proportions) was not

significant ($p = .41$). However, when considering this in conjunction with the other model fit indicators (i.e., SABIC, AIC, entropy, and significant LMR values at a 5-profile solution), goodness of fit indices suggested a solution with additional profiles.

The LMR test showed a 6-profile solution was not significant. Additionally, the 6-profile solution had three small profiles only accounting for 9%, 8.5%, and 7.6% of the sample, which led to concerns about replicability and model solution instability (See Table 8 for 6-profile solution proportions; Morovati, 2014; Nylund & Choi, 2018). These findings provided support against a 6-profile solution. When evaluating the proportions of a 5-profile solution, proportions were within expected ranges, with the smallest profile accounting for 8% of the sample, a value that does not raise concerns about replicability or model instability (see Table 9 for 5-profile solution proportions). Additionally, a 5-profile solution had lower SABIC and AIC values, a significant LMR test, and reflected a marked increase in entropy compared to a 4-profile solution. Taken together, these findings supported a 5-profile solution.

Five Profile Model Solution

Once the five-profile solution was selected, each profile's performance on the variables of interest was examined (For profile distribution, see Table 9; for profile performance on variables of interest see Table 10, Figure 1, and Figure 2; for posterior probabilities see Table 11). For profile-specific demographics see Table 12. Information regarding psychological and physical concerns is presented in Table 13. For within profile variable correlations see Table 14.

Within the 5-profile solution, the first profile (P1) was marked by difficulties on specific measures of attention, executive functioning tasks with a psychomotor component (i.e., TMT-A and TMT-B), and measures of immediate memory and delayed memory. Additionally, this profile had the lowest overall scores on most measures, including letter and semantic fluency, and another measure of executive function (i.e., WCST perseverative errors). Notably, this profile did not have the lowest overall scores on Digits Forward or Backward, possibly indicating that the difficulties in attention and executive functioning may be driven by psychomotor slowing. As such, this profile was labeled as *the broadly impaired profile, marked by memory impairments and psychomotor slowing*.

The second profile (P2) within the 5-profile solution did not display any values above or below a standard deviation of the sample. However, this profile had the lowest overall scores on measures of attention and executive function (i.e., DF and DB). This profile also had the second lowest overall scores on measures of attention and executive function with a psychomotor component (i.e., TMT-A and TMT-B), perseverative errors, and measures of language fluency. Notably, P2's immediate and delayed memory scores were in the middle of the distribution among the five profiles, suggesting that its memory performance was somewhat average relative to other profiles. Overall, when compared to other profiles, this profile was marked by weaknesses in simple attention and auditory processing and aspects of executive functioning related to mental flexibility and the ability to form and maintain mental images from auditory stimuli. Given these patterns of performance, this profile was called *the mildly impaired profile with attention, executive function, and language weaknesses*.

The third profile (P3) had broadly average scores with scores on attention, executive function, and language fluency falling in the middle of the distribution. Notably, P3 had the second-lowest scores on memory out of all profiles and their scores on verbal measures of attention and executive function were the second highest although broadly average. This profile was referred to as *the average performance profile with slight memory difficulties*.

The fourth profile (P4) was characterized by scores within normal limits on measures of attention, executive function, and language fluency. Notably, despite having largely average scores, P4's scores on DF and DB were slightly *lower* than P3. Additionally, P4 had the overall second-highest memory scores out of all profiles. Taking into account this profile's pattern of weaknesses and strengths, this profile was called *the moderately strong executive function and memory profile*.

The fifth profile (P5) was characterized by having the highest scores across domains, with a particular sample level strength (> 1 SD) on DF, DB, and immediate memory. Overall, this profile demonstrated consistently strong performance across domains with population- and individual-level strengths in working memory and the memory domain. As such, this profile was called *the high-performing memory and executive function profile*.

Associations between profile membership and covariates

As mentioned previously, Aim 2 was to assess the relationship between profiles and covariates of interest. These covariates included demographic variables (e.g., sex, race, ethnicity, years of education), psychological variables (i.e., depression, anxiety, personality), and physical variables (i.e., sleep difficulties and chronic pain). The hypothesis driving this aim stated that profiles with marked cognitive impairment would be significantly associated with higher scores on depression, anxiety, personality, and higher reports of sleep difficulties and chronic pain. Of note, cases with missing data were excluded via listwise deletion, resulting in a final sample of $N = 268$ for these analyses.

This aim was assessed via step 3 of the 3-step LPA, in which the relationship between profile membership and external variables was examined while accounting for profile classification uncertainty. This method utilizes a multinomial logistic regression using the R3STEP method to examine whether select variables differentiated profile membership in the 5-profile solution. This method can also assess if specific variables had a significant predictive relationship with a specific profile even if the variables did not have a significant relationship with other profiles.

Notably, differences in memory tests were not significant among profiles. Regardless, profile specific data for memory tests administered are summarized on Table 13. There were no significant findings regarding the associations between profile membership and demographic variables, such as race and ethnicity, which was not unexpected, given the homogeneity. There were also no significant findings regarding sex. However, years of education was a significant predictor of profile membership.

P1 ($M = 12.56$; $SD = 2.6$) had significantly lower educational attainment when compared to P3 ($M = 14.00$, $SD = 2.48$; $\beta = -1.022$, $p = .010$, $OR = 0.365$, 95% CI [0.122, 1.092]) and P4 ($M = 14.18$, $SD = 2.39$; $\beta = -0.880$, $p = .023$, $OR = 0.414$, 95% CI [0.141, 1.276]). Additionally, P5 ($M = 15.91$, $SD = 2.34$) had significantly higher educational attainment than P1 ($\beta = 1.269$, $SE = 0.409$, $p = .002$, $OR = 3.469$, 95% CI [1.139, 10.562]). P3 ($\beta = -0.247$, $p = .028$, $OR = 1.281$, 95% CI [1.028, 1.595]) and P4 ($\beta = -0.389$, $p = .001$, $OR = 1.476$, 95% CI [1.167, 1.853]) had significantly lower years of education in comparison to P5.

Similarly, neither anxiety nor depression was significantly associated with profile membership within the LPA. Notably, differences in the type of anxiety or depression measures administered had no effect on profile membership. Additionally, it is worth noting that a limited number of individuals in this sample had an anxiety measure included as part of their neuropsychological assessment ($N=164$) which may have limited our ability to detect a significant relationship between anxiety and profile membership.

P1 had 16 out of 36 datapoints available for anxiety measures (*BAI*: $N = 5$, $M = 28$, $SD = 14.46$; *GAD-7*: $N = 11$, $M = 12.36$, $SD = 5.51$). P2 had 33 out of 84 datapoints (*BAI*: $N = 10$, $M = 20.30$, $SD = 16.06$; *GAD-7*: $N = 23$, $M = 6.26$, $SD = 5.37$). P3 had 37 out of 95 datapoints (*BAI*: $N = 16$, $M = 23.44$, $SD = 15.60$; *GAD-7*: $N = 21$, $M = 6.62$, $SD = 6.04$). P4 had 48 out of 151 datapoints (*BAI*: $N = 33$, $M = 16.79$, $SD = 10.92$; *GAD-7*: $N = 15$, $M = 7.93$, $SD = 6.51$). P5 had 30 out of 55 datapoints (*BAI*: $N = 15$, $M = 17.07$, $SD = 9.68$; *GAD-7*: $N = 15$, $M = 7.33$, $SD = 5.08$).

To aid in interpretability, scores across anxiety measures were converted into minimal, mild, moderate, and severe. In P1, 11.1% endorsed minimal anxiety, 8.3% endorsed mild or moderate, and 13.9% endorsed severe. For P2, 16.7% reported minimal, 7.1% mild, 11.9% moderate and 3.6% severe anxiety. In P3, 10.5% reported minimal anxiety, 11.6% mild, 9.5% moderate, and 7.4% severe. P4 showed similar rates of mild (6.0%) and moderate (6.6%) anxiety, with 11.3% reporting minimal and 7.9% reporting severe anxiety. P5 had higher proportions of minimal (16.4%), mild (12.7%), and moderate (18.2%) anxiety, with 7.3% severe anxiety.

Conversely, while most participants had a depression questionnaire, depression did not significantly predict profile membership. For context, 35 out of 36 individuals in P1 had a depression measure (*BDI-II*: $N = 32$, $M = 25.19$, $SD = 12.47$; *GDS-15*: $N = 1$, $M = 6.00$, $SD = 0$; *PHQ-9*: $N = 2$, $M = 4.00$, $SD = 2.83$). All 84 individuals in P2 had data (*BDI-II*: $N = 78$, $M = 19.90$, $SD = 11.88$; *GDS-15*: $N = 2$, $M = 2.50$, $SD = 0.71$; *PHQ-9*: $N = 4$, $M = 9.00$, $SD = 9.27$). P3 had 93 out of 95 individuals (*BDI-II*: $N = 84$, $M = 19.87$, $SD = 10.92$; *GDS-15*: $N = 6$, $M = 4.83$, $SD = 4.17$; *PHQ-9*: $N = 3$, $M = 7.33$, $SD = 0.12$). In P4, 147 out of 151 individuals had data (*BDI-II*: $N = 143$, $M = 20.27$, $SD = 11.28$; *GDS-15*: $N = 1$, $M = 1.00$, $SD = 0$; *PHQ-9*: $N = 3$, $M = 10.67$, $SD =$

2.89), and 53 out of 55 individuals in P5 had depression measures (*BDI-II*: $N = 49$, $M = 18.86$, $SD = 9.62$; *GDS-15*: $N = 3$, $M = 3.00$, $SD = 2.65$; *PHQ-9*: $N = 1$, $M = 12.00$, $SD = 0$).

To aid interpretability, depression scores were categorized into minimal, mild, moderate, and severe symptom levels. In P1, 25.0% of individuals reported minimal or moderate depressive symptoms, 13.9% reported mild, and 33.4% reported severe symptoms. In P2, 34.5% had minimal symptoms, 21.4% mild, 22.6% moderate, and 20.2% severe. In P3, 34.7% reported minimal symptoms, 18.9% mild, 25.3% moderate, and 18.9% severe. In P4, 30.5% had minimal depressive symptoms, 22.5% mild, 21.9% moderate, and 22.5% severe. In P5, 40.0% of individuals had minimal symptoms, 7.3% mild, 32.7% moderate, and 14.5% severe.

Similarly, there were no significant associations between chronic pain and profile membership. Chronic pain was endorsed at lower rates, ranging from 33.7% to 41.7%. P4 had a 41.7% endorsement of chronic pain, followed by P1 (39%), P5 (38.2%), P2 (38.1%), and P3 (33.7%). While sleep difficulties were generally not significantly associated with profile membership, one unexpected pattern did emerge. Individuals in P5 reported significantly greater sleep difficulties than those in P1 ($\beta = 2.304$, $SE = 1.129$, $p = .041$). Overall, some levels of sleep difficulties were reported across all profiles, ranging from 64.2% to 72.7%. P5 had the highest rate of sleep difficulties (72.7%), followed by P2 (70%), P1 (67%), P4 (65.6%), and P3 (64.2%).

Lastly, in examining the relationship between PAI scales and profile membership there were no significant relationships with several scales such as infrequency, positive impression management, trait anxiety and depression, somatic concerns, paranoia, borderline features, suicidality, and warmth. However, negative impression management (*NIM*) and inconsistent response styles (*ICN*) were significantly associated with profile membership. More specifically, P1 ($M = 68.6$, $SD = 19.42$) demonstrated significantly higher *NIM* scores than P3 ($M = 58.9$, $SD = 11.90$; $\beta = 0.115$, $SE = 0.045$, $p = .011$, $OR = 1.122$, 95% CI [1.027, 1.226]), P4 ($M = 58.93$, $SD = 13.97$; $\beta = 0.123$, $SE = 0.043$, $p = .004$, $OR = 1.131$, 95% CI [1.040, 1.229]), and P5 ($M = 54.73$, $SD = 9.28$; $\beta = 0.174$, $SE = 0.049$, $p < .001$, $OR = 1.190$, 95% CI [1.086, 1.304]). Furthermore, P2 had significantly lower *NIM* scores than P1 ($\beta = -0.147$, $SE = 0.065$, $p = .025$, $OR = 0.863$, 95% CI [0.764, 0.975]).

P2 ($M = 62.75$, $SD = 14.67$) had significantly higher ICN scores than P1 ($M = 54.64$, $SD = 9.50$; $\beta = 0.184$, $SE = 0.083$, $p = .027$, $OR = 1.202$, 95% CI [1.021, 1.416]), P3 ($M = 52.25$, $SD = 9.47$; $\beta = 0.158$, $SE = 0.075$, $p = .034$, $OR = 1.171$, 95% CI [1.017, 1.353]), and P4 ($M = 50.54$, $SD = 7.69$; $\beta = 0.190$, $SE = 0.074$, $p = .010$, $OR = 1.209$, 95% CI [1.075, 1.361]). Importantly, neither scale exceeded the acceptable range, and thus there were no concerns regarding the validity of the PAI responses.

Regarding other personality- and psychopathology-based concerns, schizophrenia-related concerns (*SCZ*) significantly differentiated profile membership. Specifically, higher *SCZ* scores were associated with increased odds of belonging to P2 ($M = 65.43$, $SD = 13.46$) relative to P1 ($M = 67.00$, $SD = 15.90$; $\beta = 0.248$, $SE = 0.080$, $p = .002$, $OR = 1.282$, 95% CI [1.093, 1.503]), P3 ($M = 61.46$, $SD = 11.53$; $\beta = -0.191$, $SE = 0.072$, $p = .008$, $OR = 0.826$, 95% CI [0.708, 0.963]), and P4 ($M = 61.18$, $SD = 12.73$; $\beta = -0.172$, $SE = 0.069$, $p = .013$, $OR = 0.842$, 95% CI [0.727, 0.976]). Although the mean *SCZ* score for P2 ($M = 65.43$, $SD = 13.46$) was slightly lower than that of P1 ($M = 67.00$, $SD = 15.90$), the regression findings suggest that higher *SCZ* scores were more consistently associated with P2 membership. This may reflect a more uniform elevation of schizophrenia-related traits within P2 compared to greater variability in P1. Additionally, the mean score for P2 on *SCZ* reflected a mild clinical elevation. These results suggest that individuals in P2 may be more withdrawn and aloof and may be cautious or hostile within the few interpersonal relationships they have.

Additionally, antisocial features (*ANT*) were significantly higher in P1 ($M = 48.72$, $SD = 9.08$) compared to P4 ($M = 46.69$, $SD = 8.78$; $\beta = 0.116$, $SE = 0.055$, $p = .033$, $OR = 1.123$, 95% CI [1.010, 1.249]), with individuals having greater odds of being classified in P1 based on higher *ANT* scores. In contrast, P4 ($M = 47.84$, $SD = 10.51$) had significantly higher interpersonal dominance (*DOM*) than P1 ($M = 40.56$, $SD = 9.74$; $\beta = 0.144$, $SE = 0.066$, $p = .028$, $OR = 1.155$, 95% CI [1.015, 1.315]), with higher dominance scores associated with greater odds of being classified in P4 compared to P1. Lastly, P3 ($M = 46.83$, $SD = 8.83$) and P1 ($M = 48.04$, $SD = 11.43$) were significantly differentiated based on aggression (*AGG*; $\beta = 0.113$, $SE = 0.052$, $p = .029$, $OR = 1.120$, 95% CI [1.012, 1.240]), with individuals exhibiting higher aggression scores having greater odds of being

classified in P1 compared to P3. It is important to note that while these domains were statistically significant, they were not at a clinically meaningful level (i.e., $M < 50$).

Diagnostic Distribution of Profiles

The final exploratory aim of this study was to understand the diagnostic distribution of the cognitive profiles generated by the LPA. P1 ($N = 35$) had an 8.3% ($N = 3$) incidence of an MCI diagnosis and much larger incidences of major depressive disorder (*MDD*; $N = 19$) and generalized anxiety disorder (*GAD*; $N = 7$), 52.8% and 19.4%, respectively. Additionally, 13.9% ($N = 5$) of individuals in this profile had a history of substance abuse and a history of bipolar disorder ($N = 5$), while 11.1% had a diagnosis of adjustment disorder with mixed mood ($N = 4$), and 8.3% had post-traumatic stress disorder (*PTSD*; $N = 3$). A total of 5.6% ($N = 2$) of individuals had attention-deficit/hyperactivity disorder (unspecified [$N = 1$; 2.8%] and combined type [$N = 1$; 2.8%]), panic disorder without agoraphobia, hydrocephalus, and postural orthostatic tachycardia syndrome (*POTS*). In addition, other disorders present at lesser rates were Pontine Cavernomas, Multiple Sclerosis (*MS*), Anorexia Nervosa, Borderline Personality Disorder (*BPD*), and cancer-related impairments ($N = 1$; 2.8% each). Of note, this profile had the highest mean number of diagnoses ($M = 1.97$, $SD = 1.00$) among all profiles. Most of the individuals in this profile had one or two diagnoses, 33.3% ($N = 12$) and 36.1% ($N = 13$), respectively. A smaller subset had no diagnoses ($N = 1$; 2.8%), while 19.7% ($N = 3$) had three diagnoses and 8.3% ($N = 3$) had four diagnoses. These findings indicate a relatively higher diagnostic burden within this profile than the rest of the sample.

P2 ($N = 84$) had an 8.3% ($N = 7$) incidence of MCI, the second largest incidence out of all profiles. This profile also had large incidences of psychological concerns, specifically, *MDD* with 40.5% ($N = 34$), *GAD* with 19% ($N = 16$), bipolar disorder with 14.3% ($N = 12$), and adjustment disorders with 13.1% ($N = 11$; including with mixed mood [$N = 9$; 10.7%], with depressed mood [$N = 1$; 1.2%], and anxious mood [$N = 1$; 1.2%]). Individuals within this profile also had incidences of *ADHD* ($N = 9$; 10.8%), including 4.8% ($N = 4$) with unspecified *ADHD*, 4.8% ($N = 4$) with inattentive type, and 1.2% ($N = 1$) with combined type. Additionally, 3.6% ($N = 3$) of individuals within this profile had *MS* or obsessive-compulsive disorder, 7.1% ($N = 6$) had

PTSD, 6% ($N = 5$) had a history of substance abuse, and 4.8% ($N = 4$) had schizoaffective disorder. This profile exhibited lower incidences of the following diagnoses ($N = 2$; 2.4%): panic disorder without agoraphobia, borderline personality disorder (BPD), and human immunodeficiency virus (HIV). Even lower incidences ($N = 1$; 1.2%) were observed for hydrocephalus, encephalopathy, spinocerebellar ataxia, and chronic obstructive pulmonary disease (COPD). Lastly, P2 had a mean total diagnosis of $M = 1.88$ ($SD = 1.02$), with 4.8% ($N = 4$) having no diagnoses, 33.3% ($N = 28$) having one diagnosis, 40.5% ($N = 34$) having two diagnoses, 13.1% ($N = 11$) having three diagnoses, 7.1% ($N = 6$) having four diagnoses, and 1.2% ($N = 1$) having five diagnoses.

P3 ($N = 135$) had the largest incidence of MCI (14.7%; $N = 14$), a relatively high proportion of individuals with MDD ($N = 46$; 48.40%) and a lower proportion with GAD ($N = 22$; 23.20%). Similarly, 19.10% ($N = 18$) of the sample had an ADHD diagnosis, with 9.50% ($N = 9$) having ADHD inattentive type, 5.30% ($N = 5$) having unspecified ADHD, 3.20% ($N = 3$) having ADHD combined type, and 1.10% ($N = 1$) having ADHD hyperactive type. P3 also had an incidence rate of 7.40% ($N = 7$) for adjustment disorders, varying in type. More specifically, 4.20% had an adjustment disorder with mixed mood and 3.20% had an adjustment disorder with anxious mood. TS and panic disorder had a 3.20% ($N = 3$) incidence rate, while MS, PTSD, bipolar disorder, and a history of substance abuse each had an incidence rate of 4.20% ($N = 4$). Conversely, a lower proportion ($N = 2$; 2.10%) of individuals had diagnoses of COPD, narcolepsy, HIV, or schizoaffective disorder. The following diagnoses were also endorsed at an even lower rate ($N = 1$; 1.1%): hydrocephalus, Huntington's disease, neurofibromatosis type 1, autism spectrum disorder (ASD), OCD, or conversion disorder. Regarding total diagnoses, P3 had a mean of $M = 1.71$ ($SD = 1.09$), with many individuals having one or two diagnoses, 38.8% and 27.4%, respectively. The rest of the profile had no diagnoses ($N = 11$; 11.6%), three diagnoses ($N = 17$; 17.9%), or four diagnoses ($N = 6$; 6.3%).

P4 ($N = 151$) had a high incidence of MDD ($N = 72$; 47.7%), ADHD ($N = 30$; 19.8%), and GAD ($N = 29$; 19.20%). The ADHD diagnoses can be broken down into unspecified ($N = 14$; 9.30%), inattentive type ($N = 12$; 7.90%), hyperactive type ($N = 2$; 1.30%), and combined type ($N = 2$; 1.30%). Interestingly, the incidence of MS ($N = 8$; 5.30%), PTSD ($N = 16$; 10.60%), and bipolar disorder ($N = 13$; 8.60%) was larger than in any other

profile. This profile also had reports of adjustment disorders, with 5.40% ($N = 8$) of the profile having a diagnosis—4% of these were classified as adjustment disorder with mixed mood, while 0.7% ($N = 1$) were diagnosed with adjustment disorder with anxious mood and 0.7% ($N = 1$) with depressed mood. Additionally, 4.6% ($N = 7$) of individuals in this profile had a history of significant substance abuse. Further, 2.60% ($N = 4$) of the profile had panic disorder without agoraphobia or COPD, while 1.30% ($N = 2$) of the profile had anorexia nervosa, BPD, schizoaffective disorder, dissociative identity disorder, or MCI. Lower proportions ($N = 1$; 0.70%) of the profile had HIV, POTS, cancer-related cognitive impairment, Tourette's disorder, and social anxiety. Lastly, the mean number of diagnoses in this profile was $M = 1.56$ ($SD = 1.16$). Similarly to P1, P2, and P3, the vast majority of participants in this profile had one or two diagnoses—32.5% ($N = 49$) and 29.1% ($N = 44$), respectively. The other large percentages were individuals with no diagnoses ($N = 29$; 19.2%) or three diagnoses ($N = 20$; 13.2%). Conversely, a smaller percentage of individuals had four ($N = 7$; 4.6%) or five diagnoses ($N = 2$; 1.3%).

As might be expected, P5 ($N = 52$) had no individuals with an MCI diagnosis. However, there was a high proportion of individuals with MDD ($N = 20$; 36.40%) and GAD ($N = 11$; 11%). The other diagnoses with high proportions within this profile were ADHD ($N = 9$; 16.40% [unspecified: $N = 3$; 5.5%; combined: $N = 3$; 5.5%; inattentive: $N = 2$; 3.6%; hyperactive: $N = 1$; 1.8%]) and PTSD ($N = 6$; 10.9%). Additionally, 7.3% ($N = 4$) of individuals had bipolar disorder, and 3.6% had an adjustment disorder (total $N = 2$; $N = 1$ with anxious mood; $N = 1$ with mixed mood). Other diagnoses present in lesser proportions were functional neurological disorder, POTS, hydrocephalus, MS, COPD, narcolepsy, ASD, panic disorder without agoraphobia, OCD, avoidant personality disorder, and cancer-related impairment ($N = 1$; 1.8% each).

P5 had the lowest mean number of diagnoses ($M = 1.25$, $SD = 1.17$) among all profiles in the sample. A substantial portion of individuals in this profile had either no diagnoses ($N = 20$; 36.4%) or two diagnoses ($N = 16$; 29.1%). Similarly, 20.0% ($N = 11$) had one diagnosis, while a smaller percentage had three diagnoses ($N = 6$; 10.9%). Notably, few individuals in this profile had four diagnoses ($N = 2$; 3.6%). These findings suggest P5 had an overall lower diagnostic burden compared to other profiles in the sample.

Discussion

The primary purpose of this study was to identify neurocognitive profiles among an adult patient population with cognitive concerns using LPA, to offer a more precise classification of neurocognitive difficulties than what is currently available. The secondary aim of this study was to assess if psychological and physical factors were differentially associated with profile membership and lastly, to explore the diagnostic distribution of the profiles that arose from the LPA. As hypothesized, a five-profile solution was supported by goodness-of-fit indices, entropy values, and profile proportions, which collectively indicated sufficient interpretability and stability. These groups were distinguishable by significant differences in performance across the neurocognitive domains.

As expected, there was a notable gradient of cognitive impairment within the sample. Of note, none of the profiles had any impairments of 2 SD and based on the Luck et al. (2017) criteria did not meet criteria for dementia or a cognitive difficulty similar to what would be expected in dementia. P1 and P2 were notably more impaired than the rest of the sample; P1's impairment was driven by psychomotor and memory impairments, whereas P2's impairment was milder and driven by difficulties in language, attention, and executive function. P3 was cognitively average group with mild difficulties in memory, while P4 and P5 demonstrated less impairment and higher cognitive performances. P4 was characterized by strong performances on memory whereas P5 demonstrated marked strengths in memory and executive function.

These findings reiterate the neurocognitive heterogeneity within clinical populations (Cohen-Mansfield 2000; Delano-Wood et al., 2009; Eppig et al., 2017; Libon et al. 2014; Ramirez-Gomez et al. 2017; Thomas et al., 2023). The five distinct profiles and their unique pattern of weaknesses and strengths support the notion that neurocognitive concerns exist along a continuum rather than within discrete diagnostic categories, which often fail to account for within-group variabilities that may influence clinical outcomes and disease progression (Boots et al., 2020; Cohen-Mansfield, 2000; Delano-Wood et al., 2009; Eppig et al., 2017; Lamar et al., 2021; Libon et al., 2014; Liew et al., 2018; Thomas et al., 2023; Verdi et al., 2021). These profiles may provide an initial

framework for tailoring individualized clinical recommendations based on specific cognitive strengths and weaknesses.

The different areas of impairment within these profiles highlight potential areas for personalized targeted clinical interventions. For example, P1 is a largely impaired profile with marked impairments in psychomotor slowing and memory, resembling patterns commonly observed in individuals with subcortical impairments, VD, and AD (Berardi et al., 2005; Bublak et al., 2011; Chau et al., 2015; McGuinness et al., 2010; Perry & Hodges, 2000; Suades-González et al., 2009; Van Kan et al., 2017). Moreover, the cognitive difficulties experienced by this profile (i.e., 1 SD above the population; Luck et al., 2017) may be indicative of multidomain MCI as P1 had widespread difficulties. Individuals in P1 may benefit from cognitive rehabilitation strategies focused on external memory aids (e.g., calendars, reminders), task segmentation, external cueing, and structured routines. Additionally, while most individuals can benefit from engaging in behaviors that promote optimal brain health, it may be even more important for individuals in this profile to engage in these behaviors given the impairment pattern resemblance to VD and AD. For example, providers may carefully consider the potential anticholinergic load to decrease the risk of dementia (Coupland et al., 2019).

P2 demonstrated broad difficulties with weaknesses in attention and executive functioning. This combination of impairments is similar to common features of VD and FTD (Attix & Welsh-Bohmer, 2006; Carlin et al., 2000; Duara et al., 1999; Heilman & Valenstein, 2003; Heyanka et al., 2010; Hou et al., 2004; McGuinness et al., 2010; Miller et al., 2003; Perry & Hodges, 2000; Rahman et al., 1999; Sieroff et al., 2004; Ying et al., 2016). Individuals in P2 may benefit from cognitive compensatory strategies such as note-taking, mindfulness, completing one task at a time and when appropriate, trials with stimulant or nonstimulant medications to aid in attention difficulties. Additionally, given that individuals in P2 demonstrated cognitive difficulties approaching one standard deviation below the sample mean, future research should examine the stability and progression of similar profiles over time.

P3 was generally unimpaired, albeit defined by having slight memory difficulties; suggesting individuals in this profile may benefit from memory strategies and compensatory techniques. P4 had generally strong

performances, with slight challenges in attention and executive function, suggesting targeting these personal weaknesses could be beneficial. P5 was largely intact with strengths in several domains. This profile also had the highest education, possibly suggesting education is a protective factor or that individuals with more education perform better on neuropsychological evaluations.

The second aim of this study sought to evaluate whether profile membership was differentially associated with psychological (i.e., depression, anxiety, and personality) and physical factors (i.e., sleep difficulties and chronic pain). The hypothesis for this aim was that higher scores on measures of depression, anxiety, and personality scales (e.g., Somatic Complaints, Anxiety, Depression, and Borderline Features) and reports of sleep difficulties and chronic pain would be associated with membership in cognitive profiles characterized by marked cognitive impairment. This hypothesis was largely unsupported as higher scores on demographics variables, on measures of depression, anxiety, and reports chronic pain were not significantly associated with profile membership. However, years of education did appear to differentiate between some groups. Individuals in P1, the most cognitively impaired profile, had significantly lower levels of educational attainment compared to P3, and P5. Similarly, average (P3) to slightly above average (P4) cognitive performers had significantly lower years of education compared to the highest performing profile (P5). This finding, like previous research, (Rehnberg et al., 2024) indicates a relationship between education and cognitive performance, as having a higher level of education is related to better performance cognitive testing.

It is possible the lack of significant relationships between depression, anxiety and chronic pain was due to the overall high endorsement rates of these concerns across the sample, making it difficult to differentiate between profiles on this basis. However, more impaired profiles tended to have higher endorsement rates of these concerns. P1 had the highest proportion of severe scores in depression measures among all profiles, and depression can be accompanied by psychomotor slowing (APA, 2013), a key characteristic of this profile. This could suggest that targeted depression interventions for individuals in this profile may improve psychomotor slowing and overall functioning. Additionally, this profile had the highest proportion of chronic pain reports, which can contribute to difficulties in executive function, attention and indirectly affect memory (Berryman et

al., 2014; Higgins et al., 2018; Moriarty et al., 2011). Any effects of pain on cognition could be due to the experience of pain itself or medications used to manage pain symptoms (Moriarty et al., 2011). Conversely, sleep difficulties were significantly associated with P5 when compared to P1, with individuals in P5 reporting the highest levels of sleep disturbance despite being the highest cognitive performers. This association can appear counterintuitive as research supports sleep difficulties being associated with poorer cognitive performance (Xu et al., 2020). This finding may provide some insight into how or if perceived sleep difficulties actually impact cognitive performance. It is also possible that this finding may reflect differences in the *kind* of sleep difficulties endorsed by the profiles, although current study data limits our ability to thoroughly evaluate this. Future studies may benefit from a more thorough assessment of the impact sleep difficulties have on this kind of cognitive profile. Additionally, while P2 did not have significant associations with sleep difficulties it had the highest proportion of sleep difficulties relative to its sample size, suggesting that sleep-related concerns, which often cause attentional fluctuations, may be a salient feature for individuals within this group (Killgore 2010; Lim & Dinges 2010; Lowe et al 2017). These individuals may benefit from targeted sleep interventions such as sleep hygiene strategies or evidenced based treatments such as Cognitive Behavioral Therapy for Insomnia (CBT-I).

P4 had the highest proportions of moderate-to-severe depression. It could be that their relative difficulties in executive function and attentional abilities were exacerbated by depressive symptoms, as research demonstrates a relationship between depression and these domains (Kriesche et al., 2023; Rock et al., 2014; Snyder 2013). Despite this profile not having marked cognitive impairments there may be improvements in subjective cognitive concerns as a result of engaging in treatment for their depression symptoms. Specifically, individuals in this profile may benefit from treatment to address depression symptomatology such as pharmacological intervention and cognitive behavioral therapy (Keefe et al 2014).

Despite previous research finding significant relationships between personality variables (e.g., somatic concerns, depression, and borderline features; Aikman & Souheaver, 2018) we did not find a significant relationship for these variables. However, several significant findings arose related to NIM, ICN, and SCZ. P1 had significantly higher NIM scores than all other profiles, suggesting that P1 may be engaging in greater

negative impression management than the other profiles. A possible explanation for this finding may be that individuals in P1 may consciously or subconsciously amplify their difficulties to communicate the extent of their distress or their perceived need for support. Notably, the mean scores in P1 did not raise concerns of malingering and may instead reflect a common finding in which individuals heighten their report of symptoms expression possibly in response to a history of feeling dismissed or invalidated in care settings (Mechanic, 1995). In the case of P1, elevations in NIM may represent an appropriate form of help-seeking behavior rather than intentional exaggeration, as individuals in P1 had the lowest overall cognitive performance.

Additionally, inconsistency in responding, as assessed by the PAI, also had significant associations with P2 in comparison with P1, P3, and P4. These results suggest that individuals in P2 may be more inconsistent responders than the rest of the sample. This finding is of particular interest given that P2 had the second lowest cognitive performance overall, particularly regarding attention, executive functioning and language fluency domains. As such, this inconsistency may reflect genuine underlying cognitive difficulties that may have contributed to variability in response patterns (Hou et al., 2004), rather than an intentional disengagement. P2 had another interesting association with schizophrenia related concerns which may further compound their difficulties. P2 had significantly higher schizophrenia related concerns than P1, P3, P4. The mean SCZ score for P2 was also indicative of a mild clinical elevation, which suggests individuals in this profile may be more interpersonally distant, socially withdrawn, and potentially exhibit suspiciousness or odd interpersonal behaviors.

Considering that P2 also demonstrated the second lowest cognitive performance, it is possible these difficulties were further compounded by schizophrenia related concerns. From a clinical and treatment standpoint, this finding underscores the importance of considering cognitive and personality variables when tailoring interventions for individuals who present with both social withdrawal and cognitive complaints as this could interfere with treatment engagement and, subsequently, treatment outcomes.

Lastly, while there were significant associations between profile membership and antisocial features, interpersonal dominance, and aggression, these findings will not be over pathologized as the mean scores for

these scales were not of clinical significance. However, future research may consider evaluating the relationship of PAI scores in these scales and cognitive performance to assess if the significant relationships remain as the scales reach clinical significance.

The final exploratory aim of this study was to examine the diagnostic distribution across the cognitive profiles identified through LPA. This aim builds on previous findings of psychological and physical concerns within each profile.

P1 had the highest rates of depression, the highest rates of MDD, substance abuse diagnoses, and the highest mean number of diagnoses. These elevated rates may partially explain this profile's poor performance across domains. The findings underscore this profile's experience with increased diagnostic burden and psychosocial stress, suggesting a need for integrated care and multidisciplinary teams to address the complexity of their presentation.

P2 exhibited the highest rates of MCI, GAD, and adjustment disorders, along with elevated rates of bipolar disorder and schizoaffective disorder. This diagnostic pattern may reflect a profile characterized by heightened psychosocial distress and affective dysregulation, suggesting a potential need for mood stabilization strategies and targeted psychosocial support. Notably, P2 also had significantly high schizophrenia related concerns as discussed above which could relate to the frequency of schizoaffective disorders in this profile.

P3 demonstrated the highest incidence of ADHD and the second-highest incidence of MDD. In the context of this profile's subtle memory difficulties, it is plausible that attentional difficulties emblematic of ADHD (APA, 2013), in combination with depressive symptoms, may be contributing to slight disruptions in memory performance.

P4 had the highest rates of PTSD and MS, despite having the second-lowest diagnostic burden. The strong cognitive performance observed in this profile is broadly consistent with its lower diagnostic load; however, the elevated rates of PTSD were somewhat unexpected, as extant literature links PTSD to diminished cognitive

functioning (Scott et al., 2015). Due to limitations in the available diagnostic data (e.g., timing and nature of trauma exposure), a potential reason for this finding remains unclear.

However, a possible explanation could be the presence of post-traumatic growth in this group, which has been associated with improved outcomes (Dell'Osso L et al., 2022). Future research should examine longitudinal associations between PTSD, post-traumatic growth, and cognitive functioning to better elucidate these patterns.

P5 had the lowest diagnostic burden with minimal cognitive or psychiatric comorbidity and no MCI diagnoses. This profile appears to be largely unaffected across cognitive and psychosocial domains. The diagnostic distinctions observed across profiles, particularly the varying prevalence of MCI in P1 through P4, highlight significant differences in cognitive impairment within the sample. The current diagnostic categories (i.e., MCI and Major Neurocognitive Disorder), broadly emphasize impairment severity and etiology. While these classifications are useful for determining appropriate levels of care and projecting clinical outcomes, they may overlook nuanced within-group differences. Findings from the present study suggest that consideration of specific neurocognitive patterns, rather than reliance on categorical diagnoses alone, may offer a more refined and personalized approach to clinical care.

In summary, the purpose of this study was to empirically identify neurocognitive profiles in an adult patient population with cognitive concerns using LPA and to evaluate relationships with psychological and physical variables. The present study findings extend the current body of research regarding neurocognitive profiles and their relationship to psychosocial variables in several ways. Previous research has focused on evaluating profiles of neurocognition within MCI, AD vs VD, neuropsychiatric symptoms vs MCI, and non-demented populations and their relationship to WML burden, CSF biomarkers, genotype, outcomes and lifestyle factors (e.g., diet and exercise; Boots et al., 2020; Delano-Wood et al., 2009; Eppig et al., 2017; Lamar et al., 2021; Libon et al., 2014; Liew et al., 2018; Thomas et al., 2023). To our knowledge this is the first study to concurrently evaluate neurocognition and its relationship to specific psychological variables (i.e., sleep, chronic pain, depression, anxiety, personality). These findings extend extant research by identifying five distinct cognitive profiles, underscoring the heterogeneity present in neurocognitive concerns among an adult

population with concerns about their neurocognitive functioning. These results highlight the possible limitations of current diagnostic systems (mild vs major ND), which do not consider the nuanced patterns of cognitive strengths and weaknesses that can emerge across domains.

The relationships between profile membership, NIM, ICN, SCZ, and varying endorsement rates of psychological and physical health factors underscore the importance of comprehensive and integrated care. Patients may benefit from clinicians incorporating these insights into clinical decision-making to help guide treatment targets, whether by addressing depression-related psychomotor slowing, attentional disruptions tied to sleep difficulties, or compensatory strategies for memory and executive dysfunction.

However, these study findings should be interpreted in light of several limitations. First, the sample consisted of individuals referred to neuropsychological evaluations due to subjective cognitive concerns. Neuropsychological evaluations in an academic medical center are generally obtained through provider referrals (e.g., neurologists, psychologists, psychiatrists, mental health counselors). This may introduce a layer of bias based on an individual provider judgement as providers are the ones to determine what they deem clinically significant enough to warrant a neuropsychological assessment. Additionally, the sample was primarily White which limits generalizability to more racially or ethnically diverse populations. Third, the cross-sectional nature of the data restricts our ability to infer causality or examine changes over time. Although results demonstrate evidence for a significant relationship between neurocognitive profiles and several PAI variables we cannot establish or infer causality without further research. Future studies should explore the stability of these variables and how it may influence neurocognition over time. While extant research has examined PAI performance in medical populations (e.g., chronic pain, traumatic brain injuries, and in the context of presurgical evaluations; Corsica et al., 2009; Demakis et al., 2007; Karlin et al., 2005), further research is needed

to assess the temporal dynamics of these relationships and their impact on neurocognition. Additionally, while specific profiles were associated with diagnostic and psychosocial features, it was not possible to determine the nature of these relationships. Follow-up studies may consider evaluating the relationship between diagnostic burden and cognitive dysfunction. It is also important to note some variables (i.e., anxiety) had limited data available which may have restricted our ability to detect significant associations. Additionally, sleep difficulties and chronic pain were assessed via patient reports, which may have limited our ability to establish significant relationships or to fully evaluate the nature of the relationships. Future studies would benefit from incorporating comprehensive and validated measures of these constructs to better capture their clinical impact and improve interpretability. Additionally, future studies may focus on examining these profiles longitudinally to evaluate stability, predictive utility and responsiveness to interventions.

Conclusion

In sum, the present study identified five distinct neurocognitive profiles, varying in relative cognitive strengths and weaknesses. Profiles were significantly distinguished by differences in years of education, response style, and schizophrenia related concerns. These findings contribute to the extant research regarding heterogeneity in neurocognition and provide granularity regarding neurocognitive profiles and highlight the value of empirically derived profiles in capturing individual differences. This study provides an initial step toward refining the classification and treatment of cognitive difficulties through individualized, profile-based approaches, offering a foundation for more targeted and individualized clinical care.

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Tables

Table 1

Descriptive Statistics for Demographics

Variable	N (%) or <i>M</i>(<i>SD</i>)
Race	
White	391 (92.8%)
Black	24 (5.7%)
Asian	5 (1.2%)
Biracial	1 (0.2%)
Ethnicity	
Hispanic or Latine	5 (1.2%)
Caribbean	1 (0.2%)
Not Hispanic or Latine	415 (98.6%)
Sex	
Female	255 (60.6%)
Male	166 (39.4%)
Age	51.97 (11.17)
Years of Education	14.10 (2.64)

Note. N = 421

Table 2*Study Measures*

Domain	Measure	Scores
Independent Variables: Cognitive Measures		
Attention	Trails A (TMT-A) Digits Forward (DF)	t-score → z-score
Executive Functioning	Trails B (TMT-B) Digits Backward (DB)	t-score → z-score
Memory	Verbal Memory (immediate memory, delayed memory)	
	California Verbal Learning Test – Second edition (CVLT-II)	z-score
	Hopkins Verbal Learning Test–Revised (HVLТ)	t-score → z-score
	Rey Auditory Verbal Learning Test (RAVLT)	scaled score → z-score
Language	Verbal Fluency (phonemic and semantic fluency)	
	Controlled Oral Word Association Test (COWA)	t-score → z-score
	Animal Naming Test (ANT)	t-score → z-score
	Delis-Kaplan Executive Function System: Verbal Fluency (DKEFS: VF)	scaled score → z-score
Dependent Variables: Psychological and Physical Measures		
Personality	Personality Assessment Inventory (PAI)	t-score
Depression	Geriatric Depression Scale (GDS-15)	0 = Minimal 1 = Mild 2 = Moderate 3 = Severe
	Beck Depression Inventory (BDI-II)	
	Patient Health Questionnaire (PHQ-9)	
Anxiety	Generalized Anxiety Inventory 7 (GAD-7)	0 = Minimal 1 = Mild 2 = Moderate 3 = Severe
	Beck Anxiety Inventory (BAI)	
Sleep Difficulties	Participant reports of sleep concerns	0 = no sleep concerns 1 = sleep concerns
Chronic Pain	Participant reports of chronic pain	0 = no chronic pain 1 = chronic pain

Table 2 (Continued)

Covariates		
Demographics	Data on age, race, ethnicity, sex, and years of education	N/A
Test type	Coded Variables	
	Verbal Memory	1 = CVLT 2 = HVL 3 = RAVLT
	Depression	1 = BDI-II 2 = GDS-15 3 = PHQ 9
	Anxiety	1 = BAI 2 = GAD-7

Note. All measures included in the LPA were converted to z-scores. Measures are organized according to their respective domains

Table 3
Data Availability for Cognitive Measures and Covariates of Interest

Domain	Measure	N	%
Attention			
	TMT-A	421	100%
	Digits Forward	418	99.29%
Executive Functioning			
	TMT-B	421	100%
	Digits Backward	418	99.29%
	WCST Perseverative Errors	378	89.79%
Memory			
	CVLT-II	381	91.20%
	HVLT	32	7.60%
	RAVLT	5	1.20%
Language			
	Letter Fluency	421	100%
	Semantic Fluency	420	99.76%
Psychological Measures			
Depression	BDI-II	391	92.88%
	GDS-15	16	3.80%
	PHQ-9	12	2.85%
	Total Data	419	99.52%
Anxiety	BAI	79	18.76%
	GAD-7	85	20.19%
	Total Data	164	24.70%
Personality	PAI	268	63.66%
Physical Measures			
	Sleep Difficulties	421	100%
	Chronic Pain	421	100%

Note. TMT = Trail Making Test, WCST = Wisconsin Card Sorting Test.

Table 4*Descriptive Statistics and Frequencies for Psychological and Physical Variables*

Variable	N (%) or M (SD)
Depression Severity	
Minimal	139 (33.0%)
Mild	79 (18.8%)
Moderate	103 (24.5%)
Severe	89 (21.1%)
Anxiety Severity	
Minimal	54 (12.8%)
Mild	36 (8.6%)
Moderate	42 (10.0%)
Severe	31 (7.4%)
Personality Variables	
Somatic Concerns	70.13 (14.60)
Anxiety	62.96 (13.99)
Depression	67.87 (14.63)
Mania	46.67 (10.16)
Paranoia	53.03 (11.79)
Schizophrenia-Related Concerns	62.31 (12.85)
Borderline Features	56.19 (11.49)
Antisocial Features	46.55 (8.08)
Aggression	47.97 (10.08)
Suicidal Ideation	54.45 (14.01)
Dominance	46.21 (10.21)
Warmth	46.06 (11.02)
Inconsistency	51.98 (8.64)
Infrequency	51.11 (8.56)
Negative Impression	59.92 (14.12)
Positive Impression	47.46 (10.94)
Physical Variables	
Sleep Difficulties	283 (67.2%)
Chronic Pain	162 (38.5%)

Note. Total N = 421. Personality variables are based on T-scores from the Personality Assessment Inventory (PAI); N = 268 due to missing data.

Table 5*LPA Variable Psychometric Properties*

Variable	Mean	Variance	Skewness	Kurtosis	VIF
TMT-A	-0.007	0.986	-0.371	0.255	1.88
Digits Forward	0.004	1.004	0.332	0.598	1.68
TMT-B	-0.008	0.981	-0.068	0.592	1.95
Digits Backward	0.008	1.022	0.594	1.288	1.66
WCST-PE	-0.001	0.973	0.376	2.365	1.67
Letter Fluency	-0.005	0.981	0.236	0.014	1.60
Semantic Fluency	-0.006	1.011	0.045	0.585	1.03
Immediate Memory	-0.002	0.987	-0.086	-0.521	3.11
Delayed Memory	-0.005	0.987	-0.368	-0.521	2.81

Note. LPA = Latent Profile Solution. TMT = Trail Making Test. WCST = Wisconsin Card Sorting Test.

Table 6*Comparison of Model Fit Indices Across LPA Solutions*

LPA Models	AIC	SABIC	Entropy	LRT (p-value)
2	9829.35	9853.56	0.83	0.00
3	9693.43	9726.29	0.81	0.04
4	9586.61	9628.11	0.78	0.41
5	9508.54	9558.69	0.82	0.02
6	9454.21	9513.00	0.83	0.66

Note. LPA = Latent Profile Solution. AIC = Akaike Information Criterion. SABIC = Sample Size-Adjusted Bayesian Information Criterion, LMR = Lo, Mendel, and Rubin test.

Table 7*Profile Membership Proportions for Four-Profile LPA Solution*

Latent Profile	N	%
1	67	0.16
2	152	0.36
3	140	0.33
4	60	0.14

Table 8*Profile Membership Proportions for Six-Profile LPA Solution*

Latent Profile	N	%
1	67	15.99%
2	36	8.59%
3	37	8.83%
4	103	24.58%
5	144	34.37%
6	32	7.64%

Table 9*Profile Membership Proportions for Five-Profile LPA Solution*

Latent Profile	N	%
1	36	0.08
2	84	0.20
3	95	0.23
4	151	0.36
5	55	0.13

Table 10*Standardized Cognitive Variable Means by Latent Profile (Five-Profile Solution)*

Variable	Profile 1	Profile 2	Profile 3	Profile 4	Profile 5
TMT-A	-1.31	-0.78	0.24	0.35	0.61
Digits Forward	-0.46	-0.74	0.06	-0.04	1.51
TMT-B	-1.06	-0.91	0.23	0.36	0.64
Digits Backward	-0.51	-0.77	0.06	-0.03	1.60
Letter Fluency	-0.77	-0.75	0.12	0.20	0.88
Semantic Fluency	-0.84	-0.68	-0.09	0.34	0.81
WCST – Perseverative Errors	-0.42	-0.34	-0.22	0.20	0.55
Immediate Memory	-1.62	-0.48	-0.59	0.67	1.05
Delayed Memory	-1.74	-0.34	-0.69	0.77	0.81

Note. Values reflect standardized z-scores. WCST = Wisconsin Card Sorting Test; TMT = Trail Making Test.

Table 11*Average Posterior Probabilities for Most Likely Latent Profile Membership (Five-Profile Solution)*

Most Likely Profile	P1	P2	P3	P4	P5
Profile 1	0.91	0.05	0.04	0	0
Profile 2	0.05	0.84	0.09	0.02	0
Profile 3	0.01	0.07	0.87	0.05	0.004
Profile 4	0	0.02	0.04	0.91	0.03
Profile 5	0	0	0.004	0.1	0.90

Note. Values reflect the average posterior probabilities of being assigned to each profile, given the most likely latent class membership. Higher diagonal values indicate strong classification accuracy.

Table 12*Demographic Characteristics by Latent Profile (Five-Profile Solution)*

Variable	Profile 1 (n = 36)	Profile 2 (n = 84)	Profile 3 (n = 95)	Profile 4 (n = 151)	Profile 5 (n = 55)
Race					
White	35 (97.2%)	82 (97.6%)	84 (88.4%)	137 (90.8%)	53 (96.4%)
Black/African American	1 (2.8%)	2 (2.4%)	8 (8.4%)	12 (7.9%)	1 (1.8%)
Asian	—	—	2 (2.1%)	2 (1.3%)	1 (1.8%)
Biracial	—	—	1 (1.1%)	—	—
Ethnicity					
Hispanic/Latine	—	1 (1.2%)	2 (2.1%)	1 (0.7%)	1 (1.8%)
Caribbean	—	—	—	1 (0.7%)	—
Non-Hispanic or Latine	36 (100%)	83 (98.8%)	93 (97.9%)	149 (98.7%)	54 (98.2%)
Sex					
Female	21 (58.3%)	46 (54.8%)	53 (55.8%)	102 (67.5%)	33 (60.0%)
Male	15 (41.7%)	38 (45.2%)	42 (44.2%)	49 (32.5%)	22 (40.0%)
Age (years)	48.42 (13.28)	52.64 (9.47)	54.17 (11.51)	51.15 (10.76)	51.75 (12.13)
Years of Education	12.56 (2.60)	13.55 (2.83)	14.00 (2.48)	14.18 (2.39)	15.91 (2.34)

Note. Values for race, ethnicity, and sex are presented as n (%). Age and education are reported as M (SD).

Table 13*Psychological and Physical Measures by Profile (P1–P5)*

Measure	P1		P2		P3		P4		P5	
	N	M (SD)	N	M (SD)	N	M (SD)	N	M (SD)	N	M (SD)
Depression										
BDI-II	32	25.19 (12.47)	78	19.90 (11.88)	84	19.87 (10.92)	143	20.27 (11.28)	49	18.86 (9.62)
GDS-15	1	6.00 (0)	2	2.50 (0.71)	6	4.83 (4.17)	1	1.00 (0)	3	3.00 (2.65)
PHQ-9	2	4.00 (2.83)	4	9.00 (9.27)	3	7.33 (10.12)	3	10.67 (2.89)	1	12.00 (0)
Anxiety										
BAI	5	28.00 (14.46)	10	20.30 (16.06)	16	23.44 (15.60)	33	16.79 (10.92)	15	17.07 (9.68)
GAD-7	11	12.36 (18.25)	23	6.26 (5.37)	21	6.62 (6.04)	15	7.93 (6.51)	15	7.33 (5.08)
Physical Measures										
Sleep Difficulties (%)	24	67.00%	59	70.20%	61	64.20%	99	65.60%	40	72.70%
Chronic Pain Presence (%)	14	39.00%	32	38.10%	32	33.70%	63	41.70%	21	38.20%

Note. BDI-II = Beck Depression Inventory–II; GDS-15 = Geriatric Depression Scale–Short Form; PHQ-9 = Patient Health Questionnaire–9; BAI = Beck Anxiety Inventory; GAD-7 = Generalized Anxiety Disorder–7.

Table 14*Internal Correlations in Variables of Interest*

Profile 1	TMT-A	DF	TMT-B	DB	Letter Fluency	Semantic Fluency	WSCT-PE	Immediate Memory	Delayed Memory
TMT-A	-								
DF	-0.011	-							
TMT-B	.492**	0.098	-						
DB	-0.027	.442**	0.151	-					
Letter Fluency	-0.51	0.21	0.023	0.169	-				
Semantic Fluency	-0.071	0.113	-0.19	-0.135	0.293*	-			
WSCT-PE	0.113	-0.033	-0.064	-0.186	0	-0.057	-		
Immediate Memory	0.123	-0.041	-0.038	-0.001	0.038	0.078	-0.103	-	
Delayed Memory	0.182	-0.089	-0.041	-0.138	0.026	0.054	-0.115	.758**	-
Profile 2	TMT-A	DF	TMT-B	DB	Letter Fluency	Semantic Fluency	WSCT-PE	Immediate Memory	Delayed Memory
TMT-A	-								
DF	-0.029	-							
TMT-B	0.378**	0.087	-						
DB	-0.017	0.392**	0.12	-					
Letter Fluency	0.118	0.097	0.219**	0.036	-				
Semantic Fluency	0.076	-0.05	-0.031	-0.06	0.312	-			
WSCT-PE	-0.009	0.035	0.022	0.137	-0.034	0.031	-		
Immediate Memory	-0.163	0.002	-0.104	-0.071	0.071	0.268	-0.028	-	
Delayed Memory	-0.068	-0.135	-.207*	-.217**	0.018	.186*	-0.043	.409**	-
Profile 3	TMT-A	DF	TMT-B	DB	Letter Fluency	Semantic Fluency	WSCT-PE	Immediate Memory	Delayed Memory
TMT-A	-								
DF	0.080	-							
TMT-B	.424**	.171*	-						
DB	-0.023	.234**	-0.034	-					
Letter Fluency	0.165	0.064	0.134	0.134	-				
Semantic Fluency	0.124	-0.071	0.104	-0.093	.423**	-			
WSCT-PE	0.165	-0.002	-0.078	-0.120	-0.056	0.048	-		
Immediate Memory	-0.045	-0.113	-0.087	-0.123	-0.020	0.041	0.053	-	
Delayed Memory	-0.124	-0.149	-0.060	-0.092	-0.015	-0.066	0.010	.358**	-

Table 14 (Cont.)

Profile 4	TMT-A	DF	TMT-B	DB	Letter Fluency	Semantic Fluency	WCST-PE	Immediate Memory	Delayed Memory
TMT-A	-								
DF	0.110	-							
TMT-B	0.154	0.216	-						
DB	0.350	.520**	-0.189	-					
Letter Fluency	0.067	.443*	0.096	0.191	-				
Semantic Fluency	0.171	0.104	0.086	0.208	.650**	-			
WCST-PE	0.317	-0.046	0.171	0.156	0.171	.447*	-		
Immediate Memory	-0.066	0.266	-0.004	-0.034	-0.053	-0.260	-.524**	-	
Delayed Memory	-0.087	0.014	0.026	-0.152	0.049	-0.048	-0.230	.439*	-

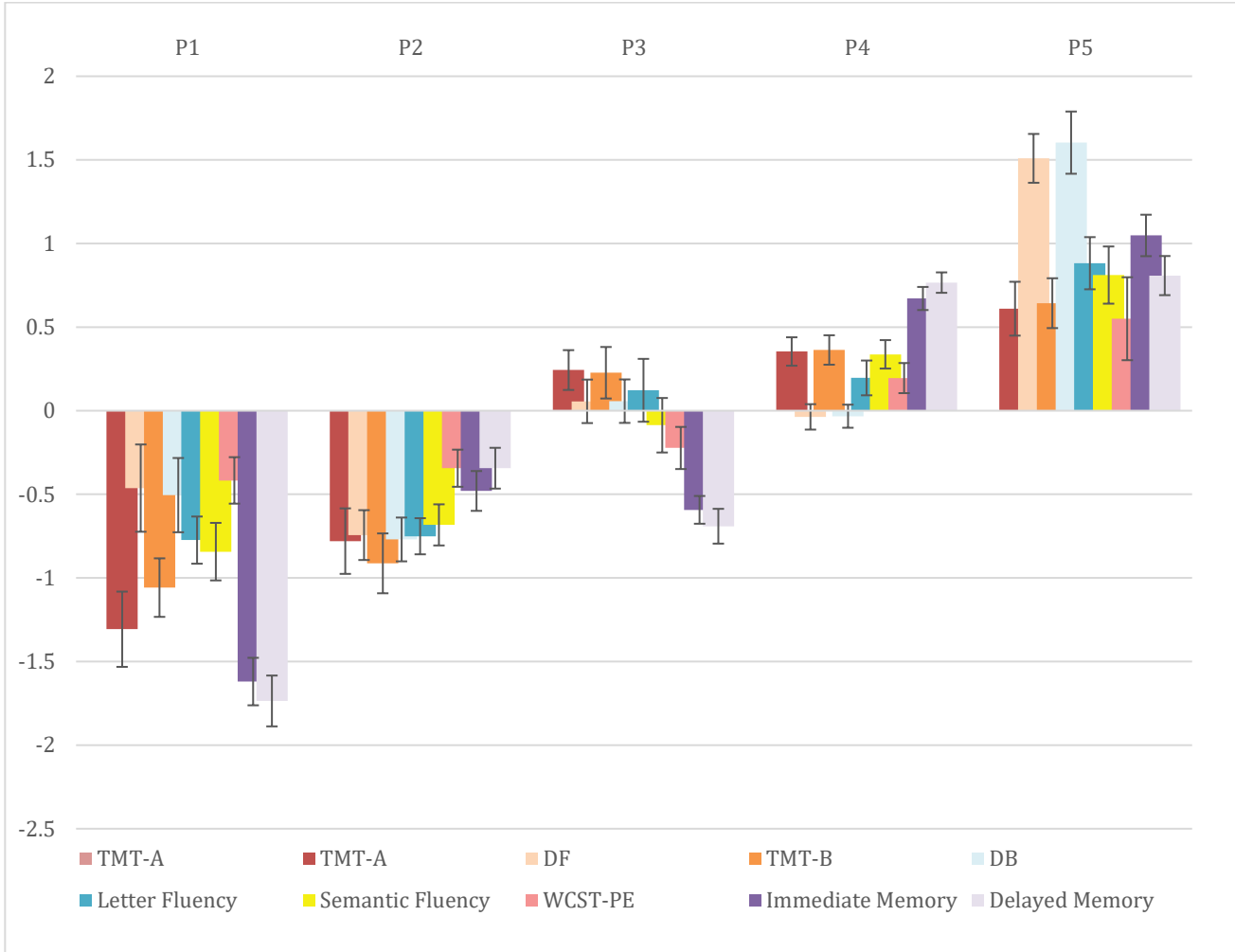
Profile 5	TMT-A	DF	TMT-B	DB	Letter Fluency	Semantic Fluency	WCST-PE	Immediate Memory	Delayed Memory
TMT-A	-								
DF	-0.073	-							
TMT-B	.647**	0.001	-						
DB	-0.231	0.245	-0.132	-					
Letter Fluency	.337*	-0.208	.390**	0.023	-				
Semantic Fluency	.428**	-0.206	0.266	-0.128	.365**	-			
WCST-PE	-0.236	0.200	-0.111	-0.171	-0.236	-0.158	-		
Immediate Memory	0.173	0.127	-0.034	0.076	0.244	.466**	0.078	-	
Delayed Memory	0.139	0.078	0.081	0.024	0.167	.485**	0.115	.800**	-

Note. **significant at the 0.01 level. *Correlation is significant at the 0.05 level (2-tailed). TMT = Trail Making Test. DF = Digits Forward. DB = Digits Backward. WCST-PE = Wisconsin Card Sorting Test -Perseverative Errors.

Figures

Figure 1

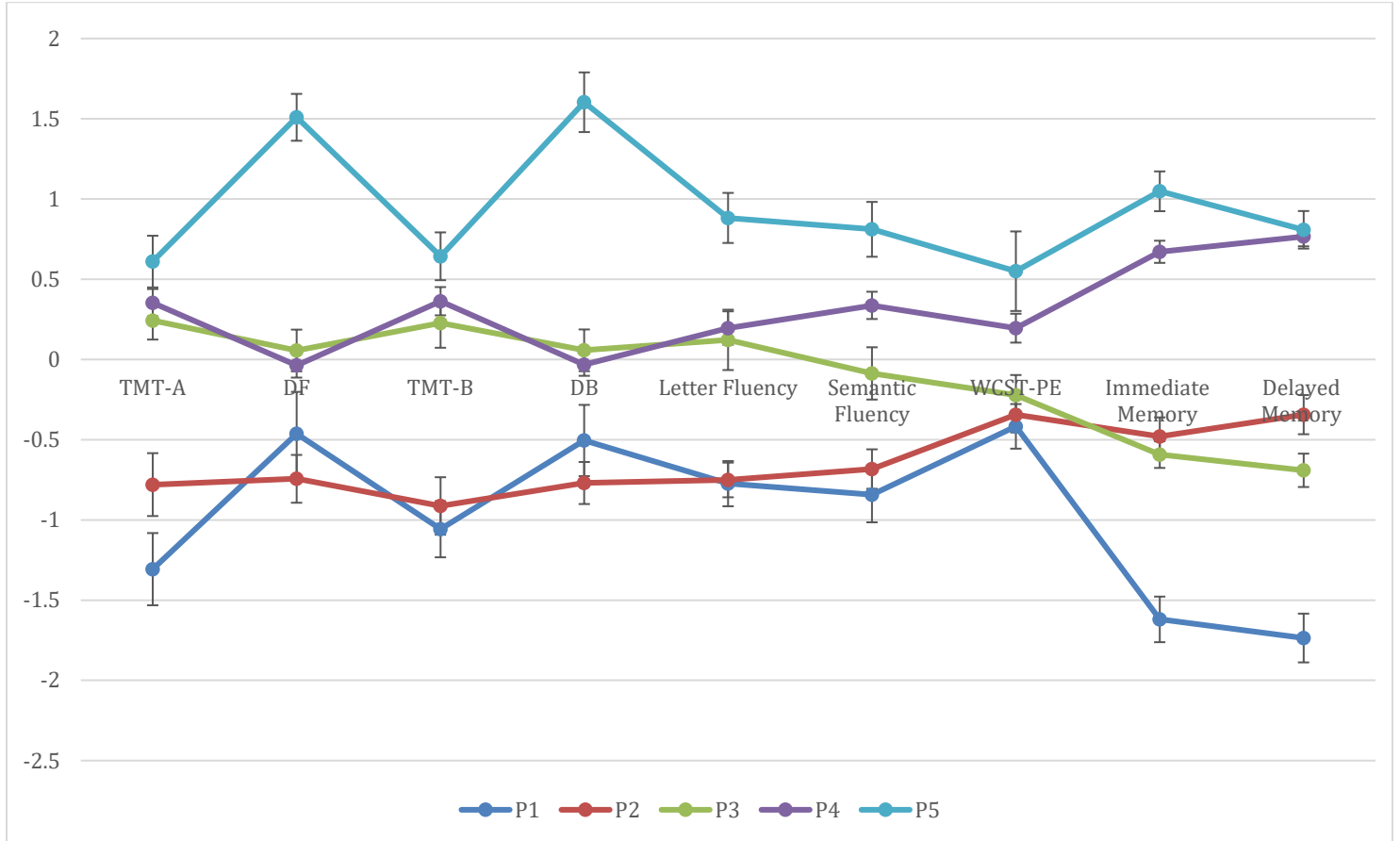
Cognitive Variable Performance Across Latent Profiles: 5-Profile Solution



Note. This figure illustrates the variable z-score by profile. TMT = Trail Making Test; DF = Digits Forward; DB = Digits Backward; WCST-PE = Wisconsin Card Sorting Test Perseverative Errors. Error bars represent standard deviations of the mean.

Figure 2

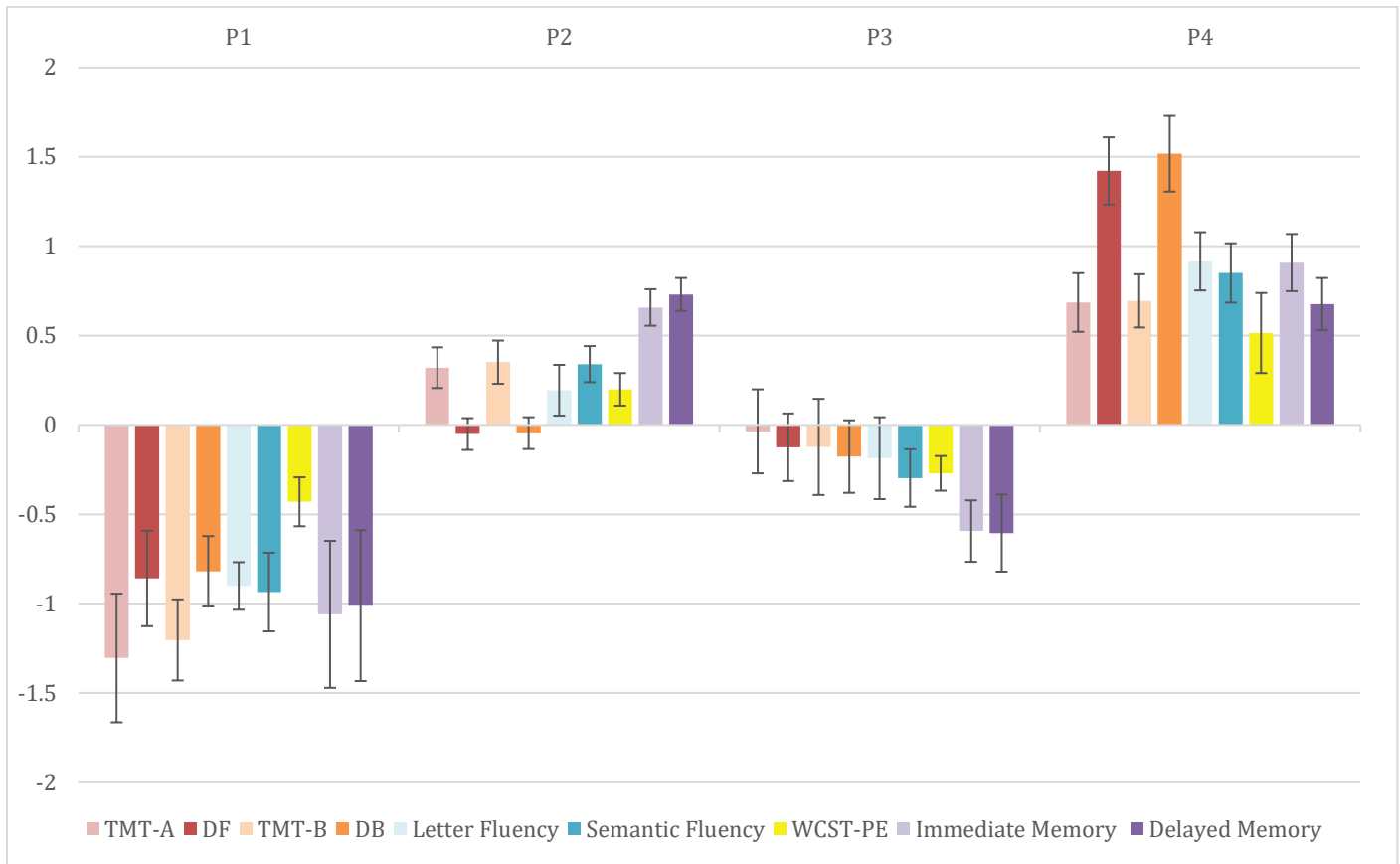
Performance Across Cognitive Variables by Latent Profile: 5-profile Solution



Note. Each line represents a latent profile group, showing performance in cognitive measures. Error bars represent standard deviations of the mean. TMT = Trail Making Test; DF = Digits Forward; DB = Digits Backward; WCST-PE = Wisconsin Card Sorting Test Perseverative Errors. Error bars represent standard deviations of the mean.

Figure 3

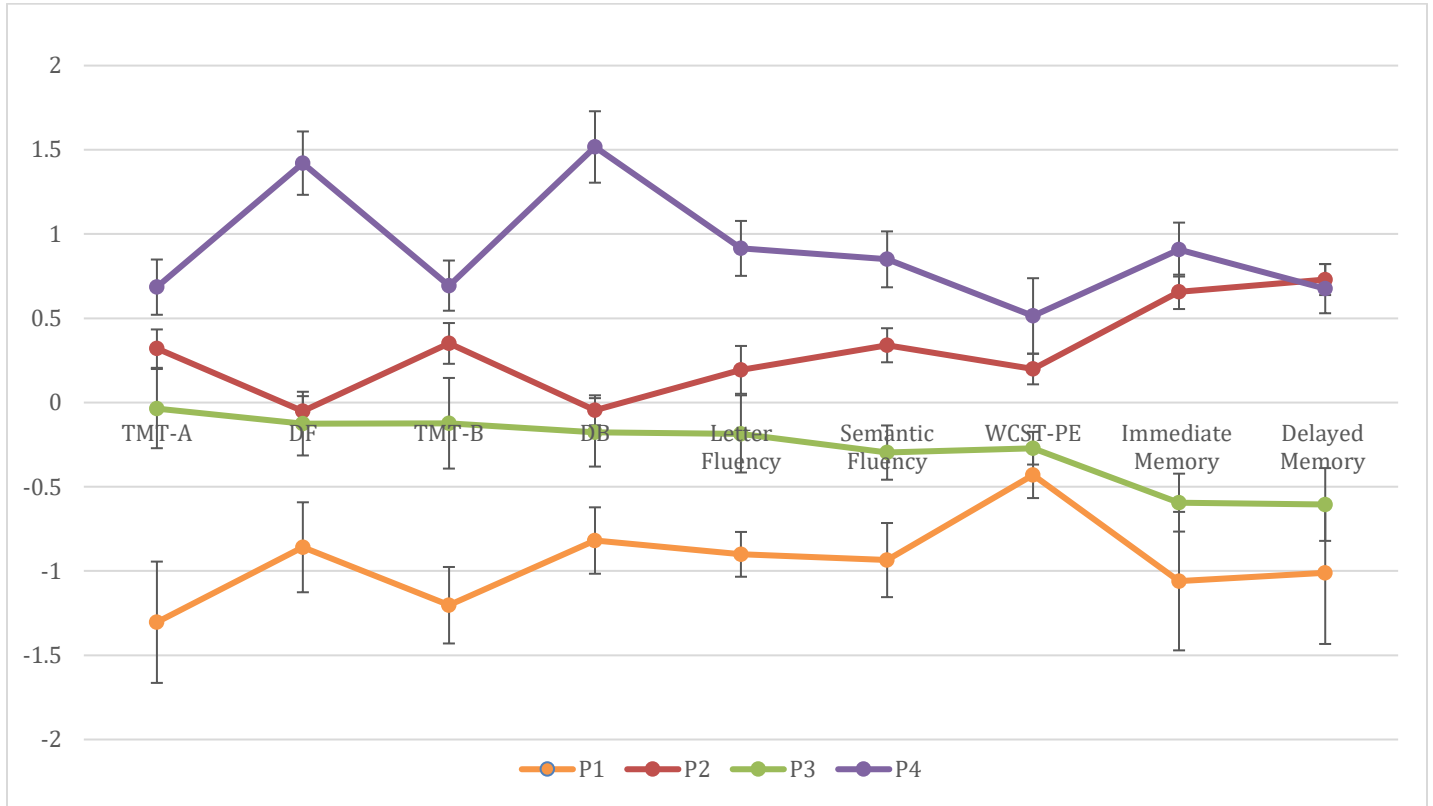
Cognitive Variable Performance Across Latent Profiles: 4-Profile Solution



Note. This figure illustrates the variable z-score by profile. TMT = Trail Making Test; DF = Digits Forward; DB = Digits Backward; WCST-PE = Wisconsin Card Sorting Test Perseverative Errors. Error bars represent standard deviations of the mean.

Figure 4

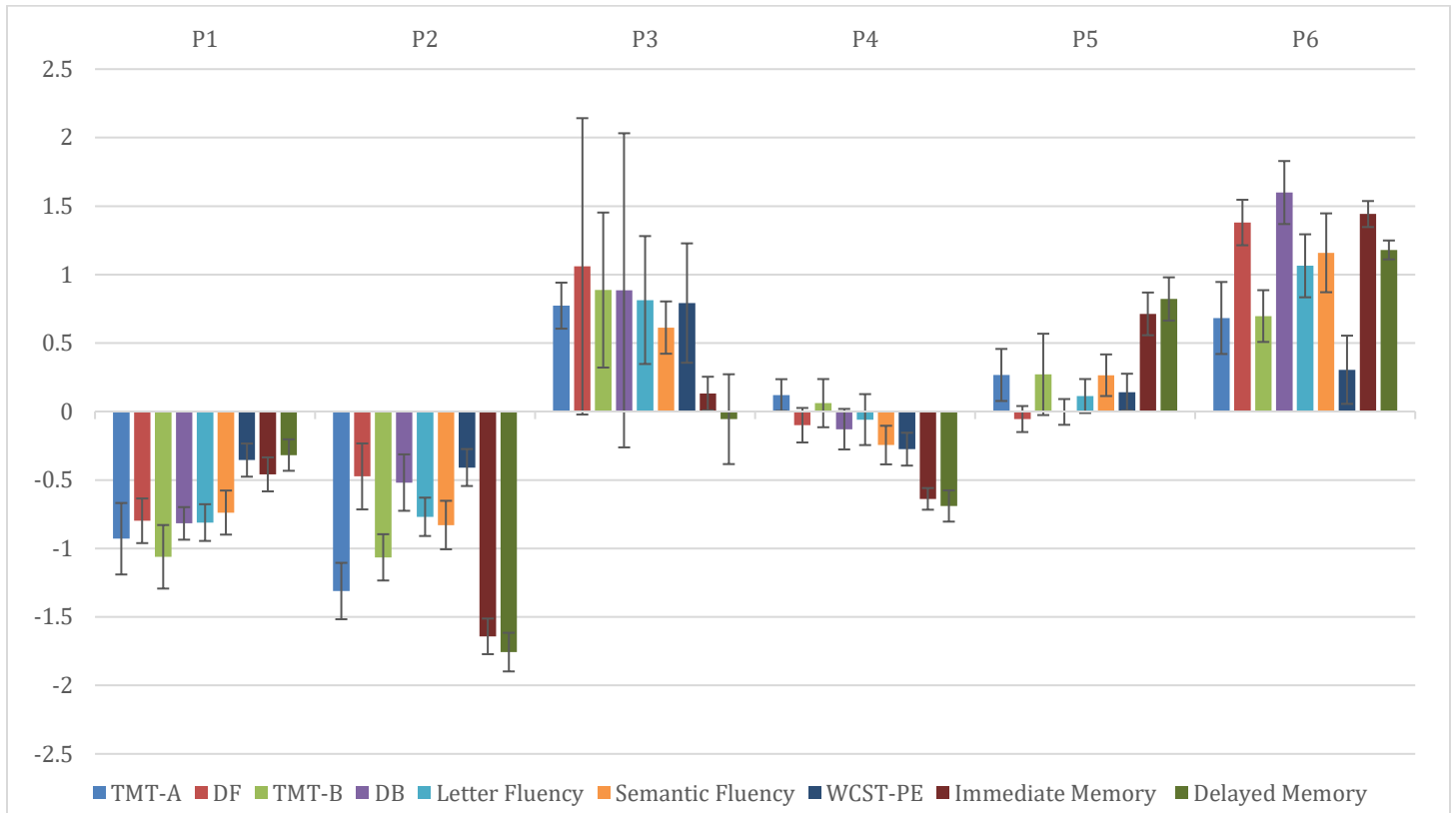
Performance Across Cognitive Variables by Latent Profile: 4-profile Solution



Note. Each line represents a latent profile group, showing performance in cognitive measures. Error bars represent standard deviations of the mean. TMT = Trail Making Test; DF = Digits Forward; DB = Digits Backward; WCST-PE = Wisconsin Card Sorting Test Perseverative Errors. Error bars represent standard deviations of the mean.

Figure 5

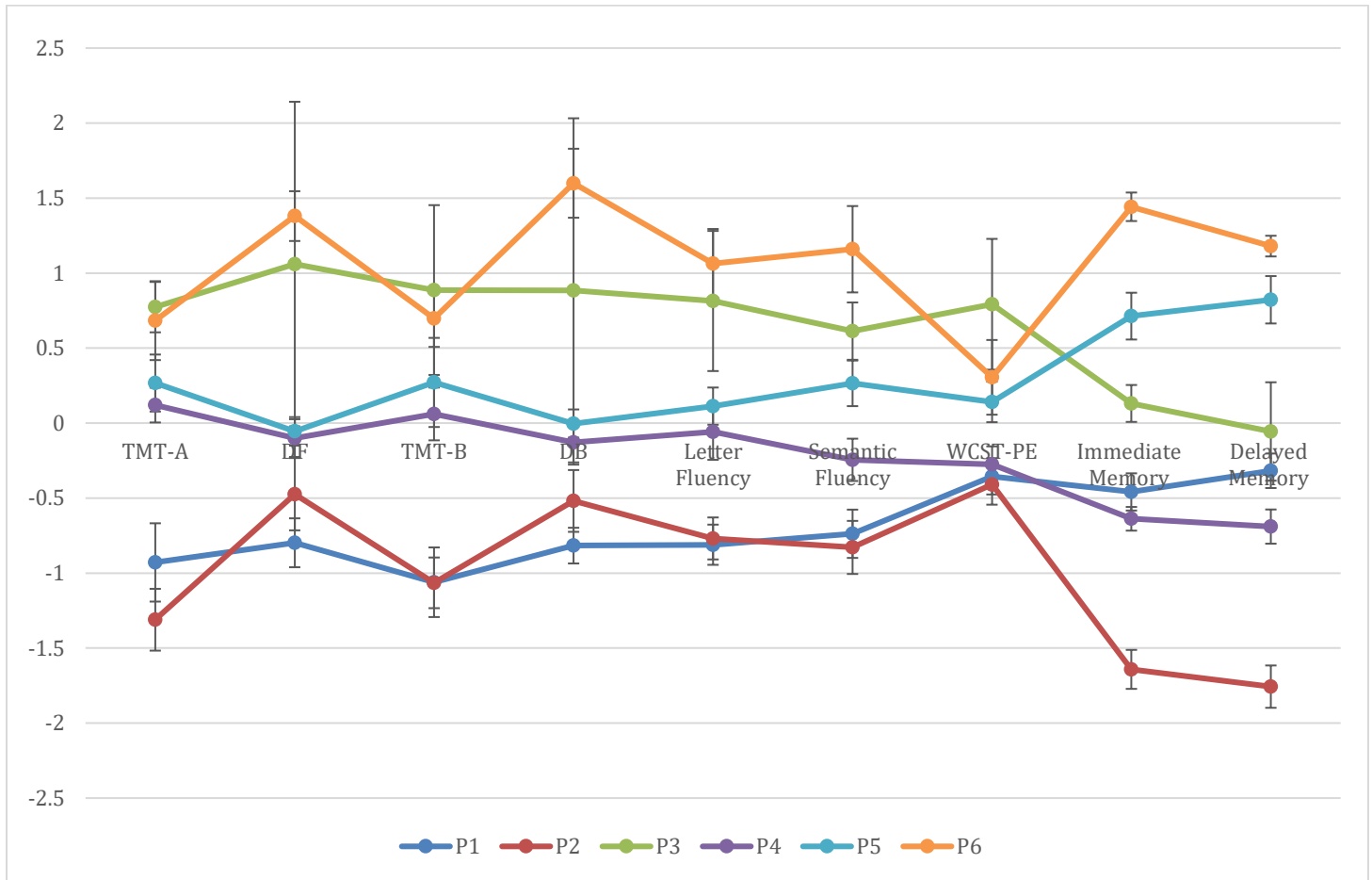
Cognitive Variable Performance Across Latent Profiles: 6-Profile Solution



Note. This figure illustrates the variable z-score by profile. TMT = Trail Making Test; DF = Digits Forward; DB = Digits Backward; WCST-PE = Wisconsin Card Sorting Test Perseverative Errors. Error bars represent standard deviations of the mean.

Figure 6

Performance Across Cognitive Variables by Latent Profile: 6-profile Solution



Note. Each line represents a latent profile group, showing performance in cognitive measures. Error bars represent standard deviations of the mean. TMT = Trail Making Test; DF = Digits Forward; DB = Digits Backward; WCST-PE = Wisconsin Card Sorting Test Perseverative Errors. Error bars represent standard deviations of the mean.