Summer 2014

Measuring apathy in a neuropsychological patient sample : factor structure and clinical correlates

Matthew Calamia
University of Iowa

Follow this and additional works at: https://ir.uiowa.edu/etd

Part of the Psychology Commons

MEASURING APATHY IN A NEUROPSYCHOLOGICAL PATIENT SAMPLE: FACTOR STRUCTURE AND CLINICAL CORRELATES

by

Matthew Calamia

A thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Psychology
in the Graduate College of
The University of Iowa

August 2014

Thesis Supervisors: Professor Daniel Tranel
Associate Professor Kristian E. Markon

Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

Matthew Calamia

has been approved by the Examining Committee
for the thesis requirement for the Doctor of Philosophy
degree in Psychology at the August 2014 graduation.

Thesis Committee: _____
Daniel Tranel, Thesis Supervisor

_____
Kristian E. Markon, Thesis Supervisor

_____
Molly A. Nikolas

_____
Michael W. O'Hara

_____
Natalie L. Denburg

To my family

ACKNOWLEDGMENTS

First, I would like to thank my advisors, Dan Tranel and Kristian Markon. Dan gave me the freedom to pursue my own research interests throughout my time at Iowa, helped me through the ups and downs of graduate school, and taught me how to shuck corn. Kristian was a constant source of support and guidance and always encouraged me to go a little further on research projects rather that settling for the easiest solution. Both were generous with their knowledge and time.

Thanks also to the members of my dissertation committee, past and current: Michael O'Hara, Molly Nikolas, Nancy Andreasen, and Natalie Denburg. Thanks as well to the undergraduate research assistants who helped collect the data for this project: Michelle Redinbaugh, Lisa Utizas, Nichole Baker, Jason Fiala, Leigh Taylor, Krista Specketer, and Hannah Hinkel. I would also like to acknowledge the American Psychological Association and University of Iowa Executive Council of Graduate and Professional Students for providing research funding.

I would also like to thank the members of my weekly Iowa writing group, Jennifer McCabe-Beane, Andrew Schrepf, Katherine Jonas, and Aaron Scherer, for their support and encouragement. Apparently sticker charts are motivating for both children and PhD students. Also, thanks to Sara Stasik for providing that same support and encouragement during internship.

Finally, I would like to thank my parents and sister for their love and support. After 7 years of weekly video chats and occasional visits, I'm so excited to finally be able to move out of the cornfields and back to the swamp.

ABSTRACT

Apathy, defined as a decrease in purposeful or goal-directed behavior, is common in many neurological disorders. The assessment of apathy in these disorders is important as apathy is associated with differential engagement and response to treatment and future cognitive and functional decline. Although apathy is often described as including three separate symptom dimensions, reflecting diminished interest, action, and emotional expression, investigations of the factor structure of apathy symptoms have been limited by the use of scales which do not comprehensively assess all of three of the proposed dimensions. The current study aimed to develop a novel informant report measure of apathy symptoms, investigate the factor structure of apathy symptoms, and examine the relationship of different types of apathy symptoms to several clinically relevant variables. Participants included 249 informants who reported on an individual with (n=210) or without (n=39) a neurological or psychiatric condition. Results showed the best fitting model of apathy symptoms was a bifactor model in which apathy could be represented as a global dimension with three separate, specific symptom factors reflecting diminished interest and initiative, asociality, and diminished emotional and verbal expression. In general, apathy was associated with poorer cognitive functioning, greater functional impairment, and higher caregiver distress. The specific symptom factors differed somewhat in their association with those same variables, highlighting the utility of measuring different types of symptoms in addition to overall apathy. Future work will refine the apathy measure developed in this study and test the obtained bifactor symptom model in an independent sample.

TABLE OF CONTENTS

LIST OF TABLES

CHAPTER I

INTRODUCTION

The term "apathy" is used to refer to decreases in behavior, specifically decreases in purposeful or goal-directed behavior (Marin, 1996). Apathy is associated with a range of cognitive, functional, and health outcomes and is present in a variety of neurological, psychiatric, and medical disorders (Chase, 2011; van Reekum, Stuss, & Ostrander, 2005). Much of the research on apathy has been conducted within the fields of neurology and neuropsychology, reflecting the facts that apathy is a very common problem following brain injury and that it creates special challenges for rehabilitation and treatment.

Although many researchers agree on the importance of studying apathy, there are significant differences in how apathy is defined and measured across studies. In a review of apathy scales, the authors concluded that "a lack of unified definition and conceptual operationalization of 'apathy' may be the foremost barrier to extending the current literature in this area" (Clarke, Ko, Kuhl, van Reekum, Salvador, & Marin, 2011, p.94). Within the literature, apathy has been "vaguely defined and broadly applied" (Chase, 2011, p.266) with studies using a "panoply of descriptors" in their characterizations of apathy (Levenson, Sturm, & Haase, 2014, p. 597).

The primary aim of this dissertation is to investigate the internal structure of apathy symptoms in a sample of patients being evaluated in a neuropsychology clinic, with the overall goal of developing a reliable and valid way of measuring apathy in such a population. Is apathy best defined as a unitary construct or is it composed of separable, but related dimensions? If separable dimensions are found, a secondary aim is to determine whether the dimensions have varying relationships to external correlates, such as cognitive and functional abilities.

Clinical Significance of Apathy

Prevalence. Studies of apathy within neurological conditions have largely treated it as a discrete disorder and compared patients "with and without apathy" rather than studying apathy symptoms dimensionally. Using this dichotomous approach, studies documenting the prevalence of apathy have varied significantly in terms of both patient characteristics (e.g, disease severity) and the criteria used to diagnose apathy (e.g. the use of different apathy scales). These differences have led to varying estimates of apathy within a disorder; for example, in Parkinson's disease, the rate of apathy has been found to range from as low as 17% and as high as 70% across studies (Aarsland, Marsh, & Schrag, 2009). In a meta-analysis of studies of stroke patients, the type of scale used moderated the prevalence estimate of apathy (van Dalen, van Charante, Nederkoorn, van Gool & Richard, 2013).

Differences in the rates of apathy within individual disorders have been compared with several replicated results. For example, multiple studies have documented lower rates of apathy in patients with Alzheimer's disease compared to patients with frontotemporal dementia (e.g. Chow, Binns, Cummings, Lam, Black, Miller…van Reekum, 2009; Levy, Miller, Cummings, Fairbanks, & Craig, 1996), vascular dementia (e.g. Chan, Lim, & Sahadevan, 2008; Fuh, Wang, & Cummings, 2005) or dementia with lewy bodies (e.g. Galvin, Malcom, Johnson, & Morris, 2007; Ricci, Guidoni, Sepe-Monti, Bomboi, Antonini, Blundo, & Giubilei, 2009). The types of apathy symptoms present within disorders can also vary. For example, in one study matching for overall apathy severity, patients with frontotemporal dementia had higher rates of emotional apathy symptoms and decreased speech (Quaranta, Marra, Rossi, Gainotti, and Masullo, 2012).

The prevalence of apathy across specific disorder subtypes has also been studied. For example, two studies have compared the rates of apathy in amnestic and non-amnestic mild cognitive impairment and have come to opposite conclusions as to which

subtype is associated with greater apathy (Geda et al., 2008; Chan et al., 2010). As will be discussed later, apathy can also be studied dimensionally and that approach has been used in examining the relation of apathy to other clinical constructs.

Factors contributing to the etiology of apathy. Apathy is related to environmental, psychological, and neurobiological factors. Patients in nursing home units where more staff time is available for patient care have lower rates of apathy than patients on units with fewer and less available staff (Zuidema, de Jonghe, Verhey, & Koopmans, 2010). Alzheimer's disease patients who formerly worked in occupations requiring high levels of "motivational ability" (e.g. jobs requiring a high level of self-planning of work-related goals) were more likely to develop apathy in a follow-up assessment than patients who previously worked in jobs requiring lower levels of "motivational ability" (Mortbly, Maercker, & Forstmeier, 2011). The authors suggested that this may be the result of those patients reacting to their disease by becoming apathetic, perhaps after experiencing failure in trying to achieve goals that are too difficult given their cognitive decline. With neurological disorders, apathy is associated with atrophy in brain regions such as the anterior cingulate, dorsolateral prefrontal cortex, and orbitofrontal cortex (e.g. Massimo et al., 2009; Zamboni, Huey, Krueger, Nichelli, & Grafman, 2008). Similarly, lesion studies have identified apathy as occurring following damage to specific regions, for example, the ventromedial and dorsolateral prefrontal cortex (Robinson, Calamia, Gläscher, Bruss, & Tranel 2013).

Cognitive impairment and decline. Apathy predicts the onset of dementia in patients with mild cognitive impairment (Chilovi et al., 2009; Palmer, Di Iulio, Varsi, Gianni, Sancesario, Caltagirone, & Spalletta, 2010; Robert, Berr, Volteau, Bertogliati, Benoit, Sarazin,…Members of the PreAL study, 2006) . This relationship persists even after controlling for factors related to both apathy and dementia, such as age and functional and cognitive status at baseline (Chilovi et al., 2009). Apathy also predicts the

onset of dementia in Parkinson's disease (Dujardin, Sockeel, Delliaux, Destee, & Defebvre, 2009).

Rates of apathy increase longitudinally with the progression of dementia (Steinberg, Shao, Zandi, Lyketsos, Welsh-Bohmer, Norton…Cache County Investigators, 2008) and diseases such as Parkinson's disease (Pedersen, Alves, Aarsland, & Larsen, 2009) and Huntington's disease (Craufurd, Thompson, & Snowden, 2001). In a sample of patients with Alzheimer's disease, while only 28% of patients with mild Alzheimer's disease were apathetic, the prevalence rose to 61% in patients with severe Alzheimer's disease. (Starkstein, Jorge, Mizrahi, & Robinson, 2006). Although apathy is related to cognitive decline, it is not synonymous with cognitive functioning; in one study, roughly half of the patients with moderate to severe dementia did not have apathy (Starkstein & Pahissa, 2014).

Apathy is especially associated with worse performance in several specific cognitive domains such as executive functioning (e.g. , Andesson & Bergedalen, 2002; Butterfield, Cimino, Oelke, Hauser,& Sanchez-Ramos, 2010), working memory (e.g., Chiaravalloti & DeLuca, 2003; Torrente, Lischinsky, Torralva, López, Roca, & Manes, 2011) and long-term verbal memory (e.g., Chiaravalloti & DeLuca, 2003; Kuzis, Sabe, Tiberti, Dorrego, & Starkstein, 1999). The magnitude of correlations between apathy and specific cognitive test scores varies significantly across studies, perhaps reflecting differences among studies in sample size, the range of cognitive and apathy scores in the sample, and the specific measure of apathy used. For example, in one study, two measures of apathy correlated significantly with the Mini Mental Status Examination (MMSE) ($r=-.42$ and $r=-.32$) while a third measure of apathy did not ($r=-.06$) (Reijnders, Scholtissen, Weber, Aalten, Verhey, & Leentjens, 2010).

Functional impairment. Apathy is associated with impairment in both basic activities of daily living (ADLs; e.g. dressing, eating) and instrumental activities of daily living (IADLs; e.g., handling money, managing medications) (Boyle, Malloy, Salloway,

Cahn-Weiner, Cohen, & Cummings, 2003). In a sample of Alzheimer's patients, those who were apathetic at both initial testing and a one-year follow-up showed a more rapid decline in IADLs compared to those without persistent apathy (Lechowski, Benoit, Chassagne, Vedel, Tortrat, Teillet, & Vellas, 2009). The association of apathy with ADLs and IADLs cannot be explained by overlap between apathy and cognitive impairment; apathy remains a significant predictor of functional impairment when cognitive impairment is added to the prediction model (Norton, Malloy, & Salloway, 2001; Zawacki, Grace, Paul, Moser, Ott, Gordon, & Cohen, 2002). Cross-sectional, correlational studies have often found a moderate relationship between apathy and functional impairment (e.g., Kiang, Christensen, Remington, & Kapur, 2003; Boyle, Malloy, Salloway, Cahn-Weiner, Cohen, & Cummings, 2003.)

Physical health. Longitudinal and cross-sectional studies have identified a link between apathy and physical health. Apathy ratings obtained at admission to physical rehabilitation programs predict patient outcomes. Patients identified as apathetic at the start of a rehabilitation program are later rated as being less involved or active those programs (Resnick, Zimmerman, Magaziner, & Adelman, 1998). Likely as a consequence of their decreased involvement, those patients show less improvement compared to non-apathetic patients (Lenze, Munin, Dew, Marin, Butters, Skidmore…Reynolds III, 2009). Apathy is associated with health management behaviors in chronic conditions. For example, in a cross-sectional study of diabetic patients, those with apathy were less likely to follow recommendations about exercise or properly manage their use of insulin (Padala et al., 2008).

Caregiver distress. The psychological and physical strain of providing care to family members with chronic illness has been referred to as "caregiver burden" (Etters, Goodall, & Harrison, 2008). Caregivers have poorer psychological and physical health than non-caregivers (Pinquart & Sörensen, 2003). Caregiver burden is also related to patient outcomes, for example, higher rates of caregiver burden are associated with a

greater likelihood of the patient becoming institutionalized (Miller, Rosenheck, & Schneider, 2011). Patient apathy has been consistently related to caregiver burden, although the magnitude of this relationship has varied greatly across studies (e.g., Allegri et al., 2006; Chiò, Mastro, Guidici, Iazzolino, Calvo, Moglia, & Montuschi, 2010; Dujardin, Sockeel, Delliaux, Destée, & Defebvre, 2008).

Summary of the clinical importance of apathy. The significance of apathy is demonstrated through its association with a host of clinically-relevant variables, including cognitive impairment, functional impairment, health behaviors, and caregiver distress. Although apathy is clearly important, there is variability in the literature as to how the construct is defined and measured. This lack of agreement has been identified as the "foremost barrier" plaguing apathy research (Clarke et al., 2011, p. 94).

Diagnosis and Measurement

Historical and current definitions. Older definitions of apathy focused primarily on emotion or interest. For example, Greenson (1949) defined apathy as a "state of affectlessness." According to Greenson (1949), "the most striking characteristic of the apathetic patient is his visible lack of emotion and drive. At first glance he seems to be depressed; closer scrutiny, however, reveals lack of affect" (p.290). Marin (1991) argued that rather than defining apathy as a loss of emotion or loss of interest, both those symptoms (as well as others) could be conceptualized as reflecting a "loss of motivation" (p. 243). More recently, authors have defined apathy in purely behavioral terms, without making reference to unobservable constructs, such as motivation. For example, Stuss, Van Reekum, and Murphy (2000) stated that "apathy is best characterized in behavioral terms as an absence of responsiveness to stimuli as demonstrated by a lack of self-initiated action" (p. 342). Similarly, Levy and Czernecki (2006) defined apathy as "a quantified and observable behavioral syndrome consisting in a quantitative reduction of voluntary (or goal-directed) behaviors." (p. 54).

Proposed diagnostic criteria. Despite the apparent differences in Marin's conceptualization of apathy as a "disorder of diminished motivation" (Marin & Wilkosz, 2005, p. 377) and definitions emphasizing observable behaviors (e.g. Stuss, Van Reekum, & Murphy, 2000), the operationalization of both of these definitions is quite similar, as Marin (1996) used observable behavioral criteria to define impairment in motivation. Marin (1996) stated that apathy is present when there is a "simultaneous diminution in the overt behavioral, cognitive, and emotional concomitants of goal-directed behavior" (p.305). The presence of these three components formed the basis of Marin's (1991) criteria for the diagnosis of apathy. Criteria for the behavioral component include "lack of time spent in activities of interest," "lack of productivity," and "diminished socialization or recreation." Criteria for cognitive component include "lack of interests" and "diminished importance or value attributed to…socialization, recreation, productivity, initative, perseverance, or curiosity." Emotional criteria include "lack of emotional responsivitiy to positive or negative events" and "absence of excitement or emotional intensity" (p.245).

A revised version of Marin's diagnostic criteria can be found in the diagnostic criteria put forth by a task force sponsored by various European associations, including the European Psychiatric Association (Robert, Onyike, Leentjens, Dujardin, Aalten, Starkstein,…Bryne, 2009). This proposed diagnosis includes cognitive, behavioral, and emotional criteria, but differs from Marin (1996) somewhat in inclusion and exclusion criteria, including a requirement of symptoms in only 2 of the 3 categories. Marin required the presence of symptoms from all 3 categories in order to make a diagnosis of apathy (Marin, 1996). The revised criteria also explicitly divide symptoms into "initiation" (e.g. "starting conversation") and "responsiveness" (e.g. "responding to a conversation") symptoms (p. 101).

Some authors have advocated for a division of apathy into subtypes based on the specific neural substrates hypothesized to underlie a particular form of apathetic

behavior. Levy and Czernecki (2006) describe three subtypes of apathy arising from prefrontal cortex or basal ganglia dysfunction. Stuss, Van Reekum, and Murphy (2000) describe seven subtypes corresponding to areas in the frontal cortex and related subcortical structures . The symptoms described in these subtypes largely overlap with the symptoms included as part of Marin's (1996) model, although in some instances they include extreme presentations. For example, akinetic mutism, which can arise following bilateral anterior cingulate damage, can be considered the most severe type of apathy (Marin & Wilkosz, 2005). Patients with this disorder are conscious and physically capable of action, but do not engage in spontaneous movement or speech (Damasio & Van Hoesen, 1983) In additional to cognitive, behavioral, and emotional symptoms, Stuss et al. (2000) propose a "more abstract form of apathy" consisting of deficts in "self and social awareness." Patients with this form of apathy are hypothesized to have "intact knowledege of behavior, even of intention, but a lack of action in one's own self-interest" (p.350).

Although apathetic symptoms such as a lack of interest in activities or constricted affect appear in several DSM-5 diagnoses (e.g. major depressive disorder and schizotypal personality disorder), the DSM-5 does not currently contain a separate apathy diagnosis in its list of mental disorders. However, "apathetic type" is listed as one subtype of "personality change due to a general medical condition" (American Psychiatric Association, 2013). In the ICD-10, apathy is listed under the heading of "symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified" and is also listed as a symptom of dementia in pick disease (World Health Organization, 1992).

Current approaches to measuring apathy in research. Despite the lack of a formal diagnosis, many researchers have studied apathy using a categorical approach and have divided patients into apathetic and non-apathetic groups based on whether patients meet diagnostic criteria or obtain a certain score on a continuous measure of apathy. Although no direct comparison of categorical and continuous models of apathy appears in

the literature, to date, there is little evidence supporting categorical models of psychopathology for the vast majority of disorders that have been studied (Haslam, Holland, & Kuppens, 2011), suggesting apathy is also likely a continuous dimension. Furthermore, recent research on physical and social anhedonia, symptoms which are similar to apathy, has supported a dimensional model. (Rawlings, Williams, Haslam, & Claridge, 2008). (However, see Haslam et al., 2011, for a discussion of older research which supports a categorical model for these symptoms). Given evidence that categorical measurement of psychopathology is less reliable and valid than continuous measurement (Markon, Chmielewski, & Miller, 2011), it seems appropriate to measure apathy using continuous measures.

While conceptualizations of apathy vary in the terminology they use (e.g. intellectual curiosity vs. interest, initiative vs. action initiation), there is general agreement across most definitions for cognitive, behavioral, and emotional components (Robert et al., 2009). Although, it should be noted that not all authors agree that those three components are dissociable. For example, in an analysis of a scale written to assess cognitive (i.e., lack of interest) and behavioral (i.e., lack of action) symptoms, empirical evidence for one factor was obtained (Esposito, Rochat, Van der Linden, Lekeu, Charnallet, & Van der Linden, 2014). In the authors' own words, "Thus, without interest, people lack a basis for acting; and without the initiation of specific activities, people lack a way of forming preferences for these activities" (p. 48). In a one factor model of apathy symptoms, both symptoms of diminished action and interest loaded highly on that one factor, with symptoms of diminished emotional expression loading weakly (Zahodone, Marsiske, Okun, & Bowers, 2012).

Apathy scales. Regardless of whether one advocates for a discrete or dimensional approach to apathy, a standardized interview or questionnaire is often used to assess the symptoms of apathy. A recent review identified the Apathy Evaluation Scale (Marin, Biedrzycki, & Firinciogullari, 1991) and apathy score on the Neuropsychiatric Interview

(Cummings, Mega, Gray, Rosenberg-Thompson, Carusi, & Gornbein, 1994) as the "most psychometrically robust and widely used measures for assessing apathy" (Clarke, Ko, Kuhl, van Reekum, Salvador, & Marin, 2011, p. 94). These scales measure apathy as a single, unitary construct, reporting the total score derived from responses to all items. In contrast, some scales, such as the Apathy Inventory (Robert, Clairet, Benoit, Koutaich, Bertogliati, Tible,…Bedoucha, 2002) and Lille Apathy Rating Scale (Sockeel, Dujardin, Devos, Denève, Destée, & Defebvre, 2006) include subscales measuring specific components of apathy (i.e. different diagnostic criteria such as loss of interest and lack of initiative). Factor analysis of these individual scales and correlational analyses of the associations among these different scales provide evidence as to the underlying latent structure of apathy symptoms.

Apathy Evaluation Scale. The Apathy Evaluation Scale (AES) is an 18 item measure of apathy (Marin et al., 1991). There are three versions of the AES: a self-report questionnaire version (AES-S), an informant-report questionnaire version (AES-I), and clinician-lead semi-structured interview version (AES-C). Marin and colleagues (1991) labeled 6 items on the AES as cognitive (e.g. s/he is interested in things; getting things started on his/her own is important to him/her; s/he is interested in having new experiences), 5 items as behavioral (e.g. s/he gets things done during the day; s/he puts little effort into anything; s/she spends time doing things that interest her/him), 2 items as emotional (i.e. s/he approaches life with intensity; when something good happens, s/he gets excited) and 3 items as "other" (i.e. s/he has an accurate understanding of her/his problems; s/he has initiative; s/he has motivation).

Principal components analyses of the AES have consistently found evidence for a large general component, representing 30-50% of the scale variance (e.g. Clarke, Van Reekum, Patel, Simard, Gomez, & Streiner, 2007; Sagen, Faerden, Haug, Melle, Finset, & Dammen, 2010; Faerden, Nesvåg, Barrett, Agartz, Finset, Friis, Rossberg, & Melle, 2008). This factor has been found in all versions of the AES (Marin, Biedrzycki, &

Foromcogullari, 1991) and in different patient groups (e.g. dementia, Clarke et al., 2007; first episode psychosis, Sagen et al., 2010). This general component often includes items from each of the three diagnostic criteria for apathy: cognitive, behavioral, and emotional symptoms.

Beyond this first component, studies have differed as to the additional components estimated in the analyses. Additional components labeled “interest” (e.g. Clarke, Ko, Lyketsos, Rebok, & Eaton, 2010), “social contacts” (e.g. Sagen et al., 2010) and “lack of insight” (e.g. Faerden et al., 2008) have been found in different studies. The composition of those components has differed significantly across different patient samples and different versions of the AES (Sagen et al., 2010, Faerden et al., 2008, Clarke et al., 2010, Marin et al., 1991). Some authors have been unable to summarize the heterogeneous content found on the second principal component in their analyses, choosing to simply label that component as “other” (Clarke et al., 2007; Sagen et al., 2010).

Although the principal components analyses of the AES suggest multiple dimensions may be needed in order to fully capture the apathy construct, limitations of the AES preclude definitive conclusions. A “lack of interest” component is consistent with the separate criteria for cognitive symptoms in diagnostic systems for apathy (Marin, 1996, Robert et al., 2009), but it should be noted that in some studies, the component labeled “interest” consisted largely or even exclusively of items which included the word “interest”, making it possible that this component merely represent that semantic commonality. The “social contacts” component is quite narrow, usually consisting of two items, both of which are about friendships. One study using the Apathy Scale, an abbreviated version of the AES, reported finding evidence for the proposed three factor structure of apathy, although it should be noted the behavior factor was represented with only two items, which correlated moderately with the cognitive factor (r=0.66) (Kay, Kirsch-Darrow, Zahodne, Okun & Bowers, 2012).

Neuropsychiatric Interview (NPI).The Neuropsychiatric Interview (NPI) was originally designed as a measure of psychopathology for use in dementia patients (Cummings et al., 1997). There are several versions of the NPI including: a structured interview (Cummings, 1997; de Medeiros, Robert, Gauthier, Stella, Politis, Leoutsakos,…the NPI-C Research Group, 2010), an abbreviated informant-report questionnaire (Kaufer, Cummings, Ketchel, Smith, MacMillian, Shelley,…DeKosky, 2000), and a structured interview designed specifically for use in nursing homes (Wood et al., 2000). Although versions differ slightly in content, they contain subscales to measure a variety of different psychotic (e.g. hallucinations, delusions), internalizing (e.g. dysphoria, anxiety), and externalizing (e.g. disinhibition, aggression) symptoms.

In the administration of the original NPI, if an informant responds positively to a screening question, the full subscale for that symptom is then administered. Scoring of the NPI is not based on a sum of responses to individual items. Rather, at the end of the subscale for a specific symptom, the informant is asked to make a rating as to the frequency of the most frequent symptom and the severity of the most severe symptom (Cummings, 1997). Given this approach to scoring, it is perhaps not surprising that analyses of the NPI have been conducted at the subscale level (i.e. principal components analyses of the severity and frequency scores of each symptom type), and not the item-level (i.e. analyses of the responses to items on an individual subscale). In the only study examining individual items of the NPI apathy subscale, 9 raters (3 neurologists, 3 neuropsychologists, and 3 psychiatrists) were asked to classify the items on the apathy subscale as reflecting either cognitive, behavioral, or emotional symptoms of apathy. Agreement (by 6 of 9 raters) was achieved only for 4 of the 9 items on the subscale (Chow, Binns, Cummings, Lam, Black, Miller, Freedman, Stuss, & van Reekum, 2009).

A revised version of the NPI, the NPI-C (de Medeiros et al., 2010) includes informant ratings of the severity and frequency of every scale item, and also includes an expanded number of items on several subscales. New items on the apathy subscales were

based on the latest version of diagnostic criteria for apathy (Robert et al., 2009). However, to date, no item-level analyses of this measure have been reported in the literature.

The items on the NPI and NPI-C were derived through expert consensus (Cummings, 1997; de Medeiros et al., 2010). Although studies have provided evidence for the convergent validity of NPI or NPI-C subscales with other established scales of the same construct (e.g. de Medeiros et al., 2010), the psychometric properties of individual items on the NPI has not been comprehensively studied. Therefore, although the NPI is one of the most frequently used measures of apathy, research on the NPI provides no data as to the internal structure of apathy symptoms.

Lille Apathy Ratings Scale (LARS). The Lille Apathy Rating Scale (LARS) was developed as a comprehensive measure of apathy (Sockeel et al., 2006). There are two structured interview versions, one for informants and one for patients (Sockeel et al., 2006; Dujardin, Sockeel, Delliaux, Destée, & Defebvre, 2008). The LARS includes 33 items written to assess the cognitive, behavioral, and emotional symptoms of apathy, as well as "extinction of self-awareness", a symptom domain included in some conceptualizations of apathy (e.g. Stuss, Van Reekum, & Murphy, 2000). Items in the self-awareness domain refer to a person's ability to question his or her decisions, change his or her opinions or actions when needed, admit when he or she is wrong, and feel guilt after being rude to someone. The 33 items were (rationally) divided into 9 subscales: "lack of interest", "novelty seeking", "motivation", "poor social life", "low everyday productivity", "lack of initiative", "blunting of emotional responses", "lack of concern", and "extinction of self-awareness." Although the authors do not provide specific criteria, they state an examination of the correlation matrix of responses to items supported their decision to create subscales (Sockeel et al., 2006).

A principal component analysis of the LARS subscales yielded four components, which the authors labeled "intellectual curiosity", "action initiation", "emotion" and

"self-awareness" (Sockeel et al., 2006). The first three components resemble the cognitive, behavioral, and emotional apathy symptom domains in proposed diagnostic criteria for apathy. These components were all significantly correlated, with the highest correlation between the cognitive ("intellectual curiosity") and behavioral ("action initiation) components. The self-awareness component was not significantly correlated with any other component and scores on the self-awareness subscale were not significantly correlated with the total LARS score. This suggests self-awareness may not be a core component of apathy.

Apathy and self-awareness. Lack of awareness of apathy is associated with cognitive impairment; in a study of patients with Alzheimer's disease, patients with Parkinson's disease, patients with mild cognitive impairment, and healthy comparison participations, informant and patient reported apathy only differed for the Alzheimer's sample, the group which had the worst MMSE score (Robert, Clairet, Benoit, Koutaich, Bertogliati, Tible, Caci, Borg, Brocker, & Bedoucha, 2002).

A lack of awareness of cognitive and behavioral deficits (i.e. anosognosia) associated with a disease process, such as Alzheimer's disease, is related to apathy. In one study including various cognitive and emotional measures, apathy had the strongest relationship to unawareness (Derouesne, Thibault, Lagha-Pierucci, Baudouin-Madec, Ancri, & Lacomblez, 1999). One longitudinal study found that anosognosia for functional impairments and mood and behavior changes at baseline was associated with a greater increase in apathy scores at follow-up (Starkstein, Brockman, Bruce, & Petracca, 2010)

This evidence suggests: 1) patients can be unaware of the severity of their apathy and 2) patients' unawareness of their cognitive, behavioral, or functional impairments is associated with their level of apathy. This leads to a question as to whether a lack of self-awareness, which is not included in many definitions of apathy, should be considered a component of apathy. Several sources of evidence do not support the inclusion of self-

awareness as a component of apathy. A lack of self-awareness is more highly related to cognitive impairment than other symptoms of apathy. For example, items on the "lack of insight" component of the AES have been found to correlate more highly with MMSE scores than total apathy scores (Lueken, Seidl, Völker, Schweiger, Kruse, & Schröder, 2007). While Parkinson's patients differ from healthy comparison participants on the cognitive, behavioral, and emotional domains of apathy on the LARS, they do not differ from healthy comparison participants in the self-awareness domain; only the subgroup of Parkinson's patients with dementia shows impairments in self-awareness (Dujardin, Sockeel, Devos, Delliaux, Krystkowiak, Destée, & Defebvre, 2007).

Correlations between different measures of apathy. Although different measures have varied significantly in their length and breadth of content, most studies have found evidence of at least a moderate degree of convergent validity. The median correlation of three studies assessing agreement between informant-report and clinician-report of apathy was r = 0.71 (Clarke et al., 2007; Dujardin et al., 2008; Marin et al., 1991). The median correlation of six studies in assessing agreement between self-report and clinician-report of apathy on was r = 0.67 (Gallagher, Lees, & Schrag, 2008; Kiang, Christensen, Remington, & Kapur, 2003; Kirsch-Darrow, Zahodne, Hass, Mikos, Okun, Fernandez, & Bowers, 2009; Marin et el., 1991; Pluck & Brown, 2002; Starkstein & Merello, 2007). All of these correlations from different pairs of raters, using different measures of apathy, support the convergent validity of apathy.

Despite evidence of good convergent validity of different apathy scales, the scales clearly contain differing degrees of cognitive, behavioral, and emotional apathy content. Two studies compared self-rated LARS domain scores to the total score of a different apathy measure (i.e., the Apathy Evaluation Scale or closely related Apathy Scale). The highest correlations in each study were between the LARS intellectual curiosity domain (cognitive domain) and total score on the second apathy measure (r=0.61 and r=0.84). The second highest correlations were between the total apathy score and the action

initiation domain (behavioral domain), r = 0.42 and r = 0.65. Finally, correlations with the emotion domain were r = 0.33 and r = 0.44, and correlations with the self-awareness domain were r = 0.15 and r = 0.22 (Sockeel et al., 2006; Zahodone et al., 2009). In a study comparing the NPI apathy subscale to the Apathy Inventory (Robert et al., 2002), a brief measure containing one cognitive apathy, one behavioral apathy, and one emotional apathy item, the highest correlation was between the NPI apathy subscale and the "lack of interest" (cognitive) score, r=0.63. The "lack of initiative" (behavioral) score correlated r=0.23 and the emotional blunting score correlated r=0.01. Proposed emotional and self-awareness symptoms of apathy appear to be the least well represented on existing apathy scales.

Convergent validity of apathy scales with other types of measurement. Scores on apathy scales have been validated using alternative measures of apathy. For example, scores on apathy measures are significantly related to measures of daily motor activity (i.e. ambulatory actigraphy) (David, Mulin, Friedman, Duff, Cygankiewicz, Deschaux,…Zeitzer, 2011; Kuhlmei, Walther, Becker, Müller, & Nikolaus, 2011; Müller, Czymmek, Thone-Otto, & Von Cramon, 2006). In experimental tasks, those with higher apathy scores spend less time looking at novel stimuli compared to those with lower apathy scores (Daffner, Mesulam, Scinto, Acar, Calvo, Faust…Holcomb, 2000; Eling, Maes, & Van Haaf, 2006). In one study, participants were placed in a waiting room with a variety of games (e.g. Pac-Man) and told they were welcome to play with the games while they waited. Informant and clinician-rated apathy scores were significantly negatively correlated with the total amount of time spent playing games (Marin et al., 1991). In a conversational task in which patients interacted with a spouse or romantic partner, apathy scores were related to decreases in eye contact (Sturm, McCarthy, Yun, Madan, Yuan, Holley, Ascher, Boxer, Miller,& Levenson, 2011). Taken together these results indicate that scores on apathy scales are related to apathetic behaviors, both in the laboratory and in the real-world.

Apathy vs. depression. Apathy and depression are partially overlapping constructs. They share symptoms such as diminished interest in activities and psychomotor retardation. However, cognitive and affective symptoms of depression, such as feelings of worthlessness or guilt and depressed mood, are not considered a part of apathy. Multiple studies support the distinction between the two constructs. For example, one study found that the best fitting model in a confirmatory factor analysis of an apathy and depression symptoms was one which included multiple factors, including separate apathy and dysphoric mood factors. (Kirsch-Darrow, Marsiske, Okun, Bauer, & Bowers, 2011). In the majority of principal components analyses of the Neuropsychiatric Inventory, apathy and dysphoria scores loaded most highly on different components (e.g. Aalten, Verhey, Boziki, Bullock, Byrne, Camus…Robert, 2007; Mirakhur, Craig, Hart, Mcllory, & Passmore, 2004; Prado-Jean, Courateir, Druet-Cabanac, Nubukpo, Bernard-Bourzeix, Thomas…Clement, 2010). Scores on apathy and depression scales are often moderately correlated (e.g., Andersson, Krogstad, & Finset, 1999; Butterfield, Cimino, Oelke, Hauser, Sanchez-Ramos, 2010), but this correlation is strongly driven by overlapping content in the scales; the correlation between apathy and cognitive and affective symptoms of depression is small (e.g., Lampe & Heeren, 2004; Landes, Sperry, & Strauss, 2005). Using diagnostic criteria, some patients only meet criteria for either apathy *or* depression (Starkstein, Ingram, Garau, & Mizrahi, 2005).

The distinction between apathy and depression is more apparent when informant-reported vs. self-reported ratings are used. For example, in a sample of patients with brain damage, self-rated apathy was significantly correlated with clinician-rated depression ($r = 0.48$, $p<.05$), but informant-rated apathy was not ($r = 0.15$, $p>.05$) (Njomboro & Deb, 2012). Similar results were found in a relatively large mixed neurological and healthy elderly comparison sample (n=107) in which a clinician-rated measure of depression excluding apathy symptoms was used (Marin, Firinciogullari, & Biedrzycki, 1993).

Distinguishing between apathy and depression can have treatment implications. Some nursing home interventions have been shown to affect apathy, but not depression (Leontjevas, Teerenstra, Smalbrugge, Vernooij-Dassen, Bohlmeijer, Gerritsen, & Koopman, 2013). In one series of case studies of patients with pituitary disease diagnosed with apathy, the patients failed to show decreased apathy symptoms when treated with a variety of antidepressant medications, but did improve when prescribed methylphenidate (Weitzner, Kanfer Booth-Jones, 2005). SSRIs, a common treatment for depression, can increase symptoms of apathy in some patients (e.g., Padala, Padala, Monga, Ramirez, and Sullivan, 2012).

Studies have provided various lines of evidence for apathy and depression as distinct constructs based on their association with other variables. For example, apathy is associated with impaired insight about one's illness and cognitive abilities while depression is associated with greater insight (Horning, Melrose, & Sultzer, 2013). Apathy and depression have different structural and functional neural correlates (Lavretsky, Ballmaier, Pham, Toga, & Kumar, 2007; Skidmore, Yang, Baxter, von Deneen, Collingwood, He, Tandon, Korenkeych, Savenkov, Heilman, Gold, & Liu, 2013). Apathy and depression differ in their ability to predict conversion to dementia in individuals with mild cognitive impairment (Chilovi, Conti, Zanetti, Mazzù, Rozzini, & Padovani, 2009).

Several studies have shown that apathy has stronger associations with cognitive and functional impairment than depression (e.g., Butterfield, Cimino, Oelke, Hauser, & Sanchez-Ramos, 2010; Hama, Yamashita, Shigenobu, Watanabe Hiramoto, Kurisu, Yamawaki & Kitaoka, 2007). For some neurodegenerative diseases, symptoms of depression have an earlier onset than symptoms of apathy, likely one reason apathy is more strongly associated with impairment (Naarding, Janzing, Eling, van der Werf, Kremer, 2009). Apathy and depression in patients are both associated with caregiver distress, although there is mixed evidence as to whether one is more strongly related to

caregiver distress than the other (e.g., Figved, Myhr, Larsen, Aarsland, 2007; Leiknes I, Tysnes O-B, Aarsland D, Larsen JP, 2010; Tun, Murman & Colenda, 2008).

Apathy vs. anhedonia. Like apathy, anhedonia is a construct that has been defined in variable ways in the literature (Shankman, Katz, DeLizza, Sarapas, Gorka, & Campbell, 2014). A broad definition of anhedonia as including loss of interest, loss of pleasure, and general reduction in emotional experience and expression makes it highly overlapping with definitions of apathy. However, when using more narrow definitions, such as "a diminution or reduction in the capacity to experience pleasure" (Fonseca-Pedrero, Gooding, Paino, Lemos- Giráldez, & Muñiz, 2014), the two constructs are clearly distinct as apathy also involves reductions in behavior and reductions in both positive and negative expressions of emotion. However, it should be noted that measures of anhedonia often include content related to reduced behavior generally, which has been criticized in articles about anhedonia (e.g., Fonseca-Pedrero et al., 2014; Kwapil, Gross, Chun, Silvia, & Barrantes-Vidal, 2014).

Studies support a support a distinction between anhedonia, defined as loss of interest or pleasure, and apathy. In a study using the Beck Depression Inventory and Apathy Scale with Parkinson's disease patients, the best fitting symptom model included separate apathy and anhedonia factors (Kirsch-Darrow, Marsiske, Okun, Bauer, & Bowers, 2011). This finding was replicated in a study using multiple measures of anhedonia and a measure of apathy that includes scales for the three proposed symptom dimensions (the Lille Apathy Rating Scale) (Zahodne, Marsiske, Okun, & Bowers, 2012). In both these studies, a reduction in interest or pleasure was distinct from behavioral symptoms of apathy (e.g., reduced motivation and engagement in activities).

Summary of the conceptualization and measurement of apathy. Research has shown that apathy is related, but partially distinct from, constructs such as depression and anhedonia. The majority of definitions of apathy have included three symptom domains: cognitive (i.e. "diminished interest"), behavioral (i.e. "diminished action), and emotional

(i.e. diminished emotional expression). An additional lack of self-awareness component has been proposed, however, results suggest that a lack of self-awareness may be better conceptualized as a correlate rather than a component of apathy.

Research using the two most popular apathy scales has provided limited information as to the internal structure of apathy symptoms. Although researchers have sought evidence for three separate domains of apathy, they have often used measures that do not include more than a couple of items for the emotional domain (e.g., Pedersen, Alves, Larsen, Tysnes, Møller , & Brønnick, 2012). The AES includes only 2 items to measure emotional symptoms and principal component analyses of the AES have yielded inconsistent results. Although the NPI-C apathy subscale was written to assess the symptoms in the latest diagnostic criteria for apathy, no analyses of its structure have been conducted. Although such analyses could in theory be conducted, with only 12 items, the NPI-C apathy subscale would have limited utility in differentiating among multiple potential latent dimensions of apathy symptoms. The LARS was designed to measure cognitive, behavioral, emotional, and self-awareness symptoms, and its component structure supports the differentiation of these symptoms. However, the cognitive, behavioral, and emotional components are correlated, and it is possible that a more parsimonious structure, with fewer separate apathy dimensions, may be a better fitting model of apathy symptoms. In fact, research on a similar construct, negative symptoms, suggests an alternative two factor structure of apathetic symptoms.

Apathy and Negative Symptoms

Researchers have described apathy as having a “striking similarity” (Foussias & Remington, 2010) to negative symptoms. The two constructs may be “synonymous” (van Reekum, Stuss, and Ostrander, 2005) or “almost identical” (Eisenberg, Aniskin, White, Stein, Harvey, & Galynker, 2009). Some authors have used the terms interchangeably (e.g. Marin, 1996; Winograd-Gurvich, Fitzgerald, Georgiou-Karistianis, Bradshaw, &

White, 2006). Using total scores on measures of apathy and negative symptom scales in patients with psychosis, studies have found moderate correlations between the two constructs (e.g., Faerden et al., 2008; Evensen, Røssberg, Barder, Haahr, Hegelstad, Joa, …McGlashan, 2012).

The term "negative symptoms" is most commonly used to refer to a constellation of symptoms found in schizophrenia. Similar to definitions of apathy emphasizing diminished interests, actions, and emotional expression, negative symptoms are defined in terms of a loss of functioning (Andreasen, 1990). These symptoms include: alogia, "loss or diminution in fluency of thought and speech"; affective blunting, "loss of the capacity to express emotions fluently"; avolition, "a diminution or loss of the ability to initiate or persist in tasks"; and anhedonia, "a loss of the capacity to feel joy and pleasure" (p. 14-15).

Measurement of negative symptoms. The first instrument developed to reliably assess negative symptoms was the Scale for the Assessment of Negative Symptoms (SANS), a clinician-administered rating scale (Andreasen, 1982). Ratings on the SANS are made on the basis of a patient interview, with many items based on the interviewer's observation of the patient's behavior during the interview. Collateral information from informants can also be used as an additional source of information to determine ratings.

The majority of principal components or factor analyses of negative symptoms have used the SANS. Aside from being the first measure to assess negative symptoms, its inclusion of multiple items to assess each specific domain distinguishes it from many other scales, leading to its popular use in structural analyses (Blanchard & Cohen, 2006). Overall, analyses suggest negative symptoms are best represented by two, moderately correlated factors; one factor representing decreased interest and engagement in activities and the other representing decreased speech and expression of emotion (Blanchard & Cohen, 2006; Messinger, Trémeau, Antonious, Mendelsohn, Prudent, Stanford, & Malaspina, 2011). The first factor, labeled as "anhedonia-asociality" (Blanchard &

Cohen, 2006) or “avolition” (Messinger et al. 2011), contains symptoms typically included in the cognitive and behavioral apathy symptom domains. The second factor, labeled as “diminished expression” (Blanchard & Cohen, 2006) or “expressive deficits” (Messinger et al., 2011), contains symptoms typically included in the emotional apathy symptom domain.

Support for a 2 factor model of negative symptoms is not limited to the SANS. The same structure was replicated with a newly developed measure of negative symptoms, the Clinical Assessment Interview for Negative Symptoms (CAINS), a measure designed to update the assessment of negative symptoms with the most recent conceptualizations of specific symptoms (Horan, Kring, Gur, Reise, & Blanchard, 2011).

Negative symptoms in disorders other than schizophrenia. In the development of the SANS, Andreasen (1990) explicitly stated that the use of the SANS was not limited to schizophrenia. The SANS was “developed in order to define and describe a wide range of symptoms reliably” and “could then be used to observe the frequency of these signs and symptoms in a variety of diagnostic categories and to observe whether they showed different patterns in various diagnostic categories or differences in change over time” (p.76).

Negative symptom scales, such as the SANS, have been used to measure negative symptoms in disorders such as temporal lobe epilepsy (Getz, Hermann, Seidenberg, Bell, Dow, Jones…Magnotta, 2002), major depressive disorder (Galynker, Coehn, & Cai, 2000), Alzheimer’s disease (Galynker, Roane, Miner, Feinberg, & Watts, 1995), and frontotemporal dementia (Ziauddeen, Dibben, Kipps, Hodges, McKenna, 2011). The negative symptoms reported in these studies include those from both of the factors proposed to underlie negative symptoms in schizophrenia, diminished interest/action and diminished emotional expression.

Other scales used to measure personality or psychopathology in neurological populaitons have also found evidence for constructs similar to negative symptoms. These

scales do not always use the term “negative symptoms”; however, the types of symptoms they measure overlap with the negative symptom construct. For example, several of the items on the Iowa Scales of Personality Change (ISPC), designed to assess a variety of personality changes that occur following brain damage, measure symptoms labeled in the schizophrenia literature as “negative symptoms.” One of the components in a principal components analysis of the ISPC in a sample of patients with focal brain damage consisted of several “negative symptom” items: blunted affect, social withdrawal, and apathy (defined primarily as lack of interest) (Barrash, Asp, Markon, Manzel, Anderson, & Tranel, 2011). An analysis of a scale developed to measure psychopathology in Alzheimer’s disease found evidence for two components roughly corresponding to the the 2 factor model of negative symptoms (Devannad, Brockingham, Moody, Brown, Mayeux, Endicott, & Sackeim, 1992).

Correlates of specific dimensions of apathy and negative symptoms. The clinical and research utility of the 2 factor model of negative symptoms is still being established (Kaiser, Heekeren, & Simon, 2011; Kirkpatrick, Fenton, Carpenter, & Marder, 2006). However, there is some evidence to suggest the 2 factors differ, at least partially, in their associations with external variables, such as cognitive and functional abilities, and in their relative prevalence across disorders.

Cognitive abilities. Similar to apathy, negative symptoms are related to several cognitive domains. A meta-analysis of negative symptoms and cognition found relationships between negative symptoms and executive functioning, verbal and visual memory, processing speed, verbal fluency, and attention (Dominguez, Viechtbauer, Simons, van Os, & Krabbendam, 2009). Few studies have directly compared different types of negative symptoms in their relationship to cognitive tests. One study using SANS with dementia patients found a large degree of overlap in the relationship between symptom domains and cognitive functioning. However, only the SANS affective flattening subscale was related to immediate and delayed verbal memory and semantic

fluency (Boone, Miller, Swartz, Lu, & Lee, 2003). Other studies have also found a relationship between restricted or blunted affect and semantic fluency (Cohen, Iglesias, & Minor 2009) phonemic fluency (Stolar, Berenbaum, Banich, & Barch, 1994), and verbal memory (Gur, Kohler, Ragland, Siegel, Lesko, Bilker, & Gur, 2006). Alogia, which along with flat affect comprises the emotional blunting factor of negative symptoms, is also associated with verbal fluency (Docherty, Berenbaum, & Kerns, 2011).

Only two studies reporting the correlation between specific types of apathy symptoms and cognitive test scores were found. In one small study of 27 patients with traumatic brain injuries, a principal components analysis of cognitive, emotional, and behavioral symptom totals of apathy and a battery of cognitive tests was done (Andersson & Bergedalen, 2002). Cognitive apathy (lack of interest) was related to worse performance on tests of memory, processing speed, and executive function. Emotional apathy was negatively associated with attention. Paradoxically, behavioral apathy was positively associated with processing speed. In a study of using the Modified Six Elements Test, a measure of executive functioning, only behavioral apathy (lack of initiative) was associated with performance (Esposito, Rochat, A. Van der Linden, Lekeu, Quittre, Charnallet, & M. Van der Linden, 2010).

Overall, there have been few studies examining the correlates of specific domains of negative symptoms or apathy, and the majority of these studies have had sample sizes less than 30. Given the correlations both among symptom domains and among cognitive abilities, studies with sample sizes this small are likely underpowered in their ability to detect unique relationships among specific negative or apathy symptoms and specific cognitive abilities. Although a relationship between components of emotional expressivity and both verbal memory and verbal fluency has been replicated in several studies, only one study has directly compared both factors of negative symptoms. Therefore, it is unclear whether verbal fluency and verbal memory are uniquely related to emotional expressivity or are significant correlates of both negative symptom factors.

Functional abilities. Although blunted affect is included in many models of apathy, as noted previously, many apathy scales fail to include much, if any, content related to these symptoms. This likely leads to the underestimation of the relationship between apathy and functional impairment. In one study, scores on a measure of both blunted affect and alogia were significantly correlated with activities of daily living (ADLs) (Meeks & Walker, 1990). Blunted affect has been shown to be significantly associated with performance on a role-playing test assessing social skills (Mueser, Pratt, Bartles, Forester, Wolfe, & Cather, 2010) and measures of social and occupational impairment (Troisi, Pompili, Binello, & Sterpone, 2007).

Two studies have supported the need to include blunted affect when investigating the relationship between negative symptoms or apathy and functional impairment. Compared to other negative symptoms, blunted affect has been found to have a greater association with interpersonal functioning (Leifker, Bowie, & Harvey, 2009). In another study investigating social and occupational impairment, blunted affect symptoms were found to account for additional predictive variance above and beyond that of the apathy (Faerden, Friis, Agartz, Barrett, Nesvag, Finset, & Melle, 2009). (Although, see Foussias, Mann, Zakzanis, van Reekum, & Remington, 2009, for an example in which blunted affect did not contribute any additional predictive power over apathy).

Prevalence across disorders. In a study using the diagnostic criteria proposed by Robert (2009), all three apathy symptom domains (cognitive, behavioral, and emotional) were highly prevalent in patients with schizophrenia. In contrast, compared to cognitive and behavioral symptoms, emotional symptoms were less prevalent in patients with Parkinson's disease, major depression, mixed dementia, mild cognitive impairment, and Alzheimer's disease (Mulin, Leone, Dujardin, Delliaux, Leentjens, Nobili, …Robert, 2011). The decreased prevalence of emotional symptoms may reflect the fact that these symptoms reflect a more severe form of apathy in some disorders; in Parkinson's disease, emotional symptoms of apathy occurred most frequently in combination with both

cognitive and behavioral symptoms (Drijgers, Dujardin, Reijnders, Defebvre, & Leentjens, 2010). However, for some disorders, emotional and expressive symptoms are much more common. In a sample of patients with temporal lobe epilepsy, blunted affect and alogia were the most prominent negative symptoms (Geary, Seidenberg, Hermann, 2009). In research on apathy and negative symptoms, it may be important to examine not only the overall level of symptoms, but also specific symptom domains.

Study Rationale and Specific Aims

Apathy and negative symptoms are similar constructs, yet while there has been a large body of research aimed at understanding the internal structure of negative symptoms, there have been comparatively few studies examining the structure of apathy symptoms. The studies that have been conducted have often used measures that do not include a sufficient number of items to fully assess all of the three proposed domains of apathy (i.e., cognitive, behavioral, and emotional symptoms). In this study, a comprehensive set of items written to assess cognitive, behavioral, and emotional symptoms of apathy was administered to relatives or other informants of patients undergoing neuropsychological assessment or participating in neuropsychological research. By utilizing a large bank of items, and administering items to a large number of people, proposed models for the structure of apathy can be tested and compared to one another. The relationship of apathy symptoms to correlates that have been previously studied in apathy research (cognitive abilities, functional impairment, and caregiver distress) was also explored. Apathy was also compared with depression in its relationship to those same correlates.

The current project also serves as the first step in the creation of an informant-report questionnaire of apathy. Informant-report measures of apathy have an advantage over self-reports in their greater discriminant validity in distinguishing between apathy and depression (e.g., Njomboro & Deb, 2012). In general, the use of informant-report

within neuropsychology can be useful because lack of awareness of symptoms is associated with many different types of neurological disorders (Lezak, Howieson, Bigler, & Tranel, 2014; Prigatano, 2010). Due to this lack of awareness, informant-report may have greater validity than self-report. For example, in a study of individuals with varying levels of cognitive impairment, informant-report of functional impairment was associated with performance on neuropsychological testing while self-report was not (Farias, Mungas, & Jagust, 2005). Although there are likely trade-offs in measuring symptoms via questionnaire rather than an interview, a questionnaire has greater clinical utility in neuropsychological assessment. A questionnaire serves the goal of increasing the amount of information that can be gained in an evaluation without greatly increasing the time spent on an evaluation. If a clinically significant level of apathy is reported, the clinician could follow-up with the informant and patient with a more detailed assessment, if needed.

Specific Aim #1: To determine the internal structure of apathy symptoms within a neuropsychology patient sample

Hypothesis 1: The best fitting factor model for apathy symptoms will be a two factor model similar to that found in analyses of negative symptoms in schizophrenia. One factor will represent cognitive (lack of interest) and behavioral (lack of action) symptoms of apathy. The second factor will represent symptoms of reduced emotional and verbal expression.

Specific Aim #2: To investigate the relationship between apathy symptoms and cognitive abilities, functional abilities, caregiver distress, positive and negative affect, and depression.

Hypothesis 2a: Apathy will be most highly associated with measures of executive functioning, working memory, and processing speed. If the best fitting model of apathy contains more than one factor, the factor(s) including emotional symptoms will be more highly related to verbal memory and verbal fluency than other factor(s) and the factor(s)

including cognitive and behavioral symptoms will be more highly related to executive functioning than the other factor(s).

Hypothesis 2b: Apathy will be significantly associated with functional impairment. If the best fitting model of apathy contains more than one factor, the factor(s) containing cognitive and behavioral symptoms will be more highly related to functional impairment than the other factor(s).

Hypothesis 2c: Apathy will be significantly associated with caregiver distress. If the best fitting model of apathy contains more than one factor, the factor(s) containing cognitive and behavioral symptoms will be more highly related to caregiver distress than the other factor(s).

Hypothesis 2d: The new measure of apathy developed for this study, which comprehensively assesses different types of apathy symptoms, will have incremental validity in its association with cognitive abilities, functional abilities, and caregiver distress, relative to an existing measure, the Apathy Evaluation Scale, which focuses primarily on cognitive and behavioral symptoms.

Specific Aim #3: To compare the relationship of apathy and depression to cognitive abilities, functional abilities, and caregiver distress, and positive and negative affect.

Hypothesis 3a: The relationship between apathy and functional impairment will be stronger than the relationship between depression and functional impairment.

Hypothesis 3b: The relationship between apathy and caregiver distress will not differ from the relationship between depression and caregiver distress.

Hypothesis 3c: Depression will have a stronger association with negative affect than apathy. Apathy will have a stronger association with positive affect than depression.

Hypothesis 3d: The relationship between apathy and cognition will be stronger than the relationship between depression and cognition.

CHAPTER II

METHODS

Participants and Recruitment

249 informant participants (66% female, 34% male) completed the study. Informants were all adults (i.e. over the age of 18 years) who reported on someone they knew well (known hereafter as a "target participant"). In the majority of cases, this was a participant recruited into the study; in other cases this was an unidentified individual; see below. The average age of informants was 62 (SD=14) and average years of education was 16 (SD=4). Informants reported interacting with the target person they were reporting on frequently; 73% reported seeing the target person daily. The remaining saw the person reported seeing the person multiple times a week (17%), once a week (6%), several times a month (2%), or monthly (2%). The majority of informants were spouses (58%) with the remaining informants being adult children (10%), dating partners (3%), friends (10%), and parents (9%), or having another type of relationship to the target person (e.g., professional caregiver) (12%). Informants reporting knowing the target participant an average of 40 years (SD=17) (range=1 year to 76 years). (Of note, information about the informant's relationship to and frequency of interaction with the target participant was not available for 46 individuals, described below.)

The majority of informants were identified by a target participant including: 1) patients being evaluated at the Benton Neuropsychology Clinic at the University of Iowa Hospitals and Clinics (n=97), 2) members of the Iowa Neurological Patient Registry, a registry of patients with focal brain damage maintained by the Division of Cognitive Neuroscience at the University of Iowa (n=48), 3) patients with Alzheimer's disease who were participating in research studies conducted in the Division of Cognitive Neuroscience at the University of Iowa (n=12), and 4) members of the Seniors Together in Aging Research (STAR) Registry who self-reported being diagnosed with a

neurological or psychiatric condition (n=46). A subset of informants were recruited directly (i.e., they were not identified as informants by another individual in the study). These informants included 1) individuals in the STAR Registry identifying themselves as caregivers of someone with dementia who were asked to report on someone they knew with dementia (n=12) and 2) members of a sample of older adults used in studies conducted by Dr. Natalie Denburg who were asked to report on someone they knew well who had not been diagnosed with a neurological disease (n=34).

Target participants (54% female, 46% male) were on average 64 years old (SD=14) and had completed an average of 15 years of education (SD=3). (Note, demographic and other personally identifying information about the target participant (e.g., age, relationship to the informant) was not collected for the two sources in which informants were recruited directly as those target participants were not consented as part of the study and therefore had to remain anonymous.) Target participants did not complete measures specifically for the study; however, a subset of participants completed neuropsychological testing as part of a clinical or research evaluation and consented to these data being used in the current study.

Procedure

After obtaining consent, the informants were given the questionnaires described below. For each informant recruited in the Benton Clinic or Iowa Neurological Patient Registry, the corresponding patient was asked to consent to the release of the information obtained from his or her neuropsychological evaluation or research record (i.e., cognitive test scores). The only information obtained from patient participants was that which had already been collected or scheduled to be collected for clinical or other research purposes. Prior to data collection, all study procedures were approved by the Institutional Review Board for Human Subjects Research at the University of Iowa.

Informant Report Measures

Background questionnaire. This questionnaire was administered in order to obtain demographic information about the informant and to classify the informant's relationship to the patient.

Apathy measures. Because no existing informant questionnaire of apathy comprehensively samples the cognitive, behavioral, and emotional components of apathy described previously, participants were given a questionnaire designed specifically for this study. Items were written based on published descriptions of these three components of apathy (e.g., Marin, 1991; Robert et al., 2009) and were based on existing measures of apathy and other relevant constructs (e.g., negative symptoms, emotional expressivity, and motivation). In total, 160 of these items were administered to participants (see Appendix B). Responses were given on a five point Likert scale (strongly agree to strongly disagree) and ratings were made based on the past four weeks.

For comparison purposes, the Apathy Evaluation Scale-Informant version (Marin et al., 1991) was also administered. As noted in the introduction, this is a widely used measure in apathy research. As noted previously, its content is largely reflective of cognitive and behavioral symptoms of apathy.

Functional impairment. The Bristol Activities of Daily Living Scale (Bucks, Ashworth, Wilcock, & Siegfried, 1996) was administered as a measure functional impairment. The scale is a 20-item questionnaire with items assessing both basic activities of daily living (ADLs) (e.g. bathing and eating independently) and instrumental activities of daily living (IADLs) (e.g. managing finances, using a telephone). In a review and critique of measures of functional impairment, the Bristol Activities of Daily Living Scale was one of two scales given the highest ratings for overall measurement quality (Sikkes, de Lange-de Klerk, Pijnenburg, Scheltens, & Uitdehaag, 2009).

Caregiver burden. The Zarit Caregiver Burden Scale (Zarit, Reever, & Bach-Peterson, 1980) was administered as a measure of caregiver burden and distress.

Although often referred to as an interview, the scale can be administered as a questionnaire (e.g., Ankri, Andrieu, Beaufils, Grand, & Henrand, 2005). The 22 item questionnaire includes items such as "do you feel your health has suffered because of your involvement with your relative?". It is the most widely used scale of caregiver burden (Parks & Novielli, 2000).

Inventory of Depression and Anxiety Depression (IDAS), General Depression Scale. The General Depression Scale of the IDAS (Watson, O'Hara, Simms, Kotov, Chmielewski, McDade-Montez…Stuart, 2007) was developed to assess depression in a manner similar to popularly used measures of depression. It contains a core of items assessing dysphoria as well as additional items assessing other relevant symptoms of depression (e.g., insomnia, appetite changes).

Positive and Negative Affect Schedule (PANAS). The PANAS (Watson, Clark, & Tellegen, 1988) was developed to briefly and reliable assess positive affect (i.e., "the extent to which a person feels enthusiastic, active, and alert", p. 1063) and negative affect (i.e., subjective distress and unpleasurable engagement", p. 1063) with two ten item scales. It is the most frequently used measure of positive and negative affect. The instructions used in the current study used "the past few weeks" as the timeframe for ratings.

Cognitive Measures

Scores from measures administered both as a part of neuropsychological assessments in the Benton Clinic and as part of research conducted within the Iowa Neurological Patient Registry were used. Tests that had been given to at least 30 participants were chosen for this study; a cut-off of n=30 was chosen to balance including enough measures to test specific hypotheses while avoiding including many measures given to only a handful of participants. Raw scores were used in all analyses as raw

scores are more appropriate than normative scores when using a test as a measure of ability to predict real-world functioning (e.g., Silverberg & Millis, 2009).

Auditory Verbal Learning Test (AVLT). The AVLT (Rey, 1964) is a list-learning measure in which a participant is presented the same list of words for 5 trials and then has to recall that list following a 30 minute delay. The total words recalled over 5 trials and long delay free recall and recognition were used in this study.

Benton Facial Discrimination Test. The FDT (Benton & Van Allen, 1968) is a measure of visual perception and discrimination in which a participant has to identify faces which match a target face under conditions of varying difficulty (e.g., the faces are obscured by a shadow). Originally called the Benton Facial Recognition Test, this test has been more recently referred to as the Benton Facial Discrimination Test given that "recognition" refers more precisely to a memory process rather than perceptual matching per se (Tranel, 2009).

Benton Visual Retention Test (BVRT). The BVRT (Benton, 1945) is a measure of immediate visual memory in which pages of three figures are displayed for 10 seconds after which a participant must draw them from memory (Administration A). The total number of errors was used in this study.

Boston Naming Test (BNT). The BNT (Kaplan, Goodglass, &Weintraub, 1983) is a 60-item measure of visual confrontation naming in which a participant is presented with black and white figure drawings and has to name the item being shown. The total number of correct responses given without a phonemic cue was used in this study.

Complex Figure Test (CFT). The CFT (Rey, 1941) is a measure of visuospatial ability and visual memory. The participant is asked to copy a complicated line drawing and then later asked to draw it again from memory following a 30 minute delay. The total number of correct points earned on both the copy trial and delayed recall trial were used in this study

Controlled Oral Word Association Test (COWA). On the COWA (Benton & Hamsher, 1989), the participant is asked to list as many words he or she can think of that begin with a certain letter of the alphabet while also following additional rules. Given the novel aspect of the task demands and need to inhibit certain responses, the COWA is often considered a measure of executive functioning (Lezak et al., 2014). The total number of correct responses across three trials was used in this study.

Judgment of Line Orientation (JLO). The JLO (Benton, Varney, Hamsher, 1998) is a test of visual perception in which a participant has to match partial line segments to a response grid containing lines oriented at different angles. The total number of correct responses was used in this study.

Trail Making Test (TMT). The TMT (Reitan, 1958) consists of two parts (A and B). TMT A is a measure of visual scanning that requires the participant to connect scattered numbered circles in numerical order. TMT B is a similar task containing both numbers and letters in which the participant has to alternate between the two categories. Given its set-switching component, Part B is used by neuropsychologists as a measure of executive functioning (Rabin, Barr, Burton et al., 2005). Time (seconds) taken to complete Part A and Part B were used in this study.

Wechsler Adult Intelligence Scale-IV (WAIS-IV) The WAIS-IV (PsychCorp, 2008) is a measure of intelligence assessing both verbal and nonverbal intellectual functions. Total correct scores from the verbal comprehension subtests (i.e., Information, Comprehension, Similarities, Vocabulary), perceptual reasoning subtests (i.e., Block Design, Matrix Reasoning, Visual Puzzles), processing speed subtests (i.e., Digit Symbol, Symbol Search) and working memory subtests (i.e., Digit Span, Arithmetic) were used in this study.

Wechsler Memory Scale-III (WMS-III). The WMS-III (Wechsler, 1997) contains several subtests measuring verbal and nonverbal memory. Total correct scores

for immediate and delayed recall trials for one verbal memory subtest, Logical Memory, and one nonverbal memory subtest, Faces, were used in this study.

Wisconsin Card Sorting Test. The WCST (Milner, 1963) is a widely used measure of executive functioning that involves learning from feedback and conceptual flexibility. The total number of perseverative errors, one of the more commonly used scores from the measure, was used in this study.

Statistical Analysis

Missing data. Missing data for analyses involving total scale scores (i.e., on the informant report measures listed above and the total scores on the new measure of apathy developed in this study) were imputed on a scale by scale basis for each participant; for participants completing at least 50% of a scale, the mean score on the completed items were used to estimate the responses to the items not completed. Missing data for the structural analyses of the apathy items (i.e., the exploratory and confirmatory analyses described below) and the calculations of factor scores from the best-fitting confirmatory model was handled through the use of full information maximum likelihood (FIML).

Internal structure of apathy. In order to assess specific aim #1, data analysis began with an exploratory factor analysis of the apathy questionnaire items. An oblique rotation (geomin) was used as factors of apathy were expected to correlate. Parallel analysis was used as an initial guide in determining the number of factors to estimate (Hayton, Allen, & Scarpello, 2004). Given the goal of the study to explore possible discrete dimensions of apathy symptoms, items with no primary loadings on any factor (i.e., < 0.30) or significant cross-loadings on a secondary factor (i.e., >0.30) were eliminated and a new exploratory factor analysis was conducted. Eliminating cross-loading items was done to help to clarify the interpretation of dimensions as much as possible. Increasing numbers of factors were estimated until arriving at a solution in which no items loaded primarily on the final factor.

Confirmatory factor analyses were then conducted to develop separate scales for the factors derived in the exploratory factor analysis. Maximum likelihood estimation with robust standard errors (MLR) was used; although the responses on the new measure of apathy are ordinal, research suggests that maximum likelihood estimation is appropriate when at least 5 response categories are used (Rhemtulla, Brosseau-Liard, & Savalei, 2012). Model comparisons were then conducted using the scales developed. Adequate fit was defined as CFI $\geq$ 0.90 (Hu & Bentler, 1999) and RMSEA $\leq$ 0.1 (Browne & Cudeck, 1993). A chi-square difference test appropriate for the MLR estimator was used to directly compare nested models (Asparouhov & Muthen, 2006). The relative fit of models was also compared using the Akaike Information Criterion (AIC) (Akaike, 1987). Testing different models of apathy symptoms using confirmatory factor analysis allows for a test of hypothesis #1 concerning the best fitting model of apathy symptoms.

External correlates of apathy dimensions. To test hypotheses 2a-2c, concerning the relationship of specific symptom factors of apathy to other variables, correlations between factor scores from the best fitting model identified in aim #1 and informant report measures and cognitive test scores were calculated.

Apathy symptoms across diagnostic groups. As an exploratory method of examining the potential clinical utility of measuring separate symptom dimensions of apathy, target participants were sorted into diagnostic groups. Given the goals of this study to examine apathy within a neuropsychological setting and to explore differences between apathy and depression, a hierarchical coding system was used to classify patients. Diagnosis was coded in the following manner: 1) neurological disorders were coded before psychiatric disorders (e.g., if a patient had Parkinson's disease and depression, he or she was placed in the Parkinson's disease group), 2) depression was coded before other psychiatric disorders (e.g., if a patient had depression and anxiety, he or she was placed in the depression group), and 3) if a patient had one or more

neurological disorders, the primary disorder was used (e.g., if a patient had a recent stroke, but a history suggesting a progressive vascular dementia, he or she was placed in the vascular dementia group; if a patient had a past head injury, but current Alzheimer's disease, he or she was placed in the Alzheimer's disease group). Some patients had diagnoses that occurred infrequently (e.g., fronto-temporal brain sagging syndrome, n = 1; electrical injury, n = 1) and were not included in the diagnostic comparisons. Mean factor scores from the best fitting model of apathy symptoms for each symptom dimensions were calculated for each diagnostic group. Given the design of the study to be broadly generalizable to neuropsychological practice, there were a number of diagnostic groups (and therefore, number of potential comparisons) and several diagnostic groups had small sample sizes. Therefore, alternative approaches which might better represent comorbidity were not used and formal statistic comparisons across groups were not conducted; rather, results are discussed qualitatively.

Comparison with an existing measure of apathy. Regression was used to test hypothesis 2d, the hypothesis that the new measure of apathy developed for this study would have incremental validity over the Apathy Evaluation Scale (AES) in predicting functional impairment, caregiver distress, and cognition. Specifically, the significance of the change in r-squared from a regression model in which the AES is the only predictor to one in which both the AES and the new measure are predictors provides evidence as to the added utility of the newer measure. A measure of effect size (f^2) was also calculated to show the difference in variance accounted for between the two models (Cohen, 1988). As a additional test of hypothesis 2d, regression models were also used to test whether the AES accounted for additional variance beyond the new apathy measure in its association with the informant report and cognitive measures.

Comparison with depression. Correlations with the variables of interest listed above were calculated for both the total score on the new apathy measure and the total score on the IDAS General Depression Scale. To address hypotheses 3a-3c, concerning

differences in the relationship of apathy and depression to caregiver distress, positive and negative affect, and functional impairment, tests for dependent correlations were performed. To address the hypothesis 3d concerning differences in the relationship of apathy and depression to cognitive functioning, a sign test was used to compare the number of times apathy had a correlation with a cognitive measure greater than the correlation between depression and that same measure.

CHAPTER III

RESULTS

Exploratory Factor Analyses of the Apathy Item Pool

As an initial step in addressing specific aim #1 concerning the structure of apathy symptoms, 8 factors were estimated in an exploratory factor analysis of apathy items written for this study based on the results of a parallel analysis. After items with no primary loading or significant cross-loadings were eliminated (n = 40), and a new exploratory factor analysis was conducted, five interpretable factors were found: reduced interest and initiative (i.e., cognitive and behavioral apathy symptoms), asociality, reduced emotional expression/alogia, lack of self-care, and exaggerated emotional expression /emotional lability. (Factor loadings can be found in Table A1). Of the 7 items loading primarily on the lack of self-care factor, 3 items included the phrase "seem to care" and 2 additional items included the word "care" or "concerned." Given this semantic overlap in these items, and the fact that items with related content (e.g., making appointments, managing health problems) that did not use the word "care" loaded most highly on another factor or no factor at all, this factor (lack of self-care) was not considered further. The exaggerated emotional expression factor had low correlations with the first three factors (r = -0.04, r = 0.06, r = -0.13) and was therefore dropped for further analyses as it appears to tap into content unrelated to apathy. Rather than assessing intact emotional expression, some items on this factor may instead be assessing expressions of emotion that go beyond normative expressions of emotion in this sample (e.g., when he is excited, he gets really animated; when he wants to make a point, he raises his voice).

Confirmatory Factor Analyses of the Apathy Item Pool

Initially, three separate confirmatory factor analyses were performed to develop separate scales for 1) reduced interest-initiative 2) asociality and 3) reduced emotional

expression/alogia. Fit indices indicated inadequate fit for these models; examination of the modification indices revealed significant additional residual correlations among items with similar content (e.g., “he likes to take on new challenges” and “he likes to take on tasks that challenge him.”). Removal of one item from these pairs resulted in models with adequate fit: reduced interest-initiative (CFI = 0.95, RMSEA = 0.06), asociality (CFI = 0.98, RMSEA = 0.05), reduced emotional expression/alogia (CFI = 0.92, RMSEA = 0.06).

Including each of these factors together in the same model (i.e., a correlated factors model) resulted in a model with adequate fit (CFI = 0.91, RMSEA = 0.05). These factors were highly correlated (r’s ranging from 0.66 to 0.74). Of note, this model is statistically equivalent to a model in which all factors are allowed to load on a single, higher order apathy factor. Given the separation of asociality from other cognitive and behavioral symptoms in the exploratory factor analyses, the model in hypothesis 1, a two factor model in which those symptoms load on the same factor and emotional symptoms load on a second factor, was not tested. Similarly, a model corresponding to the three factor cognitive, behavioral, and emotional apathy model implied by proposed diagnostic criteria was not tested given that cognitive and behavioral symptom loaded on the same factor in the exploratory factor analyses.

Given the high across-factor correlations, a bifactor model was tested to account for the overlap in common apathy variance across items while still allowing for unique variance related to specific symptom dimensions. In this model, all items were allowed to load on a general apathy factor and one of three specific factors corresponding to the three factors noted above. The bifactor model had adequate fit (CFI = 0.91, RMSEA = 0.05). As a correlated factors model is nested within a bifactor model (Reise, 2012), a chi-square difference test was performed and the bifactor model provided significantly better fit. The bifactor model also had a lower AIC value than the correlated factors

model, indicating better model fit. Fit statistics for all confirmatory models can be found in Table A2.

The bifactor model (Table A3) was used in subsequent analyses given 1) its better model fit and 2) better utility in identifying potential differences in correlates of specific symptom factors. (Symptom factors are uncorrelated in a bifactor model after accounting for the general factor.) Although different from the model proposed in hypothesis 1, the bifactor model shares some similarities with that model in that symptoms of reduced emotional expression and speech load on the same factor and symptoms of reduced interest and action load on the same factor. Contrary to expectations, symptoms specific to reduced social interest and behavior separated into their own unique factor.

Analyses of Correlates of Apathy Symptom Factors

Cognitive functioning. Descriptive statistics for cognitive test scores can be found in Table A4. Correlations between apathy symptom factors and cognitive functioning can be found in Table A5**.** Inconsistent with the hypothesis that apathy would be most highly related to executive functioning, working memory, and processing speed, the general factor of apathy was robustly associated with performance on almost all neuropsychological tests included in the analyses (with greater apathy associated with poorer performance) and the highest correlations did not cluster within any one domain. In partial support of the hypothesis that the reduced interest-initiative factor would be more highly related to executive functioning than the other factors, that specific factor only was related to performance on one measure of executive functioning (Controlled Oral Word Association test). Additionally, the reduced interest-initiative specific factor was related to performance on a measure of processing speed (WAIS-IV Digit Symbol Coding), and to performances on measures of verbal and visual delayed memory (CFT and AVLT delayed memory).

Inconsistent with the hypothesis that the reduced emotional expression symptom factor would be most highly related to verbal memory and verbal fluency, that factor was instead related to measures of verbal intelligence (WAIS-IV Similarities and Vocabulary) as well as a measure of immediate visual recall for faces (WMS-III faces) and a measure of visuospatial planning (CFT copy).

The social specific factor, for which there were no specific hypotheses because it was not anticipated to emerge as a distinct factor, was associated with greater performance on a measure of working memory and mathematical ability (WAIS-IV Arithmetic).

Informant report measures. Correlations between apathy symptom factors and informant report measures can be found in Table A6. Consistent with the hypotheses for functional impairment and caregiver distress, in addition to being correlated with general apathy, those measures were also significantly correlated with the reduced interest-initiative symptom factor.

The general factor of apathy was highly negatively correlated with positive affect and moderately positively correlated with negative affect. Both the specific reduced interest-initiative and asociality symptom factors were also negatively correlated with positive affect.

Comparison across Diagnostic Groups

Table A7 presents mean factor scores for the general factor of apathy and specific apathy factors. An examination of Table A7 illustrates the utility of measuring specific types of apathy symptoms. For example, the conditions most associated with the general factor are different types of neurodegenerative illnesses. However, these types of dementia exhibit different profiles when examining specific factors. For example, emotional apathy appears relevant to Parkinson's disease/Lewy body dementia while reduced interest and initiative is more relevant for Vascular cognitive impairment/vascular dementia. The table also highlights one important distinction

between apathy and depression. Depressed patients have reduced interest and initiative and social apathy, but their level of emotional apathy is near the mean of the sample.

A qualitative review of the clinic reports for patients in this study illustrates the clinical presentation of apathy symptoms. For example, an 80-year-old patient with Alzheimer's disease was described by the technician who tested her as "quite passive" and not engaging in "spontaneous conversation or asking questions" during the exam but rather "seeming to just 'go with the flow.'" A 31-year-old patient with epilepsy was described as someone who "didn't seem concerned by any of her test performances" and was "quiet, serious, and rarely smiled." An 80-year-old patient with a mixed dementia was "noted to give up quickly on some tests and required extra encouragement to work to the best of his abilities." Following a stroke, a 75-year-old patient who was "formerly very activity-oriented" was described as "now gravitating towards less demanding activities such as TV watching." That patient's husband described changes in her affect, saying she is "more sweet" and "less assertive."

Comparison with an Existing Measure of Apathy

Although the new measure of apathy developed in this study and Apathy Evaluation Scale (AES) correlate 0.87 with one another, consistent with the hypothesis for those comparisons, based on regression models, the new measure accounts for a small, but significant amount of additional variance in its association with functional impairment and caregiver burden. The new measure also accounts for additional variance in depression and positive affect. These results can be found in Table A8.

Results were also consistent with the hypothesis that the new measure would have incremental validity in predicting cognitive functioning above the AES for a number of cognitive measures (Table A9). For significant differences, the f^2 values ranged from small (0.02) to medium (0.29).

In contrast, while the AES had a small amount of incremental validity beyond the new apathy measure in its association with several informant report measures (Table

A10), it did not account for a significant amount of additional variance for any cognitive measure (Table A11).

Comparison of Apathy and Depression

Results for the comparison between apathy and depression can be found in Tables A12 and A13. Consistent with the hypothesis that apathy would be more highly related to functional impairment, the relationship between apathy and functional impairment ($r = 0.61$) was greater than the relationship between depression and functional impairment ($r = 0.49$) ($p < 0.05$). Also consistent with the hypothesis that apathy and depression would relate similarly to caregiver burden, the relationship between apathy and caregiver distress ($r=0.57$) did not differ from the relationship between depression and caregiver distress ($r = 0.54$) ($p > 0.05$). Results also confirmed the hypotheses for differential relationships of apathy and depression with positive and negative affect. Apathy was more strongly associated with positive affect ($r = -0.77$) than was depression ($r = -0.57$) ($p < 0.05$). In contrast, depression was more strongly associated with negative affect ($r=0.73$) than was apathy ($r = 0.37$) ($p < 0.05$). In regard to the prediction that apathy would have a stronger association with cognition than depression, although apathy had a higher correlation than depression for 20/29 cognitive measures, using a sign test, this finding only approached significance ($p = 0.06$).

CHAPTER IV

DISCUSSION

Apathy is prevalent in a number of psychiatric and neurological conditions and is associated with clinically relevant outcomes such as cognitive and functional impairment (Boyle et al., 2003; Chiaravalloti & DeLuca, 2003). Prospectively, in progressive dementias, apathy has prognostic value in predicting future cognitive decline (Steinberg et al. 2008). Apathy also predicts a lack of engagement and decreased success in rehabilitation treatment and is associated with failure to follow recommendations given to improve health in those with chronic health conditions (Lenze et al., 2009; Padala et al., 2008; Resnick et al., 1998).

Proposed diagnostic criteria for apathy (Marin, 1996; Robert et al., 2009) have focused on three different types of symptoms: behavioral symptoms, or lack of action, cognition symptoms, or lack of interest, and emotional symptoms, or lack of emotional expression. Unfortunately, studies using questionnaires to measure apathy symptoms have not been able to test this proposed model adequately because existing apathy measures do not comprehensively assess all of these types of symptoms. For example, the most popular measure of apathy, the Apathy Evaluation Scale (Marin et al., 1991), uses only two items to assess emotional symptoms of apathy.

The primary aim of this study was to examine the structure of apathy symptoms using a comprehensive measure fully assessing the three proposed domains of apathy symptoms. Additional aims were to examine the relationship between specific factors of apathy and a set of variables previously shown to be related to apathy: caregiver distress, functional impairment, and cognition. Lastly, the relationship between apathy and depression, a construct which apathy overlaps with, was examined.

Factor Structure of Apathy Symptoms

The best-fitting model of apathy symptoms was partially consistent with the hypothesis that the factor structure of apathy would resemble the factor structure of negative symptoms. In particular, a diminished expressivity factor was found that includes symptoms of both reduced emotional expression and reduced speech. Symptoms of reduced speech have previously been labeled as behavioral symptoms in the apathy literature (e.g., Robert et al., 2009). It has been suggested that this symptom dimension is relevant to a range of psychiatric disorders (Cohen, Kim, & Najolia, 2013). The current findings extend this work into the domain of neurological disorders.

This combined reduced interest-initiative apathy factor replicates recent findings from a newly developed measure of those cognitive and behavioral symptoms (Esposito et al., 2014). Similar to the current study, those items were written based on proposed diagnostic criteria and their content is similar to the factor found in the current study. Also, similar to the current study, the measure used was an informant report measure and the majority of target participants were recruited from a neuropsychological setting.

The best-fitting model of apathy symptoms differed from the negative symptom model in that symptoms of reduced social interest and behavior were separate from other symptoms of reduced interest and behavior. These two types of symptoms typically merge together into one factor in the negative symptom literature (Blanchard & Cohen, 2006; Messinger et al., 2011). In the diagnostic criteria for apathy, reduced social interest and behavior is also not considered independent of other cognitive or behavioral symptoms.

One relevant distinction between the current measure of apathy and many negative symptom scales is that the current measure of apathy is based entirely on informant report while many negative symptom scales include both observer ratings and self-report. In fact, two alternative explanations for the two factor model obtained for negative symptoms have been offered, one based on the possibility the two factors reflect

meaningful differences and the other that they arise due to differences in measurement. In particular, the "avolition" factor is often made up of self-report items and the "expressivity" factor is often made up of behavioral observations. The use of one method to assess all symptoms could have contributed to the differences observed in the current study from the traditional model of negative symptoms.

The reduced interest and initiative, diminished expressivity, and asociality factors were all moderately correlated with one another. When compared to this correlated factors model, a bifactor model, in which items assessing these symptoms were allowed to load on both a general apathy factor and one of three specific factors, provided the better fit. Bifactor modeling does not appear to have been applied yet in the negative symptom literature so comparisons cannot be made in that regard. However, bifactor models are being increasingly applied in the study of psychopathology more broadly (e.g., Burns, de Moura, Beauchaine, & McBurnett, 2013; Krueger, Markon, Patrick, Benning, & Kramer, 2007; Simms, Grös, Watson, & O'Hara, 2008). Although these models can sometimes be challenging to interpret, they do provide some benefits in teasing apart the importance of specific clusters of symptoms.

Correlates of Apathy Symptom Factors

Apathy was associated with increased caregiver burden and functional impairment and consistent with the hypothesis for reduced interest and initiative, those specific symptoms were also associated with increased functional impairment and caregiver burden. In contrast to the hypothesis that overall apathy would be most highly related to working memory, processing speed, and executive functioning, apathy was broadly related to cognition in general and no specific domain of functioning showed consistent high correlations relative to the other domains. As predicted, the reduced interest-initiative factor was related to a measure of executive functioning. It was also related to a measure of processing speed and delayed measures of verbal and visual

memory. Although the emotional symptom factor was not related to verbal memory or fluency as hypothesized, it was related to other verbal tests, specifically measures of verbal intelligence. It was also related to two measures of visual measures, WMS-III Faces and CFT copy.

Relationships with the asociality factor are more difficult to interpret. While asociality is a core negative symptom, it is not usually studied independently, but rather is often grouped together with anhedonia more broadly (e.g., using measures such as the asociality-anhedonia subscale of the Scale for the Assessment of Negative Symptoms). In the current study, asociality differed from the other factors in its relationship to cognitive functioning; it had a significant positive relationship with one measure of cognition and several non-significant, but positive relationships with additional cognitive measures. This finding may be related to previous studies documenting a negative relationship between extraversion and some aspects of cognitive functioning (e.g., Graham & Lachman, 2014; Soubelet & Salthouse, 2011; Wolf & Ackerman, 2005).

Although specific factors had some unique correlates, in the current study, the general factor of apathy had the greatest and most robust associations to the outcome variables included in the current study. For the set of outcomes included in the current study, It is important to note that the general factor of apathy in this study is not synonymous with the total score on other measures of apathy. For example, the apathy measure developed in this study contains a greater amount of content related to reduced emotional expression. Including this content appears to have given the measure increased clinical utility; it accounted for a significant amount of incremental variance in cognitive test scores beyond the most popular existing measure of apathy. The correlates of specific factors may have some clinical utility. For example, past research has shown that symptoms of reduced interest in particular are associated with conversion from mild cognitive impairment to Alzheimer's disease (Robert et al., 2008); in the current study,

the reduced interest and initiative factor was negatively associated with delayed memory, a neuropsychological symptom of Alzheimer's disease.

The specific factors may also have clinical utility in differential diagnosis and treatment planning. These factors appeared to vary in their relevance to various clinical diagnoses. Although progressive neurological diseases were associated with increased general apathy, they differed in the profile of specific factor elevations. For example, with prior research, reduced expressivity was higher in the Parkinson's disease/Lewy body dementia and vascular cognitive impairment/vascular dementia groups (e.g., Möbes, Joppich, Stiebritz, Dengler, & Schröder, 2008; Smith, Smith, & Ellgring, 2009; Sulzer, Levin, Mahler, High, & Cummings, 1993). Although not confirmed in the present study, possibly due to a small sample size (n=4), prior research has shown that patients with frontotemporal dementia have greater levels of reduced emotional expression and alogia compared to patients with Alzheimer's disease (Quaranta et al., 2012).

Given the degree to which apathy was correlated with positive affect, one might question whether or not apathy is conceptually distinct from low positive affect. Although the two constructs certainly overlap, one important distinction can be seen when examining specific apathy symptom dimensions. While interest-initiative symptoms and asociality symptoms are both significantly negatively related to positive affect, emotional expression symptoms are not. Diminished emotional expression in apathy is an overall reduction in both positive and negative emotional expression; low positive affect refers only to diminished positive emotions.

Apathy and Depression

The results of this study provide additional evidence that apathy and depression are distinct, but related constructs. Although both are positively associated with negative affect and negatively associated with positive affect, the relationship between depression and negative affect is much stronger than the relationship between apathy and negative

affect. Similarly, the relationship between apathy and positive affect is much stronger than the relationship between depression and positive affect. Previous studies have shown that while the two conditions frequently co-occur, they can also be independent of one another (e.g., Starkstein et al., 2005; van Dalen et al, 2013). Some treatments have also been showed to be effective for one condition but not the other (e.g., Leontjevas et al., 2013; Weitzner et al., 2005).

Consistent with prior literature (e.g., Hama et al. 2007), apathy showed a stronger relationship with functional impairment that depression. This highlights the important of assessing apathy in a neuropsychological setting. However, contrary to expectations, although apathy had a greater correlation with more measures of cognitive functioning than depression, the difference was not statistically significant. Consistent with expectations, apathy and depression were both related to caregiver burden to almost the same degree. Caregiver burden is important for both caregiver wellbeing and also patients themselves; for example, in a longitudinal study, higher burden was associated a greater likelihood of the patient becoming institutionalized than would be expected based only on the patient's health status (Miller et al., 2011).

Strengths and Limitations

This study has a number of strengths. To address limitations in the content of existing scales, a large, comprehensive item pool was written. The number of participants in the study (n=249) is large relative to existing studies examining the properties of apathy scales. The use of informant report allows for the assessment of apathy in patients that may have impaired insight in their condition and also has clinical utility in allowing for more information to be gathered in a neuropsychological evaluation without requiring increased burden on the patient.

The study also has a number of limitations. The sample size, while large within the literature of apathy scales, is modest compared to many scale development studies.

Given the difficulty in recruiting patients, only one round of scale development was conducted and the exploratory and confirmatory analyses were conducted within the same sample. Additionally, the sample size for cognitive measures varied widely, from 35 to 130, therefore, associations between apathy and specific cognitive measures were measured with differing levels of precision. While recruiting a heterogeneous sample of patients (and some healthy individuals) improves the generalizability of the results to neuropsychological practice as a whole (vs. with a particular patient population), that sampling strategy also limited the ability to assess for differences of in the types of apathy symptoms most relevant to particular diagnostic groups. To maintain consistency across the method of assessment, only informant report measures of patient symptoms were used and studies have shown that certain types of symptoms are more difficult to rate than other types of symptoms. For example, the study included a measure of depression, and in assessing depression, informants rate more visible symptoms such as "talked more slowly than usual" as easier to rate than symptoms reflecting internal experiences such as "felt inadequate" (McDade-Montez, Watson, O'Hara, & Denburg, 2008). Including self-report may have led to a more valid assessment of certain types of symptoms (at least for those participants without significant cognitive impairment and/or impaired insight). The use of different types of informants may have also affected results. For example, one study found that when asked to make ratings about a patient's memory, spouses who lived with a patient provided much more accurate results than informants who did not live with the patient (Ready, Ott, & Grace, 2004).

Future Directions

Future work will refine the apathy measure developed in this study and test whether the model found replicates in an independent sample. With a larger set of participants, additional psychometric analyses can be done to shorten the measure for clinical and research use. If a shorten measure were developed, it could be included as

part of clinical practice, which would allow for the accumulation of data for specific diagnoses and longitudinal relationships between apathy and cognition.

Future work can also explore the relationship of specific types of apathy symptoms to other types of psychopathology found within neurological disorders. In structural analyses, apathy is not reliably associated with other syndromes (e.g., Canevelli, Adali, Voisin, Soto, Bruno, Cesari, & Vellas, 2012) and it is possible that examining relationships at the level of specific types of apathy symptoms may be beneficial in understanding how apathy relates to psychopathology more broadly. Apathy has also been related to a number of correlates not explored in this study such as prospective memory (Esposito, Rochat, Juillerat, Van der Linden, & Van der Linden, 2012) and decision making (Poletti, Lucetti, Logi, Baldacci, Cipriani, Nuti,…Bonuccelli, 2013). Future studies could explore the relationship between specific symptom factors and these or other correlates. Additionally, the collection of self-report data would allow for studies comparing the clinical utility of self vs. informant report.

The different symptom profiles across different neurological diseases suggest that specific types of apathy symptoms may have different neural correlates. A structural MRI study in patients with progressive neurological diseases showed relationships between emotional apathy and the left insula and behavioral apathy and the anterior cingulate (Stanton, Leigh, Howard, Barker, & Brown, 2013). In the future, more patients with focal brain damage can be recruited in order to examine the neuroanatomical correlates of specific types of apathy symptoms based on the model of symptoms obtained in this study.

REFERENCES

Aalten, P., Verhey, F. R. J., Boziki, M., Bullock, R., Byrne, E. J., Camus, V., . . . Elina, K. (2007). Neuropsychiatric syndromes in dementia. *Dementia and Geriatric Cognitive Disorders, 24*, 457-463. doi:10.1159/000110738

Aarsland, D., Marsh, L., & Schrag, A. (2009). Neuropsychiatric symptoms in Parkinson's disease. *Movement Disorders, 24*, 2175-2186. doi:10.1002/mds.22589

Akaike, H. (1987). Factor analysis and AIC. *Psychometrika, 52*, 317-332.

Allegri, R. F., Sarasola, D., Serrano, C. M., Taragano, F. E., Arizaga, R. L., Butman, J., & Loñ, L. (2006). Neuropsychiatric symptoms as a predictor of caregiver burden in Alzheimer's disease. *Neuropsychiatric Disease and Treatment, 2*, 105-110.

Alves, G. S., Alves, C. E. O., Lanna, M. E. O., Ericeira-Valente, L., Sudo, F. K., Moreira, D., . . . Laks, J. (2009). Clinical characteristics in subcortical ischemic white matter disease. *Arquivos De Neuro-Psiquiatria, 67*, 173-178. doi:10.1590/S0004-282X2009000200001

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition.* American Psychiatric Association.

Andersson, S., & Bergedalen, A. M. (2002). Cognitive correlates of apathy in traumatic brain injury. *Cognitive and Behavioral Neurology, 15*, 184-191.

Andersson, S., & Finset, A. (1999). Electrodermal responsiveness and negative symptoms in brain injured patients. *Journal of Psychophysiology, 13*, 109-116. doi:10.1027//0269-8803.13.2.109

Andreasen, N. C. (1982). Negative symptoms in schizophrenia: definition and reliability. *Archives of General Psychiatry, 39* 784. doi:10.1001/archpsyc.1982.04290070020005

Andreasen, N. C. (1990). Positive and negative symptoms: Historical and conceptual aspects. *Modern Problems of Pharmacopsychiatry, 24*, 1– 42.

Ankri, J., Andrieu, S., Beaufils, B., Grand, A., & Henrard, J. C. (2005). Beyond the global score of the Zarit Burden Interview: Useful dimensions for clinicians. *International Journal of Geriatric Psychiatry, 20*, 254–260. doi: 10.1002/gps.1275.

Asparouhov, T., & Muthe´n, B. (2006). Robust chi square difference testing with mean and adjusted test statistics. In Mplus web notes (p. 9). Los Angeles: University of California Los Angeles.

Barrash, J., Asp, E., Markon, K., Manzel, K., Anderson, S. W., & Tranel, D. (2011). Dimensions of personality disturbance after focal brain damage: Investigation with the Iowa Scales of Personality Change. *Journal of Clinical and Experimental Neuropsychology, 33*, 833-852. doi:10.1080/13803395.2011.561300

Barrash J., Tranel D., Anderson, S.W. (2000). Acquired personality distrubances associated with bilateral damage to the ventromedial prefrontal region. *Developmental Neuropsychology, 18*, 355–381.

Benton, A.L. (1945). A visual retention test for clinical use. *Archives of Neurology and Psychiatry, 54,* 212-216.

Benton, A.L., Hamsher, K., & Sivan, A. (1989). Multilingual Aphasia Examination. Iowa City, IA: AJA Associates.

Benton, A.L., & Van Allen, M.W. (1968). Impairment in facial recognition in patients with cerebral disease. *Cortex, 4,* 344-358. doi: 10.1016/S0010-9452(68)80018-8

Benton, A.L., Varney, N.R., & Hamsher, K.D. (1978). Visuospatial judgment: a clinical test. *Archives of Neurology, 35,* 364 –367. doi:10.1001/archneur.1978.00500300038006

Blanchard, J. J., & Cohen, A. S. (2006). The structure of negative symptoms within schizophrenia: implications for assessment. *Schizophrenia Bulletin, 32,* 238-245. doi:10.1093/schbul/sbj013

Boone, K. B., Miller, B. L., Swartz, R., Lu, P., & Lee, A. (2003). Relationship between positive and negative symptoms and neuropsychological scores in frontotemporal dementia and Alzheimer's disease. *Journal of the International Neuropsychological Society, 9,* 698-709. doi:10.1017/S135561770395003X

Boyle, P. A., Malloy, P. F., Salloway, S., Cahn-Weiner, D. A., Cohen, R., & Cummings, J. L. (2003). Executive dysfunction and apathy predict functional impairment in Alzheimer disease. *American Journal of Geriatric Psychiatry, 11,* 214-221. doi:10.1176/appi.ajgp.11.2.214

Brodaty, H., & Burns, K. (2011). Nonpharmacological Management of Apathy in Dementia: A Systematic Review. *American Journal of Geriatric Psychiatry.* doi: 10.1097/JGP.0b013e31822be242

Brodaty, H., Sachdev, P. S., Withall, A., Altendorf, A., Valenzuela, M. J., & Lorentz, L. (2005). Frequency and clinical, neuropsychological and neuroimaging correlates of apathy following stroke-the Sydney Stroke Study. *Psychological Medicine, 35,* 1707-1716. doi:10.1017/S0033291705006173

Browne M.W. & Cudeck R. (1993) Alternative ways of assessing model fit. In Testing Structural Equation Models (Bollen K.A. & Long J.S., eds), Sage Publications, Thousand Oaks, CA, pp. 136–162.

Brun, A., Englund, B., Gustafson, L., Passant, U., Mann, D. M. A., Neary, D., & Snowden, J. S. (1994). Consensus statement. Clinical and neuropathological criteria for frontotemporal dementia. Lund and Manchester groups. *Journal of Neurology, Neurosurgery, and Psychiatry, 57,* 416-418.

Bucks, R., Ashworth, D., Wilcock, G., & Siegfried, K. (1996). Assessment of activities of daily living in dementia: development of the Bristol Activities of Daily Living Scale. *Age and Ageing, 25,* 113-120. doi:10.1093/ageing/25.2.113

Butterfield, L. C., Cimino, C. R., Oelke, L. E., Hauser, R. A., & Sanchez-Ramos, J. (2010). The independent influence of apathy and depression on cognitive functioning in Parkinson's disease. *Neuropsychology, 24,* 721-730. doi:10.1037/a0019650

Caeiro, L., Santos, C., Ferro, J., & Figueira, M. (2011). Neuropsychiatric disturbances in acute subarachnoid haemorrhage. *European Journal of Neurology, 18,* 857-864. doi:10.1111/j.1468-1331.2010.03271.x

Canevelli, M,, Adali, N., Voisin, T., Soto, M.E., Bruno, G., Cesari, M., & Vellas, B. (2012). Behavioral and psychological subsyndromes in Alzheimer's disease using the Neuropsychiatric Inventory. *International Journal of Geriatric Psychiatry, 28,* 795–803. doi: 10.1002/gps.3904.

Castellon, S. A., Hinkin, C. H., & Myers, H. F. (2000). Neuropsychiatric disturbance is associated with executive dysfunction in HIV-1 infection. *Journal of the International Neuropsychological Society, 6,* 336-347. doi:10.1017/S1355617700633088

Chan, M., Lim, W. S., & Sahadevan, S. (2008). Stage-independent and stage-specific phenotypic differences between vascular dementia and Alzheimer's Disease. *Dementia and Geriatric Cognitive Disorders, 26,* 513-521. doi:10.1159/000178755

Chan, W. C., Lam, L. C. W., Tam, C. W. C., Lui, V. W. C., Chan, S. S. M., Chan, W. M., & Chiu, H. F. K. (2010). Prevalence of neuropsychiatric symptoms in Chinese older persons with mild cognitive impairment-a population-based study. *American Journal of Geriatric Psych, 18,* 948-954. doi:10.1097/JGP.0b013e3181d69467

Chase, T. N. (2011). Apathy in neuropsychiatric disease: diagnosis, pathophysiology, and treatment. *Neurotoxicity Research, 19,* 266-278. doi:10.1007/s12640-010-9196-9

Chatterjee, A., Anderson, K. E., Moskowitz, C. B., Hauser, W. A., & Marder, K. S. (2005). A comparison of self-report and caregiver assessment of depression, apathy, and irritability in Huntington's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences, 17,* 378-383. doi:10.1176/appi.neuropsych.17.3.378

Cheng, S. T., & Chan, A. C. M. (2007). Withdrawal, apathy and lack of vigor in late life depression: Factorial validity and relationship to diagnosis. *Aging and Mental Health, 11,* 532-537. doi:10.1080/13607860601086447

Chiaravalloti, N. D., & DeLuca, J. (2003). Assessing the behavioral consequences of multiple sclerosis: An application of the Frontal Systems Behavior Scale (FrSBe). *Cognitive and Behavioral Neurology, 16,* 54-67. doi:10.1097/00146965-200303000-00007

Chiò, A., Vignola, A., Mastro, E., Giudici, A. D., Iazzolino, B., Calvo, A., . . . Montuschi, A. (2010). Neurobehavioral symptoms in ALS are negatively related to caregivers' burden and quality of life. *European Journal of Neurology, 17,* 1298-1303. doi:10.1111/j.1468-1331.2010.03016.x

Chow, T. W., Binns, M. A., Cummings, J. L., Lam, I., Black, S. E., Miller, B. L., . . . van Reekum, R. (2009). Apathy symptom profile and behavioral associations in frontotemporal dementia vs dementia of Alzheimer type. *Archives of Neurology, 66,* 888-893. doi:10.1001/archneurol.2009.92

Clark, L. A., & Watson, D. (1995). Constructing validity: Basic issues in objective scale development. *Psychological Assessment, 7,* 309-319. doi:10.1037/1040-3590.7.3.309

Clarke, D., Reekum, R., Simard, M., Streiner, D., Freedman, M., & Conn, D. (2007). Apathy in dementia: an examination of the psychometric properties of the apathy evaluation scale. *The Journal of Neuropsychiatry and Clinical Neurosciences, 19*, 57-64. doi:10.1176/appi.neuropsych.19.1.57

Clarke, D. E., Ko, J. Y., Kuhl, E. A., van Reekum, R., Salvador, R., & Marin, R. S. (2011). Are the available apathy measures reliable and valid? A review of the psychometric evidence. *Journal of Psychosomatic Research, 70*, 73-97. doi:10.1016/j.jpsychores.2010.01.012

Clarke, D. E., Ko, J. Y., Lyketsos, C., Rebok, G. W., & Eaton, W. W. (2010). Apathy and cognitive and functional decline in community-dwelling older adults: results from the Baltimore ECA longitudinal study. *International Psychogeriatrics, 22*, 819-829. doi:10.1017/S1041610209991402

Clarke, D. E., Van Reekum, R., Patel, J., Simard, M., Gomez, E., & Streiner, D. L. (2007). An appraisal of the psychometric properties of the Clinician version of the Apathy Evaluation Scale (AES-C). *International Journal of Methods in Psychiatric Research, 16*, 97-110. doi: 10.1002/mpr.207

Cohen, A. S., Iglesias, B., & Minor, K. S. (2009). The neurocognitive underpinnings of diminished expressivity in schizotypy: What the voice reveals. *Schizophrenia Research, 109*, 38-45. doi:10.1016/j.schres.2009.01.010

Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Erlbaum.

Craufurd, D., Thompson, J. C., & Snowden, J. S. (2001). Behavioral changes in Huntington disease. *Cognitive and Behavioral Neurology, 14*, 219-226.

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D., & Gornbein, J. (1994). The neuropsychiatric inventory : comprehensive assessment of psychopathology in dementia. *Neurology, 44*, 2308-2308.

Daffner, K. R., Mesulam, M., Scinto, L., Acar, D., Calvo, V., Faust, R., . . . Holcomb, P. (2000). The central role of the prefrontal cortex in directing attention to novel events .*Brain, 123*, 927-939. doi:10.1093/brain/123.5.927

Damasio, A.R. & Van Hoesen, GW. (1983). Emotional disturbances associated with focal lesions of the limbic frontal lobe. In: Heilman, KM.; Satz, P., editors. Neuropsychology of Human Emotion. New York: Guilford; p. 85-110

David, R., Mulin, E., Friedman, L., Duff, F. L., Cygankiewicz, E., Deschaux, O., . . . Zeitzer, J. M. (2011). Decreased Daytime Motor Activity Associated With Apathy in Alzheimer Disease: An Actigraphic Study. *American Journal of Geriatric Psychiatry*. doi: 10.1097/JGP.0b013e31823038af

de Gracia Dominguez, M., Viechtbauer, W., Simons, C. J. P., van Os, J., & Krabbendam, L. (2009). Are psychotic psychopathology and neurocognition orthogonal? A systematic review of their associations. *Psychological Bulletin, 135*, 157-171. doi: 10.1037/a0014415

De Medeiros, K., Robert, P., Gauthier, S., Stella, F., Politis, A., Leoutsakos, J., . . . Porsteinsson, A. (2010). The Neuropsychiatric Inventory-Clinician rating scale (NPI-C):

reliability and validity of a revised assessment of neuropsychiatric symptoms in dementia. *International Psychogeriatrics, 22,* 984-994. doi:10.1017/S1041610210000876

Derouesne, C., Thibault, S., Lagha-Pierucci, S., Baudouin-Madec, V., Ancri, D., & Lacomblez, L. (1999). Decreased awareness of cognitive deficits in patients with mild dementia of the Alzheimer type. *International Journal of Geriatric Psychiatry, 14,* 1019-1030. doi:10.1002/(SICI)1099-1166(199912)14:12<1019::AID-GPS61>3.3.CO;2-6

Devanand, D., Broekington, C., Moody, B. J., & Brown, R. P. (1992). Behavioral syndromes in Alzheimer's disease. *International Psychogeriatrics, 4,* 161-184.

Docherty, A. R., Berenbaum, H., & Kerns, J. G. (2011). Alogia and formal thought disorder: Differential patterns of verbal fluency task performance. *Journal of Psychiatric Research, 45,* 1352-1357. doi:10.1016/j.jpsychires.2011.04.004

Drijgers, R. L., Aalten, P., Winogrodzka, A., Verhey, F. R. J., & Leentjens, A. F. G. (2009). Pharmacological treatment of apathy in neurodegenerative diseases: a systematic review. *Dementia and Geriatric Cognitive Disorders, 28,* 13-22. doi:10.1159/000228840

Drijgers, R. L., Dujardin, K., Reijnders, J. S. A. M., Defebvre, L., & Leentjens, A. F. G. (2010). Validation of diagnostic criteria for apathy in Parkinson's disease. *Parkinsonism & Related Disorders, 16,* 656-660. doi:10.1016/j.parkreldis.2010.08.015

Dujardin, K., Sockeel, P., Delliaux, M., Destée, A., & Defebvre, L. (2008). The Lille Apathy Rating Scale: Validation of a caregiver-based version. *Movement Disorders, 23,* 845-849. doi: 10.1002/mds.21968

Dujardin, K., Sockeel, P., Delliaux, M., Destée, A., & Defebvre, L. (2009). Apathy may herald cognitive decline and dementia in Parkinson's disease. *Movement Disorders, 24,* 2391-2397. doi: 10.1002/mds.22843

Dujardin, K., Sockeel, P., Devos, D., Delliaux, M., Krystkowiak, P., Destée, A., & Defebvre, L. (2007). Characteristics of apathy in Parkinson's disease. *Movement Disorders, 22,* 778-784. doi: 10.1002/mds.21316

Eisenberg, D. P., Aniskin, D. B., White, L., Stein, J. A., Harvey, P. D., & Galynker, I. I. (2009). Structural differences within negative and depressive syndrome dimensions in schizophrenia, organic brain disease, and major depression: a confirmatory factor analysis of the positive and negative syndrome scale. *Psychopathology, 42,* 242-248. doi: 10.1159/000218522

Eling, P., Maes, J., & Van Haaf, M. (2006). Processing of emotionally toned pictures in dementia. *International Journal of Geriatric Psychiatry, 21,* 831-837. doi:10.1002/gps.1568

Eslinger, P., Dennis, K., Moore, P., Antani, S., Hauck, R., & Grossman, M. (2005). Metacognitive deficits in frontotemporal dementia. *Journal of Neurology, Neurosurgery & Psychiatry, 76,* 1630-1635. doi:10.1136/jnnp.2004.053157

Esposito, F., Rochat, L., Juillerat Van der Linden, A.C.., & Van der Linden, M. (2012). Apathy and prospective memory in aging. *Dementia and Geriatric Cognitive Disorders, 2,* 456–467. doi: 10.1159/000345037

Esposito, F., Rochat, L., Van der Linden, A. C. J., Lekeu, F., Quittre, A., Charnallet, A., & Van der Linden, M. (2010). Apathy and executive dysfunction in Alzheimer Disease. *Alzheimer Disease & Associated Disorders, 24*, 131. doi:10.1097/WAD.0b013e3181c9c168

Etters, L., Goodall, D., & Harrison, B. E. (2008). Caregiver burden among dementia patient caregivers: a review of the literature. *Journal of the American Academy of Nurse Practitioners, 20*, 423-428. doi:10.1111/j.1745-7599.2008.00342.x

Evensen, J., Røssberg, J.I., Barder, H., Haahr, U., Hegelstad, W.T., Joa, I., Johannessen, J.O., Larsen, T.K., Melle, I., Opjordsmoen, S., Rund, B.R., Simonsen, E., Sundet, K., Vaglum,P., Friis, S., McGlashan, T. (2012). Apathy in first episode psychosis patients: a ten year longitudinal follow-up study. *Schizophrenia Research, 136*, 19–24. doi: 10.1016/j.schres.2012.04.019

Faerden, A., Friis, S., Agartz, I., Barrett, E. A., Nesvåg, R., Finset, A., & Melle, I. (2009). Apathy and functioning in first-episode psychosis. *Psychiatric Services, 60*, 1495-1503. doi:10.1176/appi.ps.60.11.1495

Faerden, A., Nesvåg, R., Barrett, E. A., Agartz, I., Finset, A., Friis, S., . . . Melle, I. (2008). Assessing apathy: the use of the Apathy Evaluation Scale in first episode psychosis. *European Psychiatry, 23*, 33-39. doi:10.1016/j.eurpsy.2007.09.002

Fava, M. (2006). Pharmacological approaches to the treatment of residual symptoms. *Journal of Psychopharmacology, 20*, 29-34. doi:10.1177/1359786806064325

Fellows, L. K., & Farah, M. J. (2005). Dissociable elements of human foresight: a role for the ventromedial frontal lobes in framing the future, but not in discounting future rewards. *Neuropsychologia, 43*, 1214-1221. doi:10.1016/j.neuropsychologia.2004.07.018

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). " Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research,12*, 189-198. doi: 10.1016/0022-3956(75)90026-6

Foussias, G., Mann, S., Zakzanis, K., Van Reekum, R., & Remington, G. (2009). Motivational deficits as the central link to functioning in schizophrenia: A pilot study. *Schizophrenia Research, 115*, 333-337. doi:10.1016/j.schres.2009.09.020

Foussias, G., & Remington, G. (2010). Negative symptoms in schizophrenia: avolition and Occam's razor. *Schizophrenia Bulletin, 36*, 359-369. doi:10.1093/schbul/sbn094

Fuh, J., Wang, S., & Cummings, J. (2005). Neuropsychiatric profiles in patients with Alzheimer's disease and vascular dementia. *Journal of Neurology, Neurosurgery & Psychiatry, 76*, 1337-1341. doi:10.1136/jnnp.2004.056408

Gallagher, D., Lees, A., & Schrag, A. (2008). Unified Parkinson's Disease Rating Scale (UPDRS) part I as a screening and diagnostic instrument for apathy in patients with Parkinson's disease. *Parkinsonism and Related Disorders, 14*, 586-587. doi:10.1016/j.parkreldis.2008.01.005

Galvin, J. E., Malcom, H., Johnson, D., & Morris, J. C. (2007). Personality traits distinguishing dementia with Lewy bodies from Alzheimer disease. *Neurology, 68*, 1895-1901. doi:10.1212/01.wnl.0000263131.80945.ad

Galynker, I. I., Cohen, L. J., & Cai, J. (2000). Negative symptoms in patients with major depressive disorder: a preliminary report. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 13*, 171-176.

Galynker, I. I., Roane, D. M., Miner, C. R., & Feinberg, T. E. (1995). Negative symptoms in patients with Alzheimer's disease. *The American Journal of Geriatric Psychiatry, 153,* 424-426. doi:10.1016/0006-3223(94)90705-6

Geary, E. K., Seidenberg, M., & Hermann, B. (2009). Atrophy of basal ganglia nuclei and negative symptoms in temporal lobe epilepsy. *The Journal of Neuropsychiatry and Clinical Neurosciences, 21*, 152-159. doi:10.1176/appi.neuropsych.21.2.152

Geda, Y. E., Roberts, R. O., Knopman, D. S., Petersen, R. C., Christianson, T. J. H., Pankratz, V. S., . . . Tangalos, E. G. (2008). Prevalence of neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging: population-based study. *Archives of General Psychiatry, 65*, 1193-1198. doi:10.1001/archpsyc.65.10.1193

Glenn, M. B., Burke, D. T., O'Neil-Pirozzi, T., Goldstein, R., Jacob, L., & Kettell, J. (2002). Cutoff score on the apathy evaluation scale in subjects with traumatic brain injury. *Brain Injury, 16*, 509-516. doi:10.1080/02699050110119132

Graham, E., & Lachman, M. E. Personality traits, facets and cognitive performance: Age differences in their relations. (2014). *Personality and Individual Differences, 59,* 89-95. doi: 10.1016/j.paid.2013.11.011

Greenson, R. R. (1949). The psychology of apathy. *Psychoanalytic Quarterly, 18*, 290-302.

Gur, R. E., Kohler, C. G., Ragland, J. D., Siegel, S. J., Lesko, K., Bilker, W. B., & Gur, R. C. (2006). Flat affect in schizophrenia: relation to emotion processing and neurocognitive measures. *Schizophrenia Bulletin, 32*, 279-287. doi:10.1093/schbul/sbj041

Haslam, N., Holland, E., & Kuppens, P. (2011). Categories versus dimensions in personality and psychopathology: A quantitative review of taxometric research. *Psychological Medicine, 42*, 903-920. doi:10.1017/S0033291711001966

Hayton, J. C., Allen, D. G., & Scarpello, V. (2004). Factor retention decisions in exploratory factor analysis: A tutorial on parallel analysis. *Organizational Research Methods, 7*, 191-205. doi: 10.1177/1094428104263675

Horan, W. P., Kring, A. M., Gur, R. E., Reise, S. P., & Blanchard, J. J. (2011). Development and psychometric validation of the Clinical Assessment Interview for Negative Symptoms (CAINS). *Schizophrenia Research, 132*, 140-145. doi:10.1016/j.schres.2011.06.030

Isella, V., Melzi, P., Grimaldi, M., Iurlaro, S., Piolti, R., Ferrarese, C., . . . Appollonio, I. (2002). Clinical, neuropsychological, and morphometric correlates of apathy in Parkinson's disease. *Movement Disorders, 17*, 366-371. doi:10.1002/mds.10041

Kaiser, S., Heekeren, K., & Simon, J. J. (2011). The Negative Symptoms of Schizophrenia: Category or Continuum? *Psychopathology, 44*, 345-353. doi:10.1159/000325912

Kaji, Y., Hirata, K., & Ebata, A. (2006). Characteristics of poststroke depression in Japanese patients. *Neuropsychobiology, 53*, 148-152. doi:10.1159/000093340

Kanauss, K., Schatz, P., & Puente, A. E. (2005). Current trends in the reimbursement of professional neuropsychological services. *Archives of Clinical Neuropsychology, 20*, 341-353. doi:10.1016/j.acn.2004.09.002

Kant, R., Duffy, J., & Pivovarnik, A. (1998). Prevalence of apathy following head injury. *Brain Injury, 12*, 87-92. doi:10.1080/026990598122908

Kaplan, E. F., Goodglass, H., &Weintraub, S. (1983). *The Boston Naming Test (2nd ed).* Philadelphia, PA: Lea & Febiger.

Kay, D.B., Kirsch-Darrow, L., Zahonde, L., Okun, M., & Bowers, D. (2012). Dimensions of apathy in Parkinson's disease: exploratory factor analysis of the apathy scale. *Journal of Parkinson's Disease, 2,* 161-166. doi: 10.3233/JPD-2012-12085

Kaufer, D. I., Cummings, J. L., Ketchel, P., Smith, V., MacMillan, A., Shelley, T., . . . DeKosky, S. T. (2000). Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. *The Journal of Neuropsychiatry and Clinical Neurosciences, 12*, 233-239. doi:10.1176/appi.neuropsych.12.2.233

Kiang, M., Christensen, B. K., Remington, G., & Kapur, S. (2003). Apathy in schizophrenia: clinical correlates and association with functional outcome. *Schizophrenia Research, 63*, 79-88. doi:10.1016/S0920-9964(02)00433-4

Kirkpatrick, B., Fenton, W. S., Carpenter Jr, W. T., & Marder, S. R. (2006). The NIMH-MATRICS consensus statement on negative symptoms. *Schizophrenia Bulletin, 32*, 214-219. doi:10.1093/schbul/sbj053

Kirsch-Darrow, L., Marsiske, M., Okun, M. S., Bauer, R., & Bowers, D. (2011). Apathy and Depression: Separate Factors in Parkinson's Disease. *Journal of the International Neuropsychological Society, 17*, 1058-1066. doi 10.1017/S1355617711001068

Kirsch-Darrow, L., Zahodne, L. B., Hass, C., Mikos, A., Okun, M. S., Fernandez, H. H., & Bowers, D. (2009). How cautious should we be when assessing apathy with the Unified Parkinson's Disease Rating Scale? *Movement Disorders, 24*, 684-688. doi:10.1002/mds.22437

Kostic, V. S., & Filippi, M. (2011). Neuroanatomical correlates of depression and apathy in Parkinson's disease: Magnetic resonance imaging studies. *Journal of the Neurological Sciences, 310*, 61-63. doi:10.1016/j.jns.2011.05.036

Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. Journal of Abnormal Psychology, 116, 645-66. . doi: 10.1037/0021-843X.116.4.645

Kuhlmei, A., Walther, B., Becker, T., Müller, U., & Nikolaus, T. (2011). Actigraphic daytime activity is reduced in patients with cognitive impairment and apathy. *European Psychiatry.* doi:10.1016/j.eurpsy.2011.04.006

Kuzis, G., Sabe, L., Tiberti, C., Dorrego, F., & Starkstein, S. (1999). Neuropsychological correlates of apathy and depression in patients with dementia. *Neurology, 52,* 1403-1403.

Lampe, I. K., & Heeren, T. J. (2004). Is apathy in late-life depressive illness related to age-at-onset, cognitive function or vascular risk? *International Psychogeriatrics,16,* 481-486. doi:10.1017/S1041610204000766

Landes, A. M., Sperry, S. D., & Strauss, M. E. (2005). Prevalence of apathy, dysphoria, and depression in relation to dementia severity in Alzheimer's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences, 17,* 342-349. doi:10.1176/appi.neuropsych.17.3.342

Lane-Brown, A., & Tate, R. (2009). Measuring apathy after traumatic brain injury: Psychometric properties of the Apathy Evaluation Scale and the Frontal Systems Behavior Scale. *Brain Injur*y, *23,* 999-1007. doi:10.3109/02699050903379347

Lechowski, L., Benoit, M., Chassagne, P., Vedel, I., Tortrat, D., Teillet, L., & Vellas, B. (2009). Persistent apathy in Alzheimer's disease as an independent factor of rapid functional decline: the REAL longitudinal cohort study. *International Journal of Geriatric Psychiatry, 24,* 341-346. doi:10.1002/gps.2125

Leifker, F. R., Bowie, C. R., & Harvey, P. D. (2009). Determinants of everyday outcomes in schizophrenia: the influences of cognitive impairment, functional capacity, and symptoms. *Schizophrenia Research, 115,* 82-87. doi:10.1016/j.schres.2009.09.004

Lenze, E. J., Munin, M. C., Dew, M. A., Marin, R. S., Butters, M. A., Skidmore, E. R., . . . Reynolds III, C. F. (2009). Apathy after hip fracture: a potential target for intervention to improve functional outcomes. *The Journal of Neuropsychiatry and Clinical Neurosciences, 21,* 271. doi:10.1176/appi.neuropsych.21.3.271

Leontjevas, R., Evers-Stephan, A., Smalbrugge, M., Pot, A. M., Thewissen, V., Gerritsen, D. L., & Koopmans, R. T. C. M. (2011). A Comparative Validation of the Abbreviated Apathy Evaluation Scale (AES-10) With the Neuropsychiatric Inventory Apathy Subscale Against Diagnostic Criteria of Apathy. *Journal of the American Medical Directors Association, 13,* 308.e1-308.e6. doi:10.1016/j.jamda.2011.06.003

Leontjevas, R., Teerenstra, S., Smalbrugge, M., Vernooij-Dassen, M. Bohlmeijer, E.T., Gerritsen, D.L., & Koopman, R. (2013). More insight into the conept of apathy: a multidisciplinary depression program has a different effects on depressive symptoms and apathy in nursing homes. *International Psychogeriatrics, 25,* 1941-1952. doi: 10.1017/S1041610213001440

Leontjevas, R., van Hooren, S., Waterink, W., & Mulders, A. (2009). Apathy and Depressive Mood in Nursing Home Patients With Early-Onset Dementia. *American Journal of Alzheimer's Disease and Other Dementias, 24,* 341-348. doi:10.1177/1533317509333905

Leroi, I., Ahearn, D. J., Andrews, M., McDonald, K. R., Byrne, E. J., & Burns, A. (2011). Behavioural disorders, disability and quality of life in Parkinson's disease. *Age and Ageing, 40,* 614-621. doi:10.1093/ageing/afr078

Leroi, I., Harbishettar, V., Andrews, M., McDonald, K., Byrne, E. J., & Burns, A. (2012). Carer burden in apathy and impulse control disorders in Parkinson's disease. *International Journal of Geriatric Psychiatry, 27,* 160-166.doi:10.1002/gps.2704

Levy, M. L., Cummings, J. L., Fairbanks, L. A., Masterman, D., Miller, B. L., Craig, A. H., . . . Litvan, I. (1998). Apathy is not depression. *The Journal of Neuropsychiatry and Clinical Neurosciences, 10,* 314-319.

Levy, R., & Czernecki, V. (2006). Apathy and the basal ganglia. *Journal of Neurology, 253,* vii54-vii61. doi:10.1007/s00415-006-7012-5

Lezak, M.D., Howieson, D., Bigler, E., & Tranel, D. 2012. *Neuropsychological assessment*, Fifth Edition. New York: Oxford University Press.

Lueken, U., Seidl, U., Völker, L., Schweiger, E., Kruse, A., & Schröder, J. (2007). Development of a short version of the Apathy Evaluation Scale specifically adapted for demented nursing home residents. *American Journal of Geriatric Psychiatry, 15,* 376-385. doi:10.1097/JGP.0b013e3180437db3

Marin, R. S. (1991). Apathy: a neuropsychiatric syndrome. *The Journal of Neuropsychiatry and Clinical Neurosciences, 3,* 243-254.

Marin, R. S., Biedrzycki, R. C., & Firinciogullari, S. (1991). Reliability and validity of the Apathy Evaluation Scale. *Psychiatry Research, 38,* 143-162. doi: 10.1016/0165-1781(91)90040-V.

Marin, R. S., Butters, M. A., Mulsant, B. H., Pollock, B. G., & Reynolds III, C. F. (2003). Apathy and executive function in depressed elderly. *Journal of Geriatric Psychiatry and Neurology, 16,* 112-116. doi:10.1177/0891988703016002009

Marin, R. S., Firinciogullari, S., & Biedrzycki, R. C. (1993). The sources of convergence between measures of apathy and depression. *Journal of Affective Disorders, 28,* 117-124. doi:10.1016/0165-0327(93)90040-Q

Marin, R. (1996). Apathy: Concept, Syndrome, Neural Mechanisms, and Treatment. *Seminars in Clinical Neuropsychiatry, 1,* 304-314.

Markon, K. E., Chmielewski, M., & Miller, C. J. (2011). The reliability and validity of discrete and continuous measures of psychopathology: A quantitative review. *Psychological Bulletin, 137,* 856-879. doi:10.1037/a0023678

Massimo, L., Powers, C., Moore, P. N., Vesely, L., Avants, B. B., Gee, J. C., Libon, D. J., Grossman, M. (200) Neuroanatomy of apathy and disinhibition in frontotemporal lobar degeneration. *Dementia and Geriatric Cognitive Disorders, 27,* 94-104. doi: 10.1159/000194658

McDade-Montez, E. A., Watson, D., O'Hara, M. W., & Denburg, N. L. (2008). The effect of symptom visibility on informant reporting. *Psychology and Aging, 23,*940 – 946. doi:10.1037/a0014297

McKinlay, A., Grace, R. C., Dalrymple-Alford, J. C., Anderson, T. J., Fink, J., & Roger, D. (2008). Neuropsychiatric problems in Parkinson's disease: Comparisons between self and caregiver report. *Aging and Mental Health, 12,* 647-653. doi:10.1080/13607860802343225

Meeks, S., & Walker, J. S. (1990). Blunted affect, blunted lives? Negative symptoms, ADL functioning, and mental health among older adults. *International Journal of Geriatric Psychiatry, 5*, 233-238. doi:10.1002/gps.930050405

Messinger, J. W., Trémeau, F., Antonius, D., Mendelsohn, E., Prudent, V., Stanford, A. D., & Malaspina, D. (2011). Avolition and expressive deficits capture negative symptom phenomenology: implications for DSM-5 and schizophrenia research. *Clinical Psychology Review, 31*, 161-168. doi:10.1016/j.cpr.2010.09.002

Miller, E. A., Rosenheck, R. A., & Schneider, L. S. (2011). Caregiver burden, health utilities, and institutional service use in Alzheimer's disease. *International Journal of Geriatric Psychiatry, 4*, 382-393. doi:10.1002/gps.2730

Milner, B. (1963) Effects of different brain lesions on card sorting: the role of the frontal lobes, *Archives of Neurology,* 100-110.

Mirakhur, A., Craig, D., Hart, D., McLlroy, S., & Passmore, A. (2004). Behavioural and psychological syndromes in Alzheimer's disease. *International Journal of Geriatric Psychiatry, 19*, 1035-1039. doi:10.1002/gps.1203

Möbes, J., Joppich, G., Stiebritz, F., Dengler, R., & Schröder, C. (2008). Emotional speech in Parkinson's disease. *Movement Disorders, 23,* 824-829. doi: 10.1002/mds.21940

Mortbly M., Maercker, A., & Forstmeier, S. (2011). Midlife motivational abilities predict apathy and depression in Alzheimer disease: The Aging, Demographics, and Memory Study, *Journal of Geriatric Psychiatry and Neurology, 24,* 151-160. doi: 10.1177/0891988711409409

Mueser, K. T., Pratt, S. I., Bartels, S. J., Forester, B., Wolfe, R., & Cather, C. (2010). Neurocognition and social skill in older persons with schizophrenia and major mood disorders: An analysis of gender and diagnosis effects. *Journal of Neurolinguistics, 23*, 297-317. doi:10.1016/j.jneuroling.2009.08.007

Mulin, E., Leone, E., Dujardin, K., Delliaux, M., Leentjens, A., Nobili, F., . . . Osorio, R. (2011). Diagnostic criteria for apathy in clinical practice. *International Journal of Geriatric Psychiatry, 26*, 158-165. doi:10.1002/gps.2508

Müller, U., Czymmek, J., Thöne-Otto, A., & Yves Von Cramon, D. (2006). Reduced daytime activity in patients with acquired brain damage and apathy: A study with ambulatory actigraphy. *Brain Injury, 20*, 157-160. doi:10.1080/02699050500443467

Naarding, P., Janzing, J. G. E., Eling, P., van der Werf, S., & Kremer, B. (2009). Apathy Is Not Depression in Huntington's Disease. *The Journal of Neuropsychiatry and Clinical Neurosciences, 21*, 266-270. doi:10.1176/appi.neuropsych.21.3.266

Norton, L. E., Malloy, P. F., & Salloway, S. (2001). The impact of behavioral symptoms on activities of daily living in patients with dementia. *American Journal of Geriatric Psychiatry, 9*, 41-48. doi:10.1176/appi.ajgp.9.1.41

Oguru, M., Tachibana, H., Toda, K., Okuda, B., & Oka, N. (2010). Apathy and depression in Parkinson disease. *Journal of Geriatric Psychiatry and Neurology, 23*, 35-41. doi:10.1177/0891988709351834

Padala, P. R., Desouza, C. V., Almeida, S., Shivaswamy, V., Ariyarathna, K., Rouse, L., . . . Petty, F. (2008). The impact of apathy on glycemic control in diabetes: A cross-sectional study. *Diabetes Research and Clinical Practice, 79*, 37-41. doi:10.1016/j.diabres.2007.06.012

Padala, P.R., Padala, K.P., Monga, V., Ramirez, D.A., & Sullivan, D.H., (2012). Reversal of SSRI-associated apathy syndrome by discontinuation of therapy. *The Annals of Pharmacotherapy, 46,* 179-186. doi: 10.1345/aph.1Q656

Parks, S., & Novielli, K. (2000). A practical guide to caring for caregivers. *American Family Physician, 62*, 2613-2620.

Paulsen, J. S., Ready, R., Hamilton, J., Mega, M., & Cummings, J. (2001). Neuropsychiatric aspects of Huntington's disease. *Journal of Neurology, Neurosurgery & Psychiatry,71*, 310-314. doi:10.1136/jnnp.71.3.310

Pedersen, K. F., Alves, G., Aarsland, D., & Larsen, J. P. (2009). Occurrence and risk factors for apathy in Parkinson disease: a 4-year prospective longitudinal study. *Journal of Neurology, Neurosurgery & Psychiatry, 80*, 1279-1282. doi:10.1136/jnnp.2008.170043

Pedersen, K. F., Alves, G., Larsen, J. P., Tysnes, O. B., Møller, S. G., & Brønnick, K. (2012). Psychometric properties of the Starkstein Apathy Scale in patients with early untreated Parkinson disease. *American Journal of Geriatric Psychiatry, 20*, 142-148. doi:10.1097/JGP.0b013e31823038f2

Pedersen, K. F., Larsen, J. P., & Aarsland, D. (2008). Validation of the Unified Parkinson's Disease Rating Scale (UPDRS) section I as a screening and diagnostic instrument for apathy in patients with Parkinson's disease. *Parkinsonism & Related Disorders, 14*, 183-186. doi:10.1016/j.parkreldis.2007.07.015

Piamarta, F., Iurlaro, S., Isella, V., Atzeni, L., Grimaldi, M., Russo, A., . . . Appollonio, I. (2004). Unconventional affective symptoms and executive functions after stroke in the elderly. *Archives of Gerontology and Geriatrics (Supplement), 9,* 315-323. doi:10.1016/j.archger.2004.04.042

Pinquart, M., & Sörensen, S. (2003). Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. *Psychology and Aging, 18*, 250-267. doi:10.1037/0882-7974.18.2.250

Pluck, G., & Brown, R. (2002). Apathy in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 73*, 636-642. doi:10.1136/jnnp.73.6.636

Poletti, M., Lucetti, C., Logi, C. Baldacci, F., Cipriani, G., Nuti, A., Borelli, P., & Bonuccelli, U. (2013). Cognitive correlates of negative symptoms in behavioral variant frontotemporal dementia: implications for the frontal lobe syndrome. *Neurological Sciences, 11*, 1893-1896. 10.1007/s10072-013-1400-2

Politis, A. M., Mayer, L. S., Passa, M., Maillis, A., & Lyketsos, C. G. (2004). Validity and reliability of the newly translated Hellenic Neuropsychiatric Inventory (H-NPI) applied to Greek outpatients with Alzheimer's disease: a study of disturbing behaviors among referrals to a memory clinic. *International Journal of Geriatric Psychiatry, 19*, 203-208. doi: 10.1002/gps.1045

Posada, C., Moore, D. J., Woods, S. P., Vigil, O., Ake, C., Perry, W., . . . the HIV Neurobehavioral Research Center (HNRC) Group. (2010). Implications of hepatitis C virus infection for behavioral symptoms and activities of daily living. *Journal of Clinical and Experimental Neuropsychology, 32,* 637-644. doi:10.1080/13803390903418900

Prado-Jean, A., Couratier, P., Druet-Cabanac, M., Nubukpo, P., Bernard-Bourzeix, L., Thomas, P., . . . Clément, J. P. (2010). Specific psychological and behavioral symptoms of depression in patients with dementia. *International Journal of Geriatric Psychiatry, 25,* 1065-1072. doi:10.1002/gps.2468

Prigatano, G.P. (Ed.). (2010). The study of anosognosia. New York: Oxford University Press.

PsychCorp (2008). Wechsler Adult Intelligence Scale–Fourth Edition. Technical and Interpretive Manual. San Antonio, TX: Pearson

Quaranta, D., Marra, C., Rossi, C., Gainotti, G., Masullo, C. (2012). Different apathy profile in behavioral variant of frontotemporal dementia and Alzheimer's disease: a preliminary investigation. (2012). *Current Gerontology and Geriatrics Research.* doi:10.1155/2012/719250

Rabin, L., Barr, W., & Burton, L. (2005). Assessment practices of clinical neuropsychologists in the United States and Canada: A survey of INS, NAN, and APA Division 40 members. *Archives of Clinical Neuropsychology, 20,* 33–65. doi: 10.1016/j.acn.2004.02.005

Rabkin, J. G., Ferrando, S. J., van Gorp, W., Rieppi, R., McElhiney, M., & Sewell, M. (2000). Relationships among apathy, depression, and cognitive impairment in HIV/AIDS.*The Journal of Neuropsychiatry and Clinical Neurosciences, 12,* 451-457. doi:10.1176/appi.neuropsych.12.4.451

Rawlings, D., Williams, B., Haslam, N., & Claridge, G. (2008). Taxometric analysis supports a dimensional latent structure for schizotypy. *Personality and Individual Differences, 44,* 1640-1651. doi:10.1016/j.paid.2007.06.005

Ready, R., Ott, B., & Grace, J. (2004). Validity of Informant Reports About AD and MCI Patients' Memory. *Alzheimer's Disease and Associated Disorders, 18*, 11-16.

Reijnders, J. S. A. M., Scholtissen, B., Weber, W. E. J., Aalten, P., Verhey, F. R. J., & Leentjens, A. F. G. (2010). Neuroanatomical correlates of apathy in Parkinson's disease: A magnetic resonance imaging study using voxel-based morphometry. *Movement Disorders, 25,* 2318-2325.doi: 10.1002/mds.23268

Reise, S. P. (2012). The rediscovery of bifactor measurement models. *Multivariate Behavioral Research, 47,* 667–696. doi: 10.1080/00273171.2012.715555

Reitan, R. (1958). Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual and Motor Skills, 8,* 271-276. doi:10.2466/PMS.8.7.271-276

Resnick, B., Zimmerman, S. I., Magaziner, J., & Adelman, A. (1998). Use of the Apathy Evaluation Scale as a measure of motivation in elderly people. *Rehabilitation Nursing : The Official Journal of the Association of Rehabilitation Nurses, 23,* 141-147.

Rey, A. (1941). L'examen psychologique dans les cas d'encéphalopathie traumatique.(Les problems.). *Archives De Psychologie,* 215-285.

Rey, A. (1964). L'examen clinique en psychologie.. *Paris, France: Presses Universitaires De France.*

Rhemtulla, M., Brosseau-Liard, P. E., & Savalei, V. (2012). When can categorical variables be treated as continuous? A comparison of robust continuous and categorical SEM estimation methods under suboptimal conditions. *Psychological Methods, 17,* 354-373. doi: 10.1037/a0029315

Ricci, M., Guidoni, S. V., Sepe-Monti, M., Bomboi, G., Antonini, G., Blundo, C., & Giubilei, F. (2009). Clinical findings, functional abilities and caregiver distress in the early stage of dementia with Lewy bodies (DLB) and Alzheimer's disease (AD). *Archives of Gerontology and Geriatrics, 49,* e101-e104. doi:10.1016/j.archger.2008.10.001

Robert, P., Onyike, C., Leentjens, A., Dujardin, K., Aalten, P., Starkstein, S., . . . Drapier, D. (2009). Proposed diagnostic criteria for apathy in Alzheimer's disease and other neuropsychiatric disorders. *European Psychiatry, 24,* 98-104. doi:10.1016/j.eurpsy.2008.09.001

Robert, P. H., Berr, C., Volteau, M., Bertogliati, C., Benoit, M., Sarazin, M., . . . Dubois, B. (2006). Apathy in patients with mild cognitive impairment and the risk of developing dementia of Alzheimer's disease A one-year follow-up study. *Clinical Neurology and Neurosurgery, 108,* 733-736. doi:10.1016/j.clineuro.2006.02.003

Robert, P., Clairet, S., Benoit, M., Koutaich, J., Bertogliati, C., Tible, O., . . . Bedoucha, P. (2002). The apathy inventory: assessment of apathy and awareness in Alzheimer's disease, Parkinson's disease and mild cognitive impairment. *International Journal of Geriatric Psychiatry, 17,* 1099-1105. doi:10.1002/gps.755

Robinson, H., Calamia, M., Gläscher, J., Bruss, J., & Tranel, D. (2013). Neuroanatomical correlates of executive functions: a neuropsychological approach using the EXAMINER battery. *Journal of the International Neuropsychological Society, 20,* 52-63. doi:10.1017/S135561771300060X

Sagen, U., Faerden, A., Haug, T., Melle, I., Finset, A., & Dammen, T. (2010). Are there common core features of apathy in different neuropsychiatric samples as assessed by the Apathy Evaluation Scale?. *Nordic Journal of Psychiatry, 64,* 49-57. doi:10.3109/08039480903274415

Santangelo, G., Vitale, C., Trojano, L., Longo, K., Cozzolino, A., Grossi, D., & Barone, P. (2009). Relationship between depression and cognitive dysfunctions in Parkinson's disease without dementia. *Journal of Neurology, 256,* 632-638. doi:10.1007/s00415-009-0146-5

Schiehser, D. M., Delis, D. C., Filoteo, J. V., Delano-Wood, L., Han, S. D., Jak, A. J., . . . Bondi, M. W. (2011). Are self-reported symptoms of executive dysfunction associated with objective executive function performance following mild to moderate traumatic brain injury? *Journal of Clinical and Experimental Neuropsychology, 33,* 704-714. doi:10.1080/13803395.2011.553587

Senanarong, V., Poungvarin, N., Jamjumras, P., Sriboonroung, A., Danchaivijit, C., Udomphanthuruk, S., & Cummings, J. L. (2005). Neuropsychiatric symptoms,

functional impairment and executive ability in Thai patients with Alzheimer's disease. *International Psychogeriatrics, 17*, 81-90. doi:10.1017/S1041610205000980

Sikkes, S., De Lange-de Klerk, E., Pijnenburg, Y., & Scheltens, P. (2009). A systematic review of Instrumental Activities of Daily Living scales in dementia: room for improvement. *Journal of Neurology, Neurosurgery & Psychiatry, 80*, 7-12. doi:10.1136/jnnp.2008.155838

Silverberg, N. H., & Millis, S. R. (2009). Impairment versus deficiency in neuropsychological assessment: implications for ecological validity. *Journal of the International Neuropsychological Society, 15,* 94–102. doi: 10.1017/S1355617708090139

Simms, L. J., Gros, D. F., Watson, D., & O'Hara, M. W. (2008). Parsing the general and specific components of depression and anxiety with bifactor modeling. Depression and Anxiety, 25, E34-E46. doi: 10.1002/da.20432

Sivan, A. B. (1992). *Benton Visual Retention Test* Psychological Corporation San Antonio, TX.

Skidmore, F.M.., Yang,, M., Baxter, L., von Deneen, K., Collingwood, J. He, G., Tandon, D., Korenkevych, D., Savenkov, A., Heilman, K.M., Gold, M., Liu, Y. (2013) Apathy, depression, and motor symptoms have distinct and separable resting activity patterns in idiopathic Parkinson disease. *Neuroimage, 81,* 484 – 495 doi: 10.1016/j.neuroimage.2011.07.012

Smith, M. C., Smith, M. K., & Ellgring, H. (1996). Spontaneous and posed facial expressionin Parkinson's disease. *Journal of the International Neuropsychological Society, 2,* 383–391.

Sockeel, P., Dujardin, K., Devos, D., Deneve, C., Destée, A., & Defebvre, L. (2006). The Lille apathy rating scale (LARS), a new instrument for detecting and quantifying apathy: validation in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 77,* 579-584. doi:10.1136/jnnp.2005.075929

Soubelet, A., & Salthouse, T.A. (2011). Personality-cognition relations across adulthood. *Developmental Psychology, 47,* 303-310. doi: 10.1037/a0021816.

Starkstein, S., Brockman, S., Bruce, D., & Petracca, G. (2010). Anosognosia is a significant predictor of apathy in Alzheimer's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences, 22,* 378-383. doi:10.1176/appi.neuropsych.22.4.378

Starkstein, S., Jorge, R., Mizrahi, R., & Robinson, R. (2006). A prospective longitudinal study of apathy in Alzheimer's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 77,* 8-11. doi:10.1136/jnnp.2005.069575

Starkstein, S., & Merello, M. (2007). The Unified Parkinson's Disease Rating Scale: validation study of the mentation, behavior, and mood section. *Movement Disorders, 22,* 2156-2161. doi:10.1002/mds.21521

Starkstein, S., & Pahissa, J., (2013). Apathy following traumatic brain injury. *Neuropsychiatry of Traumatic Brain Injury, 37,* 103-112. doi: 10.1016/j.psc.2013.10.002

Steinberg, M., Shao, H., Zandi, P., Lyketsos, C. G., Welsh-Bohmer, K. A., Norton, M. C., . . . Tschanz, J. A. T. (2008). Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: the Cache County Study. *International Journal of Geriatric Psychiatry, 23*, 170-177. doi:10.1002/gps.1858.

Stolar, N., Berenbaum, H., Banich, M. T., & Barch, D. (1994). Neuropsychological correlates of alogia and affective flattening in schizophrenia. *Biological Psychiatry, 35*, 164-172. doi:10.1016/0006-3223(94)91148-7

Strauss, M. E., & Sperry, S. D. (2002). An informant-based assessment of apathy in Alzheimer disease. *Cognitive and Behavioral Neurology, 15*, 176-183.

Sturm, V. E., McCarthy, M. E., Yun, I., Madan, A., Yuan, J. W., Holley, S. R., . . . Levenson, R. W. (2011). Mutual gaze in Alzheimer's disease, frontotemporal and semantic dementia couples. *Social Cognitive and Affective Neuroscience, 6*, 359-367. doi:10.1093/scan/nsq055

Stuss, D. T., Van Reekum, R., & Murphy, K. J. (2000). Differentiation of states and causes of apathy. In J. C. Borod. (Ed.), The Neuropsychology of Emotion,(pp. 340–363). Oxford: Oxford University Press.

Sultzer, D.L., Levin, H.S., Mahler, M.E., High, W.M., Cummings, J.L. (1993). A comparison of psychiatric symptoms in vascular dementia and Alzheimer's disease. *American Journal of Psychiatry, 150*, 1806-1812.

Thomas, P., Clément, J. P., Hazif-Thomas, C., & Léger, J. M. (2001). Family, Alzheimer's disease and negative symptoms. *International Journal of Geriatric Psychiatry, 16*, 192-202. doi:10.1002/1099-1166(200102)16:2<192::AID-GPS301>3.0.CO;2-Y

Thompson, J. C., Snowden, J. S., Craufurd, D., & Neary, D. (2002). Behavior in Huntington's Disease Dissociating Cognition-Based and Mood-Based Changes. *The Journal of Neuropsychiatry and Clinical Neurosciences, 14*, 37-43. doi: 10.1176/appi.neuropsych.14.1.37

Torrente, F., Lischinsky, A., Torralva, T., López, P., Roca, M., & Manes, F. (2011). Not always hyperactive? Elevated apathy scores in adolescents and adults with ADHD.*Journal of Attention Disorders, 15*, 545-556. doi:10.1177/1087054709359887

Troisi, A., Pompili, E., Binello, L., & Sterpone, A. (2007). Facial expressivity during the clinical interview as a predictor functional disability in schizophrenia. A pilot study. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 31*, 475-481. doi:10.1016/j.pnpbp.2006.11.016

Van Dalen, J., van Charante, E., Nederkoorn, P., van Gool, W., Richard, E. (2013). Postroke Apathy. *Stroke, 44*, 851-860. doi: 10.1161/STROKEAHA.112.674614

van Reekum, R., Stuss, D. T., & Ostrander, L. (2005). Apathy: why care? *The Journal of Neuropsychiatry and Clinical Neurosciences, 17*, 7-19. doi:10.1176/appi.neuropsych.17.1.7

Varanese, S., Perfetti, B., & Di Rocco. A. (2011). Apathy, but not depression, reflects inefficient cognitive strategies in Parkinson's disease. *PLoS One, 6*, e17846. doi:10.1371/journal.pone.0017846

Velligan, D. I., Ritch, J. L., Sui, D., DiCocco, M., & Huntzinger, C. D. (2002). Frontal Systems Behavior Scale in schizophrenia: relationships with psychiatric symptomatology, cognition and adaptive function. *Psychiatry Research, 113*, 227-236. doi:10.1016/S0165-1781(02)00264-0

Verdejo-García, A., & Pérez-García, M. (2008). Substance abusers' self-awareness of the neurobehavioral consequences of addiction. *Psychiatry Research, 158*, 172-180. doi:10.1016/j.psychres.2006.08.001

Vicini Chilovi, B., Conti, M., Zanetti, M., Mazzù, I., Rozzini, L., & Padovani, A. (2009). Differential impact of apathy and depression in the development of dementia in mild cognitive impairment patients. *Dementia and Geriatric Cognitive Disorders, 27*, 390-398. doi:10.1159/000210045

Watson, D., Clark, L.A., & Tellegen, A.(1988).Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54,*1063-1070. doi: 10.1037/0022-3514.54.6.1063

Watson, D., O'Hara M,W., Simms, L.J., Kotov, R., Chmielewski, M., McDade-Montez, E.A., Gamez, W., Stuart, S. (2007). Development and validation of the Inventory of Depression and Anxiety Symptoms (IDAS). *Psychological Assessment, 19,* 253–268. doi: 10.1037/1040-3590.19.3.253

Wechsler D. (1997). WAIS-III, WMS-III Technical Manual. The Psychological Corporation: San Antonio, TX.

Weintraub, D., Moberg, P. J., Duda, J. E., Katz, I. R., & Stern, M. B. (2004). Effect of psychiatric and other nonmotor symptoms on disability in Parkinson's disease. *Journal of the American Geriatrics Society, 52,* 784-788. doi:10.1111/j.1532-5415.2004.52219.x

Weitzner, M. A., Kanfer, S., & Booth-Jones, M. (2005). Apathy and pituitary disease: it has nothing to do with depression. *The Journal of Neuropsychiatry and Clinical Neurosciences, 17,* 159-166. doi:10.1176/appi.neuropsych.17.2.159

Winograd-Gurvich, C., Fitzgerald, P. B., Georgiou-Karistianis, N., Bradshaw, J., & White, O. B. (2006). Negative symptoms: A review of schizophrenia, melancholic depression and Parkinson's disease. *Brain Research Bulletin, 70,* 312-321. doi:10.1016/j.brainresbull.2006.06.007

Witgert, M., Salamone, A., Strutt, A., Jawaid, A., Massman, P., Bradshaw, M., . . . Schulz, P. (2010). Frontal-lobe mediated behavioral dysfunction in amyotrophic lateral sclerosis. *European Journal of Neurology, 17,* 103-110. doi: 0.1111/j.1468-1331.2009.02801.x

Wolf, M. B. & Ackerman, P. L. (2005). Extraversion and intelligence: A meta-analytic investigation. *Personality and Individual Differences, 39,* 531–542. doi: 10.1016/j.paid.2005.02.020

Wood, S., Cummings, J. L., Hsu, M. A., Barclay, T., Wheatley, M. V., Yarema, K. T., & Schnelle, J. F. (2000). The use of the neuropsychiatric inventory in nursing home residents: characterization and measurement. *American Journal of Geriatric Psychiatry, 8,* 75-83.

World Health Organization. (1992). The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines. Geneva: World Health Organization.

Yoshizumi, M., Hirao, K., Ueda, K., & Murai, T. (2008). Insight in social behavioral dysfunction in schizophrenia: Preliminary study. *Psychiatry and Clinical Neurosciences,62,* 669-676. doi:10.1111/j.1440-1819.2008.01866.x

Zahodne, L. B., Young, S., Kirsch-Darrow, L., Nisenzon, A., Fernandez, H. H., Okun, M. S., & Bowers, D. (2009). Examination of the Lille Apathy Rating Scale in Parkinson disease. *Movement Disorders, 24,* 677-683. doi:10.1002/mds.22441

Zamboni, G., Huey, E.D., Krueger, F., Nichelli, P.F., & Grafman J. (2008). Apathy and disinhibition in frontotemporal dementia: Insights into their neural correlates. *Neurology, 71,* 736-742

Zawacki, T. M., Grace, J., Paul, R., Moser, D. J., Ott, B. R., Gordon, N., & Cohen, R. A. (2002). Behavioral problems as predictors of functional abilities of vascular dementia patients. *The Journal of Neuropsychiatry and Clinical Neurosciences, 14,* 296-302. doi:10.1176/appi.neuropsych.14.3.296

Zudema, S., de Jonghe, J. Verhey, F. & Koopmans, R. (2010). Environmental correlates of neuropsychiatric symptoms in nursing home patients with dementia. *International Journal of Geriatric Psychiatry, 25,* 14-22. doi: 10.1002/gps.2292

APPENDIX A

TABLES

Table A1. Exploratory Factor Analysis of Apathy Items

Items	1	2	3	4	5
20. He keeps working even when things get tough.	**0.94**	-0.05	-0.07	-0.10	-0.08
42. He thinks it is important to stick with a task until it is completed.	**0.93**	-0.14	0.03	-0.14	-0.07
156. He sticks with things even when they're difficult.	**0.91**	-0.04	-0.04	-0.02	-0.04
107. He takes on tasks that challenge him.	**0.88**	0.09	-0.14	0.00	0.12
3. He sets goals and works toward them.	**0.86**	0.00	-0.07	0.01	0.10
153. He is self-motivated.	**0.85**	0.12	-0.04	-0.02	0.04
97. He is a motivated worker.	**0.83**	0.02	-0.09	0.03	0.03
5. When he encounters a problem, he makes an effort to think of solutions.	**0.82**	-0.11	0.02	-0.09	0.08
63. He follows through on the plans he makes.	**0.81**	0.04	0.01	0.02	-0.15
89. When he reaches a goal, he sets a higher one.	**0.77**	0.15	-0.05	-0.07	0.05

Table A1. Continued

Items	1	2	3	4	5
62. He keeps herself busy throughout the day.	**0.77**	0.15	-0.13	0.07	-0.06
26. Getting things done during the day is important to him.	**0.76**	0.04	-0.07	0.06	0.03
132. He likes to take on new challenges.	**0.75**	0.27	-0.08	-0.04	0.09
30. He has goals for the future.	**0.74**	0.20	-0.05	0.05	0.03
9. He has trouble completing tasks because he gives up easily.	**0.74**	-0.20	0.14	-0.02	-0.23
17. He finds it important to start things on his own.	**0.73**	0.06	0.01	0.01	0.03
112. Sometimes he pushes herself harder than he should.	**0.73**	0.03	-0.11	-0.13	0.12
71. He takes an active role in planning out his day.	**0.70**	0.14	0.05	0.12	0.09
11. He starts activities on his own.	**0.70**	0.11	0.06	0.04	0.00
128. He needs other people to push him to do things.	**0.69**	-0.03	0.20	0.05	-0.22
12. He is proactive about how he wants to spend his day.	**0.68**	0.14	0.08	0.03	0.08

Table A1. Continued

Items	1	2	3	4	5
80. He has a hard time being motivated to get things done.	**0.67**	0.02	0.05	0.10	**-0.30**
108. He does things on his own without being asked to do so.	**0.66**	0.05	0.12	0.06	0.11
94. He has trouble getting started on activities by herself.	**0.64**	-0.10	0.20	0.15	-0.22
23. When he starts a task, he needs to be repeatedly encouraged by others to keep working.	**0.63**	-0.26	0.25	0.01	**-0.30**
135. It seems important to him to succeed in things.	**0.62**	0.13	0.07	-0.07	0.12
146. He tries to get by without doing any more work than he has to.	**0.61**	-0.03	0.04	0.16	-0.16
133. He gives up easily when things get difficult.	**0.61**	-0.14	0.15	0.06	-0.24
92. He needs a push to get started on things.	**0.60**	-0.02	0.14	0.21	-0.19
52. He doesn't do very much during the day.	**0.59**	0.09	-0.04	0.23	-0.20

Table A1. Continued

Items	1	2	3	4	5
150. He starts things and doesn't finish them.	**0.59**	-0.13	0.14	-0.02	-0.32
113. He waits for someone to do things for him.	**0.58**	-0.06	0.24	0.04	-0.19
82. He comes up with fun, new ideas.	**0.56**	0.29	0.07	-0.05	0.11
77. He actively manages his health problems.	**0.55**	0.01	0.10	0.10	0.03
155. He is interested in a wide variety of activities.	**0.53**	0.24	-0.02	0.03	-0.02
148. He makes an effort to try new things.	**0.52**	**0.42**	0.02	-0.01	0.07
21. He has a sense of curiosity about new things.	**0.52**	0.23	0.07	0.01	0.08
59. He doesn't get much done during the day.	**0.51**	0.07	-0.08	0.32	-0.17
142. He looks forward to a lot of things in his life.	**0.50**	**0.33**	0.05	0.08	0.10
74. He often just sits or lies around doing nothing.	**0.48**	0.05	0.05	0.26	-0.16

Table A1. Continued

Items	1	2	3	4	5
88. If left alone, he will sit for hours by herself doing nothing.	**0.48**	-0.04	0.09	**0.31**	-0.14
145. He doesn't have much energy.	**0.47**	0.09	0.07	0.18	-0.18
47. He is curious about what is going on in the world around him.	**0.44**	0.16	0.21	0.00	0.07
24. He never pushes herself to do things he doesn’t feel like doing.	**0.44**	-0.01	0.10	-0.04	**-0.35**
29. He is open to new experiences.	**0.40**	**0.43**	0.05	-0.01	-0.01
152. He is interested in news and current events.	**0.39**	0.16	0.19	-0.06	0.05
53. Before going out in public, he makes sure he is clean and dressed appropriately.	**0.39**	0.09	0.07	0.08	-0.12
124. He spends time each week doing things that interest his.	**0.38**	**0.33**	-0.07	0.29	0.14
15. He has hobbies that he is interested in.	**0.38**	0.23	0.05	0.20	0.14
36. He makes plans or asks to go places he has never been before (for example, new restaurants or stores).	**0.37**	**0.49**	-0.04	0.02	-0.01

Table A1. Continued

Items	1	2	3	4	5
140. He seems interested in his hobbies.	**0.34**	**0.32**	-0.03	**0.30**	0.14
85. Unless prompted by others, he will not engage in many recreational or leisure activities	**0.31**	0.26	0.13	0.16	-0.21
109. He looks forward to social events.	-0.04	**0.74**	0.20	-0.03	-0.13
98. He accepts invitations to spend time with others.	0.10	**0.71**	0.04	-0.03	-0.20
122. He expresses a desire to spend time with other people.	0.08	**0.69**	0.08	0.09	0.01
22. He seeks out time with friends.	0.17	**0.65**	0.01	0.06	-0.13
35. He seeks out social interaction.	0.05	**0.65**	0.16	0.08	-0.01
13. He looks forward to visits with family and/or friends.	0.00	**0.65**	0.10	0.04	-0.03
44. Having close friends is important to him.	0.01	**0.64**	0.11	-0.01	-0.08
7. He is interested in spending time with friends and family.	0.06	**0.63**	0.00	0.06	-0.01

Table A1. Continued

Items	1	2	3	4	5
41. He is proactive about spending time with friends or family.	0.17	**0.59**	-0.04	0.12	-0.08
139. When he hears about a new event he is interested in, he can hardly wait to go.	0.14	**0.49**	0.07	0.09	0.21
56. He avoids meeting new people.	-0.01	**0.45**	0.26	0.02	-0.24
111. He initiates calls or emails to friends and/or family members.	0.24	**0.42**	0.02	0.18	0.02
159. He asks for updates on the lives of his friends and/or family.	0.22	**0.42**	0.25	-0.01	0.04
151. In social situations, he prefers to keep to herself.	-0.05	**0.40**	**0.48**	-0.14	-0.28
43. He starts conversations with others.	0.17	**0.34**	**0.47**	-0.20	0.09
110. It is difficult to engage him in a conversation.	0.21	-0.05	**0.72**	0.00	-0.08
116. His emotions are “flat”.	-0.02	-0.02	**0.70**	0.19	0.12
115. His facial expressions stay the same no matter what he is talking about.	-0.01	-0.11	**0.64**	0.21	0.20

Table A1. Continued

Items	1	2	3	4	5
79. He has difficulty making eye contact with other people.	-0.01	0.08	**0.63**	-0.01	-0.02
129. When people talk to his, he often doesn't respond.	0.05	0.04	**0.61**	0.15	-0.10
90. His facial expression often looks "frozen" or “wooden”.	0.16	-0.04	**0.61**	0.10	-0.03
46. When asked a question, he usually responds with only a few words.	-0.01	0.12	**0.60**	0.01	-0.01
8. He is talkative.	0.16	0.17	**0.58**	-0.19	0.26
160. When people talk to him, he doesn't seem interested in what they have to say.	0.14	0.02	**0.56**	0.17	-0.02
64. His emotions seem much less intense compared to other people's emotions.	0.04	0.06	**0.54**	0.10	0.14
18. He doesn't say much when people try to have a conversation with him.	0.13	0.19	**0.51**	-0.03	-0.05
83. When people ask him questions, he answers them only after a long delay.	0.17	0.06	**0.50**	0.04	-0.09

Table A1. Continued

Items	1	2	3	4	5
144. He doesn't seem to notice when other people are in the room, unless they talk directly to him.	0.09	-0.01	**0.50**	0.23	-0.09
61. It's often difficult for me to know what he is feeling.	-0.06	-0.03	**0.49**	0.25	0.07
78. He often seems indifferent to what is going on around him.	0.20	0.09	**0.47**	0.23	-0.12
101. He is not very emotionally expressive.	0.01	0.14	**0.46**	0.14	0.05
91. He just isn’t interested in the people around him.	0.04	0.18	**0.44**	**0.33**	-0.01
93. He smiles when he is happy.	0.04	0.14	**0.42**	0.05	0.28
54. He rarely seems either sad or happy.	0.08	-0.02	**0.41**	0.17	-0.06
105. I have to ask him the same question more than once in order to get a reply.	0.27	0.07	**0.39**	0.13	**-0.30**
6. Very few things are able to get an emotional reaction out of him.	-0.16	0.04	**0.38**	0.19	0.02
2. When he talks, his hands stay at his sides and don't move.	0.04	-0.05	**0.38**	0.06	0.10

Table A1. Continued

Items	1	2	3	4	5
51. It's difficult for me to attract his attention.	0.01	0.05	**0.37**	**0.36**	-0.08
67. He laughs at his own jokes or funny stories.	-0.01	0.14	**0.36**	0.02	**0.33**
72. He does not seem to care about anything lately.	0.23	0.08	**0.36**	**0.32**	0.02
49. When people smile at him, he smiles back.	-0.02	0.29	**0.35**	-0.06	0.08
103. In general, he doesn't seem to care very much about things going on with family or friends.	-0.03	0.26	**0.35**	**0.37**	-0.12
119. Nothing really seems to matter much to him.	0.16	0.08	**0.32**	**0.49**	0.02
45. His emotions don't change very much, even when he hears really good or bad news.	-0.04	-0.07	**0.31**	**0.32**	0.18
154. He doesn't seem interested in his relationships with other people.	-0.07	0.25	**0.31**	**0.36**	-0.09
28. He laughs when he hears a joke.	0.25	0.24	**0.30**	-0.03	0.20

Table A1. Continued

Items	1	2	3	4	5
73. He doesn’t seem to care about his health.	0.05	0.05	0.04	**0.78**	0.03
118. He doesn't seem to care about his physical health.	0.11	-0.02	0.08	**0.70**	0.04
33. He is not taking care of herself.	0.23	-0.09	0.07	**0.62**	0.06
76. He doesn't shower or bathe regularly.	0.12	-0.01	0.03	**0.62**	0.01
75. He doesn't brush his teeth regularly.	0.17	-0.02	-0.03	**0.60**	-0.06
69. He doesn't seem to care about problems in his life.	0.15	0.00	0.14	**0.50**	-0.04
40. He doesn’t seem too concerned about his personal problems.	-0.06	-0.03	0.06	**0.37**	-0.09
96. In his day to day life, certain things can put him in a good or bad mood.	-0.02	-0.23	0.03	0.03	**0.62**
131. His voice gets louder or softer depending on how he is feeling.	0.08	-0.02	0.20	-0.11	**0.55**
81. When he wants to make a point, he raises his voice.	-0.11	-0.09	0.12	-0.12	**0.55**

Table A1. Continued

Items	1	2	3	4	5
4. When he is excited, he gets really animated.	0.17	0.07	0.12	0.02	**0.54**
106. His emotions come and go quickly.	0.08	-0.12	0.10	0.22	**0.45**
60. I can tell what he is feeling just by looking at his face.	0.02	-0.24	0.20	0.07	**0.45**
25. Being around certain people can put him in a good or bad mood.	-0.03	-0.20	-0.08	0.06	**0.43**
99. People can usually tell what kind of mood he is in.	0.02	0.01	0.28	0.01	**0.41**
37. His speaks more quickly when he is excited.	0.18	0.03	0.13	-0.06	**0.39**

Note: Factor labels are as follows: Factor 1: reduced interest and intiative, Factor 2: reduced emotional expression/alogia Factor 3: lack of self-care, Factor 4: asociality, and Factor 5: exaggerated emotional expression/emotional lability . Loadings greater than +/- 0.30 are in bold.

Table A2. Fit Statistics for Confirmatory Factor Analyses

	χ^2	*df*	CFI	RMSEA	
Individual Symptom Models					
Reduced Interest-Initiative	271	152	0.95	0.06	
Asociality	46	27	0.98	0.05	
Reduced Emotional Expression	199	104	0.92	0.06	
Overall Structural Models	χ^2	*df*	CFI	RMSEA	AIC
Correlated Factors Model	1534	899	0.90	0.05	28048
Bifactor Model	1434	858	0.91	0.05	27993

Note: CFI = confirmatory fit index; RMSEA = root mean square error of approximation; AIC = Akaike information criterion.

Table A3. Factor Loadings for the Confirmatory Bifactor Model of Apathy Symptoms

Item	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
107. He takes on tasks that challenge him.	0.55	0.62		
153. He is self-motivated.	0.66	0.60		
62. He keeps herself busy throughout the day.	0.60	0.55		
26. Getting things done during the day is important to him.	0.57	0.54		
30. He has goals for the future.	0.67	0.53		
17. He finds it important to start things on his own.	0.50	0.50		
71. He takes an active role in planning out his day.	0.74	0.46		
155. He is interested in a wide variety of activities.	0.63	0.46		
11. He starts activities on his own.	0.69	0.44		
135. It seems important to him to succeed in things.	0.56	0.43		
82. He comes up with fun, new ideas.	0.62	0.43		

Table A3. Continued

Item	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
21. He has a sense of curiosity about new things.	0.58	0.39		
15. He has hobbies that he is interested in.	0.56	0.36		
146. He tries to get by without doing any more work than he has to.	0.60	0.33		
9. He has trouble completing tasks because he gives up easily.	0.60	0.28		
77. He actively manages his health problems.	0.62	0.26		
152. He is interested in news and current events.	0.54	0.25		
113. He waits for someone to do things for him.	0.71	0.21		
53. Before going out in public, he makes sure he is clean and dressed appropriately.	0.50	0.19		

Table A3. Continued

Item	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
64. His emotions seem much less intense compared to other people's emotions.	0.50		0.57	
6. Very few things are able to get an emotional reaction out of him.	0.25		0.53	
54. He rarely seems either sad or happy.	0.45		0.48	
101. He is not very emotionally expressive.	0.52		0.39	
115. His facial expressions stay the same no matter what he is talking about.	0.54		0.32	
46. When asked a question, he usually responds with only a few words.	0.60		0.30	
2. When he talks, his hands stay at his sides and don't move.	0.32		0.27	
61. It's often difficult for me to know what he is feeling.	0.50		0.27	
8. He is talkative.	0.55		0.26	

Table A3. Continued

Item	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
18. He doesn't say much when people try to have a conversation with him.	0.65		0.22	
78. He often seems indifferent to what is going on around him.	0.79		0.20	
110. It is difficult to engage him in a conversation.	0.80		0.16	
83. When people ask him questions, he answers them only after a long delay.	0.66		0.14	
160. When people talk to him, he doesn't seem interested in what they have to say.	0.74		0.13	
144. He doesn't seem to notice when other people are in the room, unless they talk directly to him.	0.70		0.11	
49. When people smile at him, he smiles back.	0.39		0.10	
22. He seeks out time with friends.	0.56			0.63

Table A3. Continued

Item	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
98. He accepts invitations to spend time with others.	0.53			0.60
122. He expresses a desire to spend time with other people.	0.57			0.58
44. Having close friends is important to him.	0.46			0.56
109. He looks forward to social events.	0.57			0.56
35. He seeks out social interaction.	0.60			0.54
41. He is proactive about spending time with friends or family.	0.54			0.47
111. He initiates calls or emails to friends and/or family members.	0.59			0.34
56. He avoids meeting new people.	0.53			0.30

Table A4 Descriptive Statistics for Neuropsychological Measures

	n	Mean (SD)	Minimum	Maximum
Verbal Knowledge and Reasoning				
BNT	123	50.8(10.4)	2	60
WAIS-IV Comprehension	33	21.1 (9.0)	2	35
WAIS-IV Information	39	13.1 (6.0)	4	24
WAIS-IV Similarities	77	23.0 (6.1)	6	33
WAIS-IV Vocabulary	35	35.9(11.5)	5	56
Visual Reasoning				
WAIS-IV Block Design	103	31.2(13.0)	2	59
WAIS-IV Matrix Reasoning	64	12.2(5.4)	0	22
WAIS-IV Visual Puzzles	35	12.9 (4.5)	6	22
Processing Speed				
TMT, Part A*	129	62.8(74.5)	13	400
WAIS-IV Digit Symbol	93	50.3(21.0)	6	104
WAIS-IV Symbol Search	63	22.1(10.1)	0	50

Table A4. Continued

	n	Mean (SD)	Minimum	Maximum
Working Memory				
WAIS-IV Digit Span	125	21.5(6.4)	6	36
WAIS-IV Arithmetic	97	12.3(4.2)	2	22
Executive Functioning				
COWA	127	29.8(14.4)	3	65
TMT, Part B*	128	169.0(135.0)	29	400
WCST, Perseverative Errors*	53	21.9(19.5)	3	92
Visual Memory				
BVRT, Correct	121	5.3(2.2)	0	10
BVRT, Errors*	121	8.1(4.9)	0	23
CFT, Delayed Memory	129	11.9(7.3)	0	31
WMS-III Faces I	46	34.0(5.4)	24	48
WMS-III Faces II	46	34.2(7.2)	2	47
Verbal Memory				
AVLT, Total Learning	125	38.8(13.6)	7	69
AVLT, Delayed Memory	125	6.8(4.3)	0	15
AVLT, Recognition Memory	125	11.6(3.4)	1	15

Table A4. Continued

	n	Mean (SD)	Minimum	Maximum
WMS-III Logical Memory I	81	31.4(14.2)	0	60
WMS-III Logical Memory II	81	17.0(10.3)	0	43
WMS-III Logical Memory Recognition	81	23.8(4.7)	9	30
Visual Processing				
CFT, Copy	130	25.9(6.8)	6	36
Benton FDT	56	43.2(7.6)	0	51
JLO	59	23.4(6.4)	4	43

Note: SD = Standard Deviation.

Table A5 Correlates of General Apathy and Specific Apathy Factors: Cognitive Measures

	n	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
Verbal Knowledge and Reasoning					
BNT	123	**-0.39**	-0.03	-0.07	0.11
WAIS-IV Comprehension	33	**-0.68**	0.00	-0.21	0.07
WAIS-IV Information	39	-0.21	0.04	-0.24	0.29
WAIS-IV Similarities	77	**-0.40**	-0.13	**-0.25**	0.05
WAIS-IV Vocabulary	35	**-0.43**	-0.01	**-0.39**	0.04
Visual Reasoning					
WAIS-IV Block Design	103	**-0.33**	-0.12	-0.17	0.06
WAIS-IV Matrix Reasoning	64	**-0.45**	0.00	-0.13	0.10
WAIS-IV Visual Puzzles	35	-0.20	-0.10	-0.01	0.03
Processing Speed					
TMT, Part A*	129	**0.31**	0.05	0.06	-0.08
WAIS-IV Digit Symbol	93	**-0.37**	-0.13	-0.20	0.09
WAIS-IV Symbol Search	63	**-0.47**	**-0.33**	-0.17	0.02

Table A5. Continued

	n	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
Working Memory					
WAIS-IV Digit Span	125	**-0.38**	-0.13	-0.16	0.10
WAIS-IV Arithmetic	97	**-0.34**	-0.10	-0.13	**0.23**
Executive Functioning					
COWA	127	**-0.33**	**-0.24**	-0.16	-0.03
TMT, Part B*	128	**0.32**	0.10	-0.01	-0.06
WCST, Perseverative Errors*	53	0.23	-0.03	0.09	-0.08
Visual Memory					
BVRT, Correct	121	**-0.35**	-0.12	-0.10	0.18
BVRT, Errors*	121	**0.35**	0.13	0.04	-0.16
CFT, Delayed Memory	129	**-0.23**	**-0.20**	0.04	0.06
WMS-III Faces I	46	**-0.45**	-0.23	**-0.32**	-0.05
WMS-III Faces II	46	-0.16	-0.03	-0.14	0.05
Verbal Memory					
AVLT, Total Learning	125	**-0.44**	-0.10	-0.09	0.10
AVLT, Delayed Memory	125	**-0.43**	**-0.20**	-0.07	0.08
AVLT, Recognition Memory	125	**-0.34**	-0.16	0.01	0.01

Table A5. Continued

	n	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
WMS-III Logical Memory I	81	**-0.47**	-0.15	-0.12	-0.11
WMS-III Logical Memory II	81	**-0.38**	-0.19	-0.18	0.13
WMS-III Logical Memory Recognition	81	**-0.34**	-0.11	-0.06	0.01
Visual Processing					
CFT, Copy	130	**-0.27**	-0.11	**-0.18**	0.10
Benton FDT	56	**-0.46**	-0.15	0.01	0.02
JLO	59	**-0.26**	0.06	-0.26	0.09

Note: Significant correlations ($p<0.05$) are in bold.

Table A6. Correlates of General Apathy and Specific Apathy Factors: Informant Report

	n	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
Bristol Activities of Daily Living Questionnaire	242	**0.62**	**0.25**	-0.07	0.02
IDAS General Depression Scale	241	**0.62**	**0.22**	-0.02	0.09
PANAS Positive Affect	244	**-0.68**	**-0.51**	-0.04	**-0.23**
PANAS Negative Affect	244	**0.42**	0.03	-0.08	0.01
Zarit Caregiver Burden Inventory	242	**0.57**	**0.24**	-0.08	0.07

Note: Significant correlations ($p<0.05$) are in bold.

Table A7. Apathy Symptoms Across Diagnostic Groups

Diagnosis	General Apathy	Reduced Interest-Initiative	Reduced Emotional Expression	Asociality
Tumor resection (n=8)	-0.64	-0.05	0.33	0.24
Healthy/Mild Deficits (n=39)	-0.40	-0.21	0.08	-0.12
Other psychiatric disorder (n=14)	-0.40	-0.53	-0.10	-0.25
Traumatic Brain Injury (n=16)	-0.39	-0.03	-0.30	0.04
Epilepsy (n=7)	-0.26	-0.24	0.13	-0.24
Temporal Lobectomy (n=7)	-0.18	-0.30	-0.13	0.10
Stroke (n=40)	-0.10	0.00	-0.01	-0.10
Depression (n=10)	0.03	0.47	-0.04	0.30
Parkinson's Disease/Lewy Body Dementia (n=14)	0.24	0.08	0.37	-0.07
Vascular Cognitive Impairment/Vascular Dementia (n=16)	0.51	0.44	0.14	-0.34
Amnestic Mild Cognitive Impairment/Alzheimer's Disease (n=20)	0.52	0.07	-0.01	-0.08
Frontotemporal Dementia (n=4)	0.75	0.52	0.11	0.32

Note: Numbers are means of factor scores for each diagnostic group. Groups are ordered by increasing means on the general apathy factor.

Table A8. Incremental Validity of the New Apathy Measure: Informant Report Measures

	AES Only	Both Apathy Measures	f^2
Bristol Activities of Daily Living Questionnaire	0.37	**0.39**	0.03
IDAS General Depression Scale	0.37	**0.40**	0.05
PANAS Positive Affect	0.56	**0.62**	0.16
PANAS Negative Affect	0.15	0.15	0.00
Zarit Caregiver Burden Inventory	0.35	**0.36**	0.02

Note: AES=Apathy Evaluation Scale. Values are R squared values from regression models in which the (AES) was entered in step 1 and the new apathy measure was added in step 2. Values in bold are ones in which the new apathy measure added a significant amount of incremental predictive power.

Table A9. Incremental Validity of the New Apathy Measure: Cognitive Measures

	AES Only	Both Apathy Measures	f^2
Verbal Knowledge and Reasoning			
BNT	0.06	**0.13**	0.08
WAIS-IV Comprehension	0.25	**0.42**	0.29
WAIS-IV Information	0.02	0.03	0.01
WAIS-IV Similarities	0.12	**0.18**	0.07
WAIS-IV Vocabulary	0.07	**0.23**	0.21
Visual Reasoning			
WAIS-IV Block Design	0.07	**0.13**	0.07
WAIS-IV Matrix Reasoning	0.11	**0.17**	0.07
WAIS-IV Visual Puzzles	0.02	0.04	0.02
Processing Speed			
TMT, Part A*	0.10	0.10	0.00
WAIS-IV Digit Symbol	0.10	0.13	0.03
WAIS-IV Symbol Search	0.22	0.26	0.05

Table A9. Continued

	AES Only	Both Apathy Measures	f^2
Working Memory			
WAIS-IV Digit Span	0.12	**0.15**	0.04
WAIS-IV Arithmetic	0.07	0.09	0.02
Executive Functioning			
COWA	0.10	**0.13**	0.03
TMT, Part B*	0.08	0.09	0.01
WCST, Perseverative Errors*	0.06	0.08	0.02
Visual Memory			
BVRT, Correct	0.09	0.11	0.02
BVRT, Errors*	0.11	0.11	0.00
CFT, Delayed Memory	0.07	0.07	0.00
WMS-III Faces I	0.16	0.23	0.09
WMS-III Faces II	0.03	0.03	0.00
Verbal Memory			
AVLT, Total Learning	0.13	**0.16**	0.04
AVLT, Delayed Memory	0.17	0.18	0.01

Table A9. Continued

	AES Only	Both Apathy Measures	f^2
AVLT, Recognition Memory	0.08	**0.11**	0.03
WMS-III Logical Memory I	0.13	0.22	0.12
WMS-III Logical Memory II	0.11	**0.17**	0.07
WMS-III Logical Memory Recognition	0.13	0.13	0.00
Visual Processing			
CFT, Copy	0.07	0.08	0.01
Benton FDT	0.21	0.22	0.01
JLO	0.06	0.07	0.01

Note: AES=Apathy Evaluation Scale. Values are R squared values from regression models in which the (AES) was entered in step 1 and the new apathy measure was added in step 2. Values in bold are ones in which the new apathy measure added a significant amount of incremental predictive power.

Table A10 Incremental Validity of the Apathy Evaluation Scale: Informant Report Measures

	New Apathy Measure Only	Both Apathy Measures	f^2
Bristol Activities of Daily Living Questionnaire	0.36	**0.39**	0.05
IDAS General Depression Scale	0.37	**0.40**	0.05
PANAS Positive Affect	0.59	**0.62**	0.08
PANAS Negative Affect	0.14	**0.15**	0.01
Zarit Caregiver Burden Inventory	0.32	**0.36**	0.06

Note: Values are R squared values from regression models in which the new apathy measure entered in step 1 and Apathy Evaluation Scale (AES) was added in step 2. Values in bold are ones in which the AES added a significant amount of incremental predictive power.

Table A11. Incremental Validity of the Apathy Evaluation Scale: Cognitive Measures

	New Apathy Measure Only	Both Apathy Measures	f^2
Verbal Knowledge and Reasoning			
BNT	0.12	0.13	0.01
WAIS-IV Comprehension	0.41	0.42	0.02
WAIS-IV Information	0.03	0.03	0.00
WAIS-IV Similarities	0.18	0.18	0.00
WAIS-IV Vocabulary	0.18	0.23	0.06
Visual Reasoning			
WAIS-IV Block Design	0.13	0.13	0.00
WAIS-IV Matrix Reasoning	0.17	0.17	0.00
WAIS-IV Visual Puzzles	0.03	0.04	0.01
Processing Speed			
TMT, Part A*	0.08	0.10	0.02
WAIS-IV Digit Symbol	0.13	0.13	0.00
WAIS-IV Symbol Search	0.26	0.26	0.00

Table A11. Continued

	New Apathy Measure Only	Both Apathy Measures	f^2
Working Memory			
WAIS-IV Digit Span	0.15	0.15	0.00
WAIS-IV Arithmetic	0.09	0.09	0.00
Executive Functioning			
COWA	0.13	0.13	0.00
TMT, Part B*	0.08	0.09	0.01
WCST, Perseverative Errors*	0.08	0.08	0.00
Visual Memory			
BVRT, Correct	0.11	0.11	0.00
BVRT, Errors*	0.10	0.11	0.01
CFT, Delayed Memory	0.06	0.07	0.01
WMS-III Faces I	0.23	0.23	0.00
WMS-III Faces II	0.02	0.03	0.01
Verbal Memory			
AVLT, Total Learning	0.16	0.16	0.00
AVLT, Delayed Memory	0.17	0.18	0.01

Table A11. Continued

	New Apathy Measure Only	Both Apathy Measures	f^2
AVLT, Recognition Memory	0.11	0.11	0.00
WMS-III Logical Memory I	0.22	0.22	0.00
WMS-III Logical Memory II	0.17	0.17	0.00
WMS-III Logical Memory Recognition	0.12	0.13	0.01
Visual Processing			
CFT, Copy	0.07	0.08	0.01
Benton FDT	0.20	0.22	0.03
JLO	0.07	0.07	0.00

Note: Values are R squared values from regression models in which the new apathy measure was entered in step 1 and Apathy Evaluation Scale (AES) was added in step 2. Values in bold are ones in which the AES added a significant amount of incremental predictive power.

Table A12. Comparison of Apathy and Depression: Informant Report Measures

	New Apathy Measure	IDAS Depression
Bristol Activities of Daily Living Questionnaire	**0.60**	**0.49**
PANAS Positive Affect	**-0.77**	**-0.57**
PANAS Negative Affect	**0.37**	**0.73**
Zarit Caregiver Burden Inventory	**0.57**	**0.54**

Note: Values are correlations. Significant correlations ($p<0.05$) are in bold.

Table 13. Comparison of Apathy and Depression: Cognitive Measures

	New Apathy Measure	IDAS Depression
Verbal Knowledge and Reasoning		
BNT	**-0.34**	**-0.26**
WAIS-IV Comprehension	**-0.64**	**-0.66**
WAIS-IV Information	-0.18	-0.12
WAIS-IV Similarities	**-0.42**	**-0.38**
WAIS-IV Vocabulary	**-0.42**	-0.30
Visual Reasoning		
WAIS-IV Block Design	**-0.34**	-0.19
WAIS-IV Matrix Reasoning	**-0.41**	**-0.26**
WAIS-IV Visual Puzzles	-0.18	-0.16
Processing Speed		
TMT, Part A*	**0.28**	0.11
WAIS-IV Digit Symbol	**-0.36**	**-0.29**
WAIS-IV Symbol Search	**-0.51**	**-0.48**

Table A12. Continued

	New Apathy Measure	IDAS Depression
Working Memory		
WAIS-IV Digit Span	**-0.38**	**-0.34**
WAIS-IV Arithmetic	**-0.31**	**-0.34**
Executive Functioning		
COWA	**-0.36**	**-0.28**
TMT, Part B*	**0.29**	**0.24**
WCST, Perseverative Errors*	0.28	**0.28**
Visual Memory		
BVRT, Correct	**-0.33**	**-0.34**
BVRT, Errors*	**0.32**	**0.29**
CFT, Delayed Memory	**-0.24**	**-0.26**
WMS-III Faces I	**-0.48**	**-0.34**
WMS-III Faces II	-0.14	-0.28
Verbal Memory		
AVLT, Total Learning	**-0.40**	**-0.40**
AVLT, Delayed Memory	**-0.41**	**-0.44**
AVLT, Recognition Memory	**-0.33**	**-0.33**

Table A12. Continued

	New Apathy Measure	IDAS Depression
WMS-III Logical Memory I	**-0.23**	-0.21
WMS-III Logical Memory II	**-0.41**	**-0.35**
WMS-III Logical Memory Recognition	**-0.34**	**-0.30**
Visual Processing		
CFT, Copy	**-0.28**	**-0.26**
Benton FDT	**-0.44**	**-0.47**
JLO	-0.26	-0.20

Note: Values are correlations. Significant correlations ($p<0.05$) are in bold.

APPENDIX B

INITIAL ITEM POOL

Apathy Items

The items below are organized by proposed apathy domain. Participants responded to the items using a five point Likert scale (Strongly Agree to Strongly Disagree). Ratings were made based on the past four weeks. Note, the following items were written to assess female participants; a version with appropriate changes in pronouns was administered to assess male participants.

Proposed Behavioral Symptoms

She lets others tell her what to do.

She doesn't get much done during the day.

She doesn't do anything around the house.

She seeks out time with friends.

She starts conversations with others.

She starts things and doesn't finish them.

She prefers that others make decisions for her.

She is a motivated worker.

She doesn't do very much during the day.

When people talk to her, she often doesn't respond.

She has trouble completing tasks because she gives up easily.

She gets little accomplished week to week.

She has not been contacting her friends to plan things to do together.

She neglects her health.

She is not taking care of herself.

She has a hard time being motivated to get things done.

She gives up easily when things get difficult.

She keeps working even when things get tough.

She actively seeks out activities that interest her.

When she starts a task, she needs to be repeatedly encouraged by others to keep working.

She seeks out social interaction.

She doesn’t like to put much effort into things.

She needs other people to push her to do things.

She has trouble getting started on activities by herself.

She sticks with things even when they are difficult.

She uses her free time to actively pursue activities she enjoys.

She takes an active role in planning out her day.

When she is asked a question, she looks to others for guidance on how to answer it.

She initiates calls or emails to friends and/or family members.

She exercises regularly.

She spends time each week doing things that interest her.

She often relies on someone to tell her what to do.

She needs a push to get started on things.

She keeps herself busy throughout the day.

In social situations, she prefers to keep to herself.

She doesn't shower or bathe regularly.

She doesn't brush her teeth regularly.

She does things on her own without being asked to do so.

She often just sits or lies around doing nothing.

She follows through on the plans she makes.

During a discussion, she doesn't express her own opinions.

She waits for someone to do things for her.

She sets goals and works toward them.

She relies on someone to plan out her day for her.

She needs encouragement to do fun activities or hobbies.

She acts as if she has no interest in anything.

She is self-motivated.

She only does activities that others tell her to do.

She starts activities on her own.

She doesn't put any more effort into things than she has to.

She doesn't make decisions, even when others ask her to.

Sometimes she pushes herself harder than she should.

She doesn't have much energy.

If left alone, she will sit for hours by herself doing nothing.

She avoids meeting new people.

She accepts invitations to spend time with others.

She tries to get by without doing any more work than she has to.

Unless prompted by others, she will not engage in many recreational or leisure activities

She never pushes herself to do things she doesn’t feel like doing.

She is proactive about spending time with friends or family.

She is proactive about how she wants to spend her day.

She actively manages her health problems.

She waits for someone else to make appointments for her.

Before going out in public, she makes sure she is clean and dressed appropriately.

She needs to be prompted to shower or bathe regularly.

Proposed Cognitive Symptoms

She is not interested in friendships.

She is interested in news and current events.

She makes an effort to try new things.

She has hobbies that she is interested in.

She doesn't seem to care about her physical health.

She doesn't seem to care about problems in her life.

When people talk to her, she doesn't seem interested in what they have to say.

She has goals for the future.

She is interested in things going on in her community.

She does not seem to care about anything lately.

She doesn’t have many interests.

She is open to new experiences.

She doesn’t seem too concerned about her personal problems.

She expresses a desire to spend time with other people

She seems interested in her hobbies.

She just isn’t interested in the people around her.

She is curious about what is going on in the world around her.

She doesn't seem interested in her relationships with other people.

She doesn’t propose visits to family and friends.

She often sits around quietly without paying attention to things going on around her.

It has been awhile since she has expressed interest in doing anything.

She doesn't seem to notice when other people are in the room, unless they talk directly to her.

She proposes new activities she would like to do.

It’s difficult for me to attract her attention.

She is interested in a wide variety of activities.

She takes on tasks that challenge her.

She finds it important to start things on her own.

She is open to trying new things.

When she reaches a goal, she sets a higher one.

She looks forward to visits with family and/or friends.

Having close friends is important to her.

She seems bored most of the time.

She asks for updates on the lives of her friends and/or family.

She likes to try new things (e.g. new products or new foods).

Very little seems to interest her.

She seems detached from what is going on around her.

It seems important to her to succeed in things.

Getting things done during the day is important to her.

She spends time thinking about the future.

When she hears about a new event she is interested in, she can hardly wait to go.

She comes up with fun, new ideas.

When something exciting is coming up in her life, she really looks forward to it.

Nothing really seems to matter much to her.

She looks forward to a lot of things in her life.

She often seems indifferent to what is going on around her.

She makes plans or asks to go places she has never been before (for example, new restaurants or stores).

She has a list of new things or activities she would like to try one day.

In general, she doesn't seem to care very much about things going on with family or friends.

She has a sense of curiosity about new things.

She is interested in spending time with friends and family.

When she encounters a problem, she makes an effort to think of solutions.

She doesn’t seem to care about her health.

She looks forward to social events.

She rarely wants try new things.

She thinks it is important to stick with a task until it is completed.

She likes to take on new challenges.

Proposed Emotional Symptoms.

It's often difficult for me to know what she is feeling.

She doesn’t seem to have strong emotions.

She doesn't seem to react emotionally to news, good or bad.

She laughs when she hears a joke.

She doesn’t react emotionally, good or bad, in situations where other people would.

Very few things are able to get an emotional reaction out of her.

She is not very emotionally expressive.

She rarely seems either sad or happy.

Her emotions are “flat.”

She doesn’t seem to enjoy anything.

Her emotions don’t change very much, even when she hears really good or bad news.

When people ask her questions, she answers them only after a long delay.

When asked a question, she usually responds with only a few words.

It is difficult to engage her in a conversation.

She doesn't say much when people try to have a conversation with her.

I have to ask her the same question more than once in order to get a reply.

She is talkative.

I can tell what she is feeling just by looking at her face.

People can usually tell what kind of mood she is in.

When she talks, her hands stay at her sides and don't move.

When she is excited, you can hear the excitement in her voice.

Her facial expressions stay the same no matter what she is talking about.

She laughs at her own jokes or funny stories

She shows a full range of emotions.

Her facial expression often looks "frozen" or “wooden”.

When people smile at her, she smiles back.

She speaks more quickly when she is excited.

Being around certain people can put her in a good or bad mood.

In her day to day life, certain things can put her in a good or bad mood.

Her emotions seem much less intense compared to other people's emotions.

She smiles when she is happy.

When she is excited, she gets really animated.

She has difficulty making eye contact with other people.

Her voice gets louder or softer depending on how she is feeling.

When she wants to make a point, she raises her voice.

She uses hand gestures when she speaks.

Sometimes she laughs so hard she starts to cry.

Her emotions come and go quickly.

When she feels a certain way, she doesn't feel that way for very long.