

The Apathy Evaluation Scale: An ineffective tool for measuring affective, behavioural, and
cognitive dimensions of apathy

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Abstract

Apathy is the most common neuropsychiatric disorder in Alzheimer's disease (AD). Apathy in AD is related to a more rapid pattern of cognitive, behavioural, and emotional decline. Despite evidence pertaining to the multi-dimensional nature of apathy, most published studies have regarded apathy as a unitary construct. Understanding apathy as a multi-dimensional syndrome, and understanding the underlying neuropsychological mechanisms behind the distinct sub-domains (cognitive, behavioural, and affective) within the construct, can enhance treatment approaches to AD. The Apathy Evaluation Scale (AES) is the most widely used measure of apathy. The present study aimed to investigate whether the AES is an adequate measure of apathy as a multi-dimensional disorder. First, we studied apathy in a sample of 32 AD patients. Following convention established by the scale's developer, we designated each AES item as measuring affective, behavioural, or cognitive apathy, and then added the scores to create three sub-totals. We correlated the affective sub-total with score on the Cornell Scale for Depression in Dementia; the behavioural sub-total with score on the Bristol Activities of Daily Living Scale; and the cognitive sub-total with performance on the Trail Making Test. Correlational analyses predominantly provided mixed results. Second, a principal component factor analysis was performed on 111 Memory Clinic patients that showed a three factor solution, but the individual AES items did not load onto these factors in the convention established by the scale's developer. Taken together, our results illustrated that there is reason to support the claim that apathy is a multi-dimensional construct, but the AES does not effectively tap into the different sub-domains of apathy.

Keywords: apathy; Apathy Evaluation Scale; Alzheimer's disease; affective; behavioural; cognitive

The Apathy Evaluation Scale: An ineffective tool for measuring affective, behavioural, and cognitive dimensions of apathy

Over the past three decades, there has been considerable interest in the clinical importance of apathy as an independent and discrete neuropsychiatric disorder (Arnould, Rochat, Azouvi, & Van der Linden, 2013; Landes, Sperry, Strauss, & Geldmacher, 2001; Marin, 1990, 1991; Robert, Mulin, Mallea, & David, 2010; Zahodne & Tremont, 2013). At present, apathy is widely conceptualised as a neuropsychiatric disorder that involves a quantitative reduction of self-initiated voluntary acts and goal-directed behaviours (Levy & Dubois, 2006; Starkstein & Leentjens, 2008). This reduction is attributed to the disruption of affective, behavioural, and cognitive processes involved in the planning, control, and execution of goal-driven behaviours (Levy & Czernecki, 2006; Marin & Wilkosz, 2005; Robert et al., 2002). A growing body of literature provides strong evidence that apathy can be considered as a multi-dimensional disorder, categorised into distinct affective, behavioural, and cognitive domains (Esposito et al., 2014; Guimaraes, Levy, Teixeira, Beato, & Caramelli, 2008).

Although apathy is an important neuropsychiatric disorder in its own right, when combined with other disorders it often exacerbates the functional decline in patients. One such disorder is Alzheimer's disease (AD). The presence of apathy in AD is associated with a more rapid pattern of affective, behavioural, and cognitive decline, a decline that in turn leads to poor quality of life and increased dependency on caregivers (Horning, Melrose, & Sultzer, 2014; Levy & Czernecki, 2006; Marin & Wilkosz, 2005; Mulin et al., 2011; Starkstein & Leentjens, 2008; Tunnard et al., 2011). Despite this growing body of evidence emphasising the clinical importance of apathy and demonstrating its multi-dimensional nature, the disorder continues, by and large, to be understood in both clinical and research settings as uni-dimensional, and it remains excluded, to a great degree, from major psychiatric disease classification systems (Marin, 1990, 1991; Marin & Wilkosz, 2005).

The Apathy Evaluation Scale (AES) is apparently a well-validated and reliable measure of apathy, and is the most widely used measure of the construct (Arnould et al., 2013; Clarke et al., 2007, 2011; Marin, 1990, 1991; Marin & Wilkosz, 2005). However, no previous study has explored whether the AES is capable of distinguishing and measuring apathy as a multi-dimensional construct, with separable affective, behavioural, and cognitive features.

Apathy: A Multi-dimensional Disorder

Apathy is a neuropsychiatric disorder of goal-directed behaviour. It is diagnosed increasingly frequently, either as a separate syndrome or as a symptom within various psychiatric, neurological, and medical conditions (Clarke et al., 2011; Stanton, Leigh, Howard, Barker, & Brown, 2013; Starkstein & Leentjens, 2008). The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000) mentions apathy or apathetic syndromes such as loss of interest or avolition in the context of other disorders, but lacks a definition or distinction for apathy as a syndrome in and of itself (Clarke et al., 2011; Starkstein & Leentjens, 2008). Formal diagnostic criteria are proposed to include loss of motivation and diminished goal-directed cognition and behaviour compared to previous levels of functioning or personal standards (Starkstein, Petracca, Chemerisnki, & Kremer, 2001). These symptoms must persist for more than 4 weeks, must cause significant impairment or distress in functional areas of the person's life, and must not be due to substance use or decreased levels of consciousness (Arnould et al., 2013; Starkstein & Leentjens, 2008).

Current claims that apathy is a multi-dimensional neuropsychiatric disorder are based on two lines of evidence. The first involves evidence provided by studies that observe three differing manifestations of apathy in patients, and consequently suggest different conceptualizations of apathy. Apathy has therefore been conceptualised as a disturbance of emotion or feelings (Starkstein & Leentjens, 2008), as a disorder of cognitive impairment (Esposito et al., 2014; Levy & Czernecki, 2006), and as a condition closely related to lack of drive, behaviour initiation, and motivation (Arnould et al., 2013; Marin, 1990). The second line of evidence supporting the claim that apathy is a multi-dimensional construct is based the identification, using neuroimaging paradigms, of three distinct neurological pathways in apathetic patients.

The first of these is the meso-cortico-limbic dopaminergic pathway, which originates in the ventral tegmentum, runs through the anterior cingulate, and ends in the anterior cortical regions. This pathway is involved in affective processing, and thus dysfunction along it is correlated with the appearance of affective apathy. The second pathway is the nigrostriatal dopaminergic pathway, which originates in the substantia nigra and runs through the striatum. This pathway is likely involved in the selection and initiation of goal-directed activities; hence, dysfunction along it is correlated with the appearance of behavioural apathy. The third pathway is the cortical cholinergic pathway, which originates in the basal nucleus

and runs into the frontal cortex and other regions. This pathway is likely to be involved in cognitive aspects of motivation such as sustained attention and flexibility; hence, dysfunction along it is correlated with the appearance of cognitive apathy (Ishii, Weintraub, & Mervis, 2009; Levy & Czernecki, 2006; Robert et al., 2010; Starkstein & Leentjens, 2008).

Despite the growing strength of this literature, apathy is still widely regarded as a unitary syndrome. This has important implications because understanding apathy as a uni-dimensional disorder may obscure important findings, which can inform and tailor interventions specific to the patients' needs and therefore diminish the effectiveness of the intervention (Njomboro & Deb, 2014).

Sub-domains of Apathy

Affective apathy. Affective apathy symptoms manifest as a lack of concern or empathy and as indifference. An inability to interpret emotional cues and to assess their value is also an important feature of affective apathy. These symptoms appear to arise as a result of the disrupted link between emotion and experience, and they seem related to a disorder of the reward system, where sensitivity to the value of reinforcement is lost. Hence, apathetic patients exhibit emotional bluntness that reduces their readiness to regulate a task or to even predict future consequences (Arnould et al., 2013; Levy & Dubois, 2006). In addition to the meso-cortico-limbic dopaminergic pathway mentioned above, lesion sites associated with the manifestation of affective apathy symptoms may include the orbital-medial prefrontal cortex and structures of the basal ganglia such as the ventral striatum and ventral pallidum (Guimaraes et al., 2008; Hernandez et al., 2012; Levy & Dubois, 2006).

Behavioural apathy. Behavioural apathy symptoms manifest as a marked reduction in initiating and sustaining autonomous activities related to daily self-care actions. Apathetic patients therefore require continuous prompting and encouragement to achieve and maintain normal activity levels. These symptoms are often misinterpreted by caregivers as indolence or laziness, which increases caregiver distress and could negatively impact medical treatment adherence. In addition to the nigrostriatal dopaminergic pathway mentioned above, behavioural apathy symptoms appear to be related to low levels of activity in bilateral insula (Guimaraes et al., 2008; Hernandez, 2012; Levy & Dubois, 2006; Stanton et al., 2013).

Cognitive apathy. Cognitive apathy symptoms manifest as a reduction in interests, loss of initiative, and inactivity in goal-directed behaviour, so that often the apathetic individual requires assistance and prompting to complete any task (Chow et al., 2009; Esposito et al., 2014; Stanton et al., 2013; Starkstein & Leentjens, 2008). These symptoms

are related to deficits in executive functions which relate to apathetic symptoms include planning, working memory, cognitive flexibility, sustained attention, and, set-shifting with the latter function being most affected. In addition to the cortical cholinergic pathway mentioned above, lesion sites associated with the manifestation of cognitive apathy symptoms are the dorsolateral prefrontal cortex and sub-regions within the basal ganglia (Guimaraes et al., 2008; Landes et al., 2001; Levy & Dubois, 2006).

Regarding apathy as a multi-dimensional disorder has important implications for the clinical treatment and research approaches towards apathy. For instance, behavioural apathy is conceptualised as the inability to reach the threshold of activity. The most appropriate course of intervention would then be to prompt and encourage the individual to initiate an activity. This course of intervention would be less suited to, for instance, affective apathy which is a disruption of the link between experience and the emotional value of the experience. Thus being able to distinguish between the sub-domains of apathy can have significant importance when formulating tailored interventions. The Apathy Evaluation Scale (AES; Marin, Biedrzycki, & Firinciogullari, 1991) is the most widely used measure of apathy and thus the adequacy of intervention and research of apathy is tied to the effectiveness of this scale in distinguishing and tapping into the sub-domains of apathy as a multi-dimensional disorder.

Apathy Evaluation Scale

The Apathy Evaluation Scale (AES) is an 18-item scale developed by Marin et al., (1991). Each item is rated on a 4-point Likert-type scale. The item is rated based on how strongly it resonates with the current condition, thoughts, and emotions of the patient, with response options including *not at all*, *slightly*, *somewhat*, or *a lot*. Possible scores on the AES ranges from 18 to 72, with a score of 38 and above indicating that a clinical diagnosis of apathy can be made. The AES has sound psychometric properties (Hsieh, Chu, Cheng, Shen, & Lin, 2012; Marin et al., 1991; Robert et al., 2002). In terms of factor structure, Marin et al., (1991) identified a three-factor solution after gathering responses from 123 adults (either healthy or with various neurological and/or psychiatric disorders, including stroke, AD, and major depressive disorder). They thus divided the 18 items into these sub-domains: affective apathy is meant to be detected by two items, (e.g., item 7, ‘S/he approaches life with intensity’). Behavioural apathy is meant to be detected by five items (e.g., item 2, ‘S/he gets things done during the day’). Cognitive apathy is meant to be detected by eight items (e.g., item 1, ‘S/he is interested in things’). The remaining three items were designated as

belonging to a group called 'other' (Marin et al., 1991).

Other studies have, however, found divergent results. For instance, Ahearn, McDonald, Barraclough, & Leroi, (2012), reported finding a two-factor solution for the AES, based on data from a group of 99 Parkinson's disease patients. This inconsistency in the literature suggests that more examination of the AES factor structure is necessary. Apathy is often a co-morbid disorder and is one of the most commonly observed neuropsychiatric symptoms in AD patients. Apathy is one of the most commonly observed neuropsychiatric symptoms in AD patients. In mild or early-stage AD, the frequency of apathy is estimated to be 14%, whereas in severe or late-stage AD estimates of frequency range from 61% to 88% (Chase, 2011; Starkstein, Jorge, Mizrahi, & Robinson, 2006).

Summary and Rationale for the Present Study

Apathy is a neuropsychiatric disorder that negatively impacts the affective, behavioural, and cognitive functioning of an individual. Despite growing evidence pertaining to the multi-dimensional nature of this neuropsychiatric disorder, apathy continues to be understood, in both clinical and research settings, as a unitary disorder. Understanding apathy as a multi-dimensional disorder, and understanding the underlying neuropsychological mechanisms behind the distinct sub-domains (affective, behavioural, and cognitive) of the disorder, can significantly enhance treatment approaches to AD (Arnould et al., 2013; Guimaraes et al., 2008; Horning et al., 2014). Knowledge about the relative severity of affective versus behavioural or cognitive symptoms can be valuable in formulating interventions tailored to the patient's disabilities. One might argue, then, that a multi-dimensional approach gives the clinician a greater chance of managing apathy successfully, and consequently, of reducing caregiver distress and burden. Hence, understanding and approaching apathy as a multi-dimensional rather than a unitary disorder is arguably more advisable and beneficial for the patient.

The Apathy Evaluation Scale (AES; Marin et al., 1991) is the most widely used measure of apathy. At present, however, no study has explored whether the AES is capable of distinguishing and measuring the multi-dimensional characteristics of affective, behavioural, and cognitive apathy, particularly within Alzheimer's disease, a neurological disorder that is frequently marked by apathy. The current study attempted to address this gap in the literature.

Specific Aims and Hypotheses

The primary objective of this study was to investigate the effectiveness of the AES in discriminating between affective, behavioural, and cognitive sub-domains of apathy. We did so by investigating whether there are significant associations between affective, behavioural, and cognitive symptoms of apathy (as measured by the AES) and standard measures of affect, behaviour, and cognition in AD patients. An overall prediction was that each sub-domain of apathy would have different neuropsychological correlates. In addition, we investigated whether the AES loads onto three factors, and whether the items allocated by the developer to the different sub-domains loaded accordingly in our sample.

Hence, we tested these specific hypotheses:

- 1) Affective apathy symptoms in AD patients will be associated with more depressive symptomatology and generally more negative affect/mood, as manifested by lower scores on the Cornell Scale for Depression (CSDD; Alexopoulos, Abrams, Young, & Shamoian, 1988).
- 2) Behavioural apathy symptoms in AD will be associated with more impaired activities of daily living, as manifested by higher scores on the Bristol Activities of Daily Living Scale (BADLS; Bucks, Ashworth, Wilcock, & Siegfried, 1996).
- 3) Cognitive apathy symptoms in AD patients will be associated with more impaired executive functioning, as manifested by longer times to completion on the Trial Making Test (TMT; Reitan, 1958).
- 4) The AES produces a three-factor solution, with each factor mapping onto one of the sub-domains of apathy that is distinguished by evidence from clinical observation and from neuroimaging studies (viz., affective apathy, behavioural apathy, and cognitive apathy).

Methods

Design and Setting

This cross-sectional study investigated the utility of a multi-dimensional approach to apathy (as measured by the AES) in Alzheimer's disease (AD). The investigation used a quantitative, correlational design.

We collected all data from the Albertina and Walter Sisulu Institute of Ageing in Africa (IAA), which is housed in the Department of Medicine at Groote Schuur Hospital (GSH; Kalula et al., 2010).

The data collection process at the Memory Clinic is on-going and independent of this study. The mental health and medical professionals who run the Memory Clinic observe a specific procedure. Once a week, they assess a maximum of two patients at the Memory Clinic. The patient is normally accompanied by a significant other, child, or friend. The patient is usually referred to the Memory Clinic by a general practitioner or by a day hospital with questions surrounding whether observed memory problems are indicative of an incipient dementia.

The Memory Clinic procedure comprises of four components: history taking (with the patient and the informant), separate interviews with the informant, physical and neurological examination of the patient, and neuropsychological testing of the patient. In the first stage, a medical or psychiatric registrar takes the patient's relevant demographic, biographical, and medical history, and enquires about current complaints and premorbid functioning. In the second and third stages, which run simultaneously, the patient undergoes medical examination while his/her companion completes a battery of questionnaires in another room. This battery includes the AES, the CSDD, and the BADLS. In the third stage, the patient completes a battery of neuropsychological tests, including the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and the Trail Making Test (TMT; Reitan, 1958).

Finally, a variety of attending doctors, a neurologist, psychiatrist, neuropsychologist and other medical practitioners participate in a case conference and attempt to reach diagnostic consensus based on analysis of the available data. The team discusses diagnosis, prognosis, and best-suited intervention course. The resident doctor or psychiatrist then presents feedback to the patient and his/her companion.

Participants

Participant data were collected through non-probability purposive sampling. Data from 136 patients were collected from the IAA's electronic database. Of these 136 datasets, 111 included a completed AES, and is thus the total sample of this study. A total of 30 (27.02 %) patients were diagnosed with no dementia (e.g., Mild Cognitive Impairment, Major Depressive Disorder, etc.), and 81 (72.97 %) were diagnosed with a dementia (e.g., AD, Vascular Dementia, Mixed AD/Vascular Dementia, Lewy Body Dementia).

Of the 81 participants diagnosed with a dementia, we identified 38 cases of possible or probable AD¹ (46.81%). Within the AD sample, 13 (40.63%) participants did not have apathy and 38 (59.38%) were participants with apathy. All participants were resident in the Western Cape; most were from the Cape Peninsula area. The Results section provides further details of the sample characteristics. Anticipating moderate correlation (.4) between the individual AES variables and the standard measures variables the achieved sample size gives the study power of .75.

Eligibility criteria. The primary analyses of this study focused on patients diagnosed with probable or possible AD. We extracted the diagnosis for each participant from his/her hospital file. Data from patients who were diagnosed with other types of dementia were excluded from the primary analyses. Of the 38 AD cases we identified, we eliminated the data from 6 due to (a) incomplete AES questionnaires ($n = 2$) and (b) possible confounding influence of co-morbid psychiatric diagnoses of MDD ($n = 3$) and bipolar disorder ($n = 1$). Hence, our primary data analyses focused on data from 32 AD patients.

Measures

Apathy Evaluation Scale (AES). This instrument (Marin, 1990, 1991) is a well-validated and reliable measure of apathy. There are three versions of the scale, determined by the person completing it: the clinician (AES-C), the patient him/herself (AES-S), or an informant (AES-I; see Appendix B). Recent studies have found that the AES-I is more sensitive to detecting apathy than the other versions (Clarke et al., 2011, 2007). This result is unsurprising: Informants can probably report apathy symptoms most accurately because apathetic individuals often show little insight into their condition (Marin & Wilkosz, 2005). The Memory Clinic test battery includes the AES-I, and hence all AES data reported here are derived from that version.

The AES was originally validated based on sample groups of AD, stroke, MDD, and healthy adults (Marin, 1991). The most current psychometric information on the AES-I reports good reliability, with Cronbach's alpha ranging from .86 to .94. The test-retest reliability of the AES-I is reported to range between .76 and .94 (Clarke, 2011). Regarding validity, the AES-I reportedly has better convergent validity than the other versions, $r = .50$, $p = .001$. Furthermore, the AES has been used successfully around the world (e.g., in Taiwan,

¹ AD cannot be positively diagnosed, only confirmed after an autopsy (Cassimjee, 2008; Horning et al., 2014).

Japan, Portugal, China, and Oman; Clarke et al., 2011, 2007). No studies have examined the psychometric properties of the AES-I in Africa.

Cornell Scale for Depression in Dementia (CSDD). The CSDD (Alexopoulos, 1988; see Appendix C) measures mood, behaviour, physical, cyclic and ideational disturbances. It is designed to identify and measure depression in patients with dementia (Korner et al., 2006; Leontjevas, Gerritsen, Vernooij-Dassen, Smalbrugge, & Koopmans, 2012). The instrument consists of 19 items, with each rated on a 4-point Likert-type scale. The range of possible scores is 0-38. A score in the range of 10-17 indicates probable major depression; a score of 18 and above indicates definite major depression.

The reliability of the CSDD has been reported at a Cronbach's alpha of .67, with an internal consistency coefficient of .84. In terms of validity, the predictive validity of the CSDD has been reported to be .75. The CSDD has been found to demonstrate moderate to excellent detection of depression compared to other depression scales for geriatric patients (Korner et al., 2006; Leontjevas et al., 2012). No studies have examined the psychometric properties of the CSDD in African populations.

Bristol Activities of Daily Living Scale (BADLS). The BADLS (Bucks et al., 1996; see Appendix D) is the most commonly used scale to measure activities of daily living (ADL) functioning in AD patients.

The version of the BADLS used in this study was modified for use at the Memory Clinic as part of the standard assessment protocol to assess basic (e.g., preparing food) and instrumental (e.g., managing finances) ADLs. This version included 17 of the original 20 items. Here, the BADLS score ranges from 0 to 51, with higher scores representing a lower level of functioning. Hence, these scores represent a continuum which indicates the degree to which an individual is dependent on a caregiver for assistance in daily activities.

The BADLS reportedly has good test-retest reliability, with a Cronbach alpha of .95. BADLS scores correlate moderately well with MMSE scores, $r = -.67$ (Byrne, Wilson, Bucks, Hughes, & Wilcock, 2000). There is no information regarding the psychometric properties of the BADLS in South Africa, but the BADLS was developed specifically for use in screening possibly demented individuals and is widely used in South Africa clinical research, hospital, and community clinic settings (Byrne et al., 2000; Marshall et al., 2011).

Trail Making Test (TMT). The TMT (TMT; Reitan, 1958) is a frequently used paper-and-pencil cognitive test designed to measure visual perception and attention, psychomotor processing speed, and set-shifting abilities. Numerous studies have shown that

AD patients perform poorly on the TMT, perhaps due to deficits in inhibition and selective attention (Amieva et al., 1998; Lezak, Howieson, & Loring, 2004).

Part A of the test features 25 circles numbered 1-25. The test administrator instructs the testee to connect the numbers, in order and as quickly as possible. Part B of the test consists of 23 circles, with some numbered 1-13 and the others A-M. The test administrator instructs the testee to connect the first number to the first letter, then to switch to the second number, connect the second number to the second letter, and so forth. Again, the test administrator emphasises that the testee should perform the task as quickly as possible.

The TMT reportedly has good reliability, with estimates of Cronbach's alpha ranging from .60 to .90 across independent studies (Lezak et al., 2004). No psychometric properties have been reported in the South African population, although the TMT is used widely in South African clinical settings (Cassimjee, 2008).

Ethical Considerations

This study adhered to the ethical guidelines for research with human subjects defined by the Health Professions Council of South Africa (HPCSA) and the University of Cape Town (UCT) Codes for Research. This study obtained ethical approval from the Research Ethics Committee of the UCT Department of Health Sciences (see Appendix A). As part of the memory clinic procedure, participants are requested to sign a consent form and informed that the data would be used for research purposes. All information and data collected is stored electronically on a database in the IAA under specific codes and access to participant names is kept highly confidential.

Data Collection, Data Management, and Statistical Analyses

Data collection. The dataset comprised of non-randomly selected archival records from the GSH/IAA Memory Clinic. Although the Memory Clinic has been run for a number of years, and has archives dating back to at least 2005, we only selected records dated March 2012-September 2014. We used that date range because data collected prior to March 2012 did not include the Apathy Evaluation Scale (AES; Marin et al., 1991), which is central to this study.

We collected raw data from the patient files (held at the GSH Records Office) of 111 individuals who had presented for assessment at the GSH/IAA Memory Clinic, as well as from the original test booklets and from an electronic database, both of which were held at the Division of Geriatric Medicine. Hence, we were able to verify information in the database

against that in the test booklets, and we were able to find information missing from the database in the patient files.

Data management. We cleaned and sorted the data using MS Excel. We then used SPSS version 22.0 to conduct the descriptive and inferential statistical analyses. We set the Type I error rate at .05.

Independent and dependent variables. We tested each of the three hypotheses using three independent variables and three dependent variables. The three independent variables were three subscales, which pertain to the affective, behavioral, and cognitive symptoms of apathy. The dependent variables were derived from standard measures of affect, behavior, and cognition (CSDD, BADLS, and TMT respectively).

Inferential statistical analyses. The analyses proceeded across four stages. The first three stages used the 32 AD patients as a sample, and the fourth used the entire sample of 111 Memory Clinic patients as a sample. This group was utilised in the factor analysis as such a large and heterogeneous group will decrease the chance of biases.

First, we ran a set of three separate correlational analyses, describing associations between (i) AES Affective and CSDD scores, (ii) AES Behaviour and BADLS scores, and (iii) AES Cognitive score and TMT performance. We used Pearson's correlation coefficient (r) to measure the associations between variables.

Second, to investigate whether the three individual AES scores correlated more strongly with the dependent variables than the global AES score, we ran another set of three separate correlational analyses, describing associations between (i) total AES and CSDD scores, (ii) total AES and BADLS scores, and (iii) total AES and TMT performance.

Third, we performed partial correlations between all of the dependent variables and the individual AES scores. We expected them to correlate in order to illustrate the exact role the individual AES score played in the outcome of the dependent variable compared to the other AES individual scores.

Finally, we performed a factor analysis to explore whether the AES resolved into a three-factor solution, and whether, as proposed by Marin et al., (1991), specific items pertaining to affective, behavioral, and cognitive apathy load onto these factors.

Results

Sample Characteristics

As noted earlier, the primary statistical analyses involved a sample of 32 AD patients, whereas the secondary analyses involved a sample of 111 Memory Clinic patients, some of whom were diagnosed with dementia and some of whom were not. Table 1 presents a summary of the demographic characteristics for the first sample. AD patients had a mean age of almost 76 years, and the majority were women. Regarding race, most were coloured, followed by white and then Black African. Regarding language, most listed English as their preferred language, followed by Afrikaans, both English and Afrikaans, and isiXhosa. Regarding AES-based apathy diagnoses, almost 60% of the sample met the criteria for a positive diagnosis (i.e., their scores were ≥ 38). Scores of the AD patients on the MMSE range from 3 to 27 points.

Table 2 shows that the larger, more heterogeneous sample that is used in the secondary analysis had similar demographic characteristics to the sample of AD patients. That sample of Memory Clinic patients had a mean age of 69 years, and more than two-thirds of them were women. Regarding AES-based apathy diagnoses, about 55% of the sample met the criteria to for a positive diagnosis.

Of note here is that the patterns of demographic data shown in Tables 1 and 2 are similar to those reported by Kalula et al., (2010), who provided a summary of Memory Clinic intake data from 2003 to 2008. In that study, the sample of 305 patients a mean age of 70 years (± 10.26). Regarding race, most patients in that sample were coloured ($n = 198$, 65%), followed by white ($n = 88$, 29%), and then Black African ($n = 20$, 6.6%). Kalula and colleagues reported that that 44% ($n = 134$) of their patient sample had been diagnosed with AD; in the current study, a similar number (47%, $n = 143$) of the 111 patients were diagnosed with AD (Kalula et al., 2010).

Table 1

Sample Demographic Characteristics: Alzheimer's Disease patients (N = 32)

Variable	Range	Frequency	Percentage	M (SD)
Age	59-93	-	-	75.69 (7.91)
MMSE	3-27	-	-	20.09 (5.30)
AES-based diagnosis	22-65			0.59 (0.49)
Apathetic	-	19	59.38%	31.54 (5.13)
Not Apathetic	-	13	40.63%	49.37 (7.73)
Sex				
Men	-	5	15.6	
Women	-	27	84.4	
Race				
Coloured	-	22	68.8	
Black African	-	3	9.4	
White	-	7	21.9	
Preferred Language				
English	-	21	65.6	
Afrikaans	-	6	18.8	
Xhosa	-	2	6.3	
English and Afrikaans	-	3	9.4	

Table 2

Sample Demographic Characteristics: Memory Clinic patients (N = 111)

Variable	Range	Frequency	Percentage	M (SD)
Age	27-93	-	-	69.20 (12.09)
MMSE	3-30	-	-	22.59 (5.31)
Apathy				
Apathetic	-	61	54.95%	0.55 (5.31)
Not Apathetic	-	50	45.05%	
Sex				
Men	-	32	28.83%	
Women	-	79	71.17%	

Primary Analyses: Correlations

Testing Hypothesis 1. This hypothesis stated that affective apathy symptoms, measured by the AES Affective score, are significantly associated with depressive symptomatology, as measured by the CSDD. As shown in Table 3 there was a small and non-significant positive association between AES Affective and CSDD scores. Table 3 also shows that there was a moderate, positive, and significant correlation between global AES and CSDD scores. Taken together, this set of results suggests that the Global AES score is likely to be more effective than the AES Affective score at predicting the appearance of depressive symptoms in AD patients. Table 3 also displays the results of partial correlation analyses.

Table 3

Correlation and Partial Correlation Results: AES scores and CSDD scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	.237	.093	.022	.455
Behaviour score	.491**	.002	.152	.215
Cognitive score	.468**	.003	.092	.317
Global score	.511**	.001	-.038	.423

Note. AES = Apathy Evaluation Scale; CSDD = Cornell Scale for Depression in Dementia.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Hence, these correlational analyses did not confirm the a priori hypothesis that the sum of AES items measuring affective apathy would correlate positively with total CSDD score. To explore this negative finding further, and to perhaps uncover reasons for it, we conducted one additional correlational analysis. There is one CSDD item that is conceptually similar to the manifestation of affective apathy. That item enquires about whether the patient displays a lack of reactivity to pleasant events. In an analysis similar to that described above, we measured associations between scores on this single item and AES Affective, Behaviour, Cognitive, and Global scores.

Table 4 presents the results of those correlations and partial correlations. As the Table shows, all of the AES variables were significantly associated, and moderately positively correlated, with scores on the item. The Table also shows, via the partial correlation results, that the individual affective apathy score moderately correlated with scores on the item, with a strong tend toward statistical significance.

Table 4

Correlation and Partial Correlation Results: AES scores and CSDD item scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	.432*	.007	.304	.055
Behaviour score	.551**	.001	.270	.078
Cognitive score	.382*	.015	.075	.350
Global score	.492**	.002	-.094	.314

Note. AES = Apathy Evaluation Scale; CSDD item = Lack of Reactivity CSDD item

* $p < .05$, ** $p < .01$, *** $p < .001$.

Testing Hypothesis 2. This hypothesis stated that behavioural apathy symptoms, measured by the AES Behaviour score, are significantly associated with functioning in terms of activities of daily living, as measured by BADLS. As shown in Table 5, there was a significant and moderate positive correlation between AES Behaviour and BADLS scores. However, this association was not unique to the AES Behaviour score: The AES Cognitive and Global scores were also significantly, positively, and moderately correlated with BADLS scores. Regarding the partial correlations shown in Table 5, these indicated that, although the individual cognitive score correlated to the BADLS scores, none of the individual AES scores or the Global AES score correlated significantly to the same.

Table 5

Correlation and Partial Correlation Results: AES scores and ADL scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	.002	.495	-.079	.343
Behaviour score	.334*	.031	.222	.124
Cognitive score	.369*	.019	.240	.105
Global score	.348*	.026	-.175	.182

Note. AES = Apathy Evaluation Scale; ALD = Bristol's Activities of Daily Living.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Hence, these correlational analyses only partially confirmed the a priori hypothesis that the sum of AES items measuring behavioural apathy would correlate positively (and uniquely among AES scores) with total BADLS score. To explore this finding further, and to perhaps uncover reasons for it, we conducted one additional correlational analysis. Each BADLS item can be taken as contributing to a score on either basic or instrumental ADLs.

Although this distinction does not pertain to the a priori hypothesis regarding the BADLS, partial correlational analyses performed on these two sub-categories yielded interesting findings. Table 6 shows there was a small and non-significant correlation between AES Behaviour and BADLS basic ADL scores. Interestingly, the correlation between AES Cognitive and BADLS basic ADL scores was stronger, and almost reached statistical significance. Table 6 also shows that none of the partial correlations were significant.

Table 6

Correlation and Partial Correlation Results: AES scores and ALD B scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	-.099	.294	-.134	.244
Behaviour score	.109	.277	.115	.275
Cognitive score	.294	.051	.254	.092
Global score	.205	.130	-.164	.198

Note. AES = Apathy Evaluation Scale; ADL B = Bristol's Activities of Daily Living Basic

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 6 shows there was a small, positive, and non-significant correlation between AES Behaviour and BADLS basic ADL scores. Interestingly, the correlation between AES Cognitive and BADLS basic ADL scores was stronger, and almost reached statistical significance. Table 6 also shows that none of the partial correlations were significant.

Table 7 shows there was a moderately high, positive, and significant correlation between AES Behaviour and BADLS instrumental ADL scores. There was also, however, a moderate, positive, and significant correlation between AES Cognitive and BADLS instrumental ADL scores. Furthermore, although none of the partial correlations shown in Table 7 were significant, the individual behaviour apathy score showed a strong trend toward significance. It was moderately correlated with BADLS instrumental ADL scores,

Table 7

Correlation and Partial Correlation Results: AES scores and ADL I scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	.079	.333	-.005	.490
Behaviour score	.477**	.003	.304	.055
Cognitive score	.349*	.025	.197	.153
Global score	.395*	.013	-.173	.184

Note. AES = Apathy Evaluation Scale; ADL I = Bristol's Activities of Daily Living

Instrumental. * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 7 shows there was a moderately high, positive, and significant correlation AES Behaviour and BADLS instrumental ADL scores. There was also, however, a moderate, positive, and significant correlation between AES Cognitive and BADLS instrumental ADL scores. Furthermore, although none of the partial correlations shown in Table 7 were significant, the individual behaviour apathy score showed a strong trend toward significance. It was moderately correlated with BADLS instrumental ADL scores.

Testing Hypothesis 3. This hypothesis stated that cognitive apathy symptoms, measured by the AES Cognitive score, are significantly associated with more impaired executive functioning, as manifested by longer times to completion on the TMT. As shown in Table 8, there was a significant and moderate positive correlation between AES Cognitive and TMT A scores. Table 8 also shows that there was a non-significant correlation between the other independent AES scores and the TMT A. Table 8 also shows that none of the partial correlations shown in Table 8 were significant, the AES cognitive apathy score showed a strong trend toward significance.

Table 8

Correlation and Partial Correlation Results: AES scores and TMT A scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	-.144	.246	-.021	.462
Behaviour score	.082	.348	.024	.458
Cognitive score	.360*	.039	-.336	.063
Global score	-.208	.159	.197	.190

Note. AES = Apathy Evaluation Scale; TMT A = Trail Making Test A.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Regarding the partial correlations shown in Table 8, these indicated that, although the individual cognitive score correlated to the TMT A scores, none of the individual AES scores or the Global AES score correlated significantly to the same. Table 9 shows there was a moderately significant correlation between the AES Cognitive and the TMT B scores. There was also, however a moderate, negative, and significant correlation between AES Affective and TMT B scores. Table 9 also shows that none of the partial correlations were significant.

Table 9

Correlation and Partial Correlation Results: AES scores and TMT B scores (N = 32)

AES Variable	Correlations with CSDD scores		Partial correlations with CSDD scores	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Affective score	-.447*	.024	-.393	.059
Behaviour score	-.239	.155	-.279	.139
Cognitive score	-.385*	.047	-.300	.121
Global score	-.365	.057	.277	.141

Note. AES = Apathy Evaluation Scale; TMT B = Trail Making Test B.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Secondary Analyses: Principal Component Analyses

The purpose of performing a Principal Component Analysis (PCA) was to explore whether (a) the AES items do in fact load onto three factors, and (b) each item allocated to a sub-domain of affect, behaviour, and cognition by Marin (1991) loads uniquely onto the appropriate one of the three factors, so that (c) one factor might be labelled affective apathy, another behavioural apathy, and the third cognitive apathy. Here, we used the large heterogeneous sample of 111 Memory Clinic patients.

The PCA modelling proceeded following the consideration that our predominant focus is on three sub-domains of apathy and on the 15 items that Marin (1991) suggested should load onto them. Hence, at this stage of our analysis we removed the three items (numbers 15, 17 and 18) designated as belonging to the “other” category. We then ran a second PCA on the data from the remaining 15 items.

Table 10 shows that that PCA found three factors with eigenvalues above 1 and that the cumulative explained variance was 60%. Table 10 also shows that analyses of sampling adequacy and sphericity suggested that we could continue the analysis and interpretation in the conventional way. Table 11 shows that, with no rotation, most of the items (13 of the 15) loaded onto the first factor. After performing an orthogonal rotation, we found that the

eigenvalues and amount of explained variance were distributed more evenly across the four factors (see Table 10). Table 11 also shows that, with the orthogonal rotation, the items were distributed more evenly across the four factors

Table 10

Principal Components Analysis: The AES in a sample of Memory Clinic patients (N = 111)

Component	No Rotation		Orthogonal Rotation	
	Eigenvalues	Explained	Eigenvalues	Explained Variance
1	6.19	41.28%	3.93	26.23%
2	1.53	10.17%	3.48	23.19%
3	1.12	7.46%	1.42	9.50%
4	6.19	41.28%	3.93	26.23%

Note. For this model, Bartlett's test of sphericity was statistically significant, $p < .001$, and KMO's measure of sampling adequacy was high, $r = .89$. Cumulative % of explained variance = 56.91%.

Table 11

Principal Components Analysis, Component Matrix and Rotation: The AES in a sample of Memory Clinic patients (N = 111)

AES Item	No rotation			Orthogonal Rotation		
	1	2	3	1	2	3
1	.703				.608	
2	.722	-.405		.805		
3	.672			.510	.422	
4	.681	.491			.817	
5	.706				.702	
6	.762			.713		
7	.692			.442	.452	
8	.732	-.403		.786		
9	.686				5.47	
10	.574			.698		
11			.464	.439		.543
12	.462	.453			.689	
13	.523				.636	
14			.805			.859
16	.791			.776		

Note. Affective Items = Items 7 & 14. Behavioural Items = Items 2, 6, 9, 10 & 12.

Cognitive Items = Items 1, 3, 4, 5, 8, 11, 13 & 16

Discussion

The main aim of this study was to explore whether the Apathy Evaluation Scale (AES) is an adequate and effective measure of the affective, behavioural and cognitive dimensions of apathy. This was first explored by correlating scores on AES items thought to assess these three subdomains with standard measures of affect, behaviour, and cognition in AD patients. The overall prediction was that scores on each subdomain would correlate significantly with conceptually related neuropsychological measures on the standard tests. The global AES score was not expected to show significant correlations with each of the standard measures. Second, a principle component factor analysis was performed to investigate if Marin et al., (1991) categorisation of AES items into affective, behavioural, and cognitive apathy subdomains had psychometric validity. To investigate these questions, the multi-dimensionality of apathy as measured by the AES was tested using four specific hypotheses. These following sections discuss each of these hypotheses.

Affective Apathy

Hypothesis 1 stated that the AES score on affective apathy items will be significantly and positively associated with scores on the Cornell Scale for Depression (CSDD). We did not expect total AES scores or scores on the behavioural and cognitive items to be significantly associated with the CSDD score. Results from this study did not show the predicted relationships. Our data indicated a non-significant low positive correlation between scores on the AES affective apathy items and the CSDD score. However, behavioural, cognitive, and global AES scores had significant moderate relationships with the CSDD score. Our data suggests that scores on affective AES items do not relate to scores on the CSDD. Partial correlations of all the AES variables with CSDD indicated non-significant results.

The above results are consistent with studies that suggest that affective apathy symptoms are distinct from depression (Marin, 1990, 1991; Mulin et al., 2011; Starkstein & Leentjens, 2008; Zahodne & Tremont, 2013). Affective apathy symptoms manifest as a lack of concern or emotional bluntness, whereas depressive symptoms manifest as extreme sadness and hence these set of symptoms are phenomenologically distinct. A further exploration was performed on this data to investigate relations between an affective item on the CSDD relating to 'the lack of reactivity to pleasant events' and affective, behavioural, cognitive, and global AES score. This item is considered to be conceptually similar to

affective apathy symptoms so we expected it to associate with the affective AES score. The results indicated a significant moderate correlation between all the AES variables and the CSDD item, with the AES behavioural apathy score showing the highest correlation with the item. A further partial analysis showed a moderate trend towards significance between the CSDD affective item and the AES affective apathy score. The behavioural, cognitive, and global AES scores showed low non-significant correlations with the item.

Overall, these results suggest that the affective impairment in depression as assessed by the CSDD is distinct from the affective apathy symptoms measured by the AES. Taken together, the non-significant relationship between affective apathy symptoms on the AES and depressive symptoms on the CSDD found in our data may stand to confirm the importance of separating apathy and depression.

Behavioural Apathy

Hypothesis 2 stated that the AES measure of behavioural apathy symptoms in AD patients will be associated with more impaired activities of daily living, as manifested by higher scores on the Bristol Activities of Daily Living Scale (BADLS). Hypothesis 2 thus suggested that the AES measure of affective, cognitive, and global apathy score would not be significantly associated with the BADLS score. Our data partially supported the hypothesis. Correlational results indicated a significant moderately low positive correlation between the AES behavioural apathy scores and the BADLS score. However, there was also a significant moderate positive correlation between global apathy scores and the BADLS score, partially disconfirming our hypothesis. In fact the global AES score had a slightly higher significant positive correlation with the BADLS score than the AES behavioural apathy score alone. However, partial correlations provided non-significant results with all the AES variables.

These results are consistent with studies that suggest that behavioural apathy symptoms are related to a marked reduction in initiating and sustaining autonomous activities related to daily self-care actions (Guimaraes et al., 2008; Hernandez, 2012; Levy & Dubois, 2006; Stanton et al., 2013). In order to gain more clarity on the results pertaining to hypothesis 2, BADLS items were further divided into two outcomes; basic and instrumental activities of daily living. This division is common in clinical practice and has also been done in other studies (e.g., Byrne et al., 2000). A non-significant low correlation between the affective, behavioural, cognitive, global AES apathy scores and basic ADL scores was found. The partial correlations also showed no significant correlations for any of the AES variables. A significant moderately high correlation was however found between the behavioural AES

score and scores on the instrumental ADLs. Results from the partial correlation analysis showed no significant correlations. The divergent results between basic and instrumental ADLs may be accounted for by the influence of the AES cognitive apathy score on activities of daily living functioning. The AES cognitive score had the highest correlation and was closest to significance with a borderline significant moderately low correlation with basic ADLs score. The partial correlation also showed that the individual AES cognitive score had the highest correlation between all the AES variables, even though it was not significant. These results may indicate the influence of processes sampled by cognitive AES items such as those involving the planning, initiation, and sustenance of action on the performance of daily activities (Byrne et al., 2000).

Taking these results together it appears that the AES behaviour apathy score is more associated with the outcome of ADLs, particularly instrumental rather than basic, than the global apathy score. Thus our findings indicate that hypothesis 2 may be at the very least partially supported.

Cognitive apathy

Hypothesis 3 stated that cognitive AES scores will be associated with poor performance on the Trial Making test (TMT). Hypothesis 3 thus suggested that scores on affective, behavioural, and global AES scores would not be significantly associated with TMT scores. Our data partially confirmed the hypothesis. We found a significant relationship between AES cognitive apathy scores and the TMT A score. The AES cognitive apathy score was clearly shown to be the only AES variable significantly associated with the TMT A by both correlational and partial correlation analysis. Apathy has been linked to executive dysfunction by various studies and it has been suggested that cognitive apathy specifically can manifest as a dysexecutive disorder (Chow et al., 2009; Esposito et al., 2014; Stanton et al., 2013; Starkstein & Leentjens, 2008). The AES cognitive apathy score is significantly associated with both the TMT A and TMT B scores and the global apathy score is not significantly associated with either. Hence this supports Hypothesis 3.

FACTOR ANALYSIS

Hypothesis 4 stated that the AES would be expected to show a three factor structure related to the affective, behavioural, and cognitive symptoms suggested by Marin et al., (1991). Based on the results from the principle component factor analysis (PCA), our data does not confirm the hypothesis. Although the results indicated that AES items loaded onto

three factors, the individual AES items did not load onto the factors in the pattern suggested by Marin (1991). These results suggest that the AES is multidimensional but does appear to be ineffective in tapping into the distinct sub-domains of apathy symptoms as suggested by its author since the items failed to load together with items within their subdomain.

The Affective Factor

The PCA component matrix indicated that only one of the two items pertaining to affective apathy, as measured by the AES, loaded onto a factor 3, identified in this study as the affective apathy factor. Item 14, which asks whether the patient becomes excited when good events take place, is conceptually related to affective apathy in that it describes a link between emotion and experience. The item which is not loading onto this factor, item 7, assess whether the patient approaches life with intensity. Item 7 is loading onto the two other factors in the matrix, behavioural and cognitive apathy factors, almost equally strong with moderate correlations. This indicates that item 7 is conceptually more related to behavioural or cognitive apathy than affective apathy. A possible explanation for this could be that item 7 is worded poorly. Approaching life with intensity can be interpreted as approaching life with passion, which thus pertains to affective apathy as it describes a link between emotion and experience. However this statement could also be understood in terms of activity levels, such as a person who is very active and approaches life with a high motivational drive. Thus item 7 could be understood in terms of the patient's ability to initiate and maintain increased activity levels. The inability to initiate and sustain activity is a manifestation of behavioural apathy, thus item 7 could be understood in terms of behavioural apathy. This may account for why the item is loading onto the behavioural factor and not onto the affective factor as expected.

The two items loading onto the affective factor identified by the component matrix are hence both conceptually similar to the manifestations and symptoms of affective apathy and this provides support for the AES items being able to tap into the subdomain of affective apathy. The AES, however, is limited in this regard as item 7 can be misinterpreted due to poor wording and that two items are arguably not sufficient to measure affective apathy outcomes. One suggestion would be to reword item 7 to eliminate ambiguity. Another suggestion would be to include additional items from the AES into the affective apathy subdomain. The PCA component matrix indicated that item 11, which was expected to load onto the cognitive factor, loaded onto the affective factor. Item 11 asks if the patient is appropriately concerned about their problems. While concern implies cognitive aspects of

functioning, it has an inherent affective component and is conceptually closer to affective apathy in that concern shows appropriate affective value judgments and a link between emotion and experience. Our study suggests that the AES has some limited ability to tap into affective apathy and requires some revision to strengthen this ability.

The Behavioural Factor

The PCA component matrix demonstrated that three of the five behavioural AES items loaded onto a factor 1, identified as the behavioural apathy factor. These are Items 2, 6 and 10. Item 2 assesses how the patient places importance on completing tasks. Item 6 asks whether to the patient puts effort to complete tasks, and item 10 asks whether the patient needs prompting to initiate, sustaining, and completing tasks. The items which are not loading onto this factor as suggested by Marin are items 9 and 12. Item 9 asks whether the patient spends time on interests and item 12 enquires on whether the patient has friends. Both items were loading onto the cognitive apathy factor, with strong correlations. This is understandable because interests are conceptually more related to cognitive apathy than behavioural apathy. A manifestation of cognitive apathy is reduction in interests. Thus item 9 may be more suited to the cognitive factor. Item 12 is more difficult to account for as it pertains more to social aspects of life than apathy. A possible explanation for this could be that item 12 is not conceptually related to apathy and should therefore not be included in the AES.

The three items which load onto the behavioural factor identified by the component matrix are conceptually similar to the manifestations and symptoms of behavioural apathy which provides support for the AES being able to tap into the subdomain of behavioural apathy. However, as items 9 and 12 are arguably not conceptually similar to behavioural apathy and do not load onto the behavioural factor as expected it is shown that the AES can only partially tap into behavioural apathy and is thus limited.

The Cognitive Factor

The PCA component matrix indicated that only four of the eight items pertaining to cognitive apathy, as measured by the AES, loaded onto a factor 2, identified as the cognitive apathy factor. Items 1, 4, 5 and 13 are conceptually relatable to cognitive apathy. These items primarily aim to measure how important new experiences, learning opportunities, social gatherings and general interests are to the patient. These items are conceptually relatable to cognitive apathy as they describe interests, initiative and the initiation of activities.

The items which did not load onto this factor are items 3, 8, 11 and 16. At a conceptual level items 3, 8 and 16 appear to be more related to behavioural apathy than cognitive apathy. Item 3, 8 and 16 all aim to measure the importance of initiating tasks, completing tasks and completing enough tasks during the day, respectively. Reduction in initiating and sustaining tasks are an important manifestations of behavioural apathy, thus items 3, 8 and 16 are more conceptually related to behavioural apathy. Item 11 has been shown to be more conceptually related to affective apathy than cognitive apathy, as discussed under the affective factor above.

Items 3, 8 and 16 are very similar hence for a patient or informant whose first language is not English it may be difficult to answer these questions correctly. Item 16 can also be considered as a double barrel question as it measures both the amount of tasks completed during the day and the importance of this to the patients. This is a common fallacy of items on questionnaires when the item asks two questions in one. The amount of tasks completed during the day is related to behavioural apathy while the importance of this to the patient is conceptually more related to affective apathy than cognitive apathy. This item is thus flawed. Some of these items, such as items 4 and 5, are also subject to the influences of socio-economic status (SES) and age (Kalula et al., 2010). Items 4 and 5 pertain to new experiences and learning new things. Patients of low SES might not have the luxury to pursue new interests or experiences due to their situation rather than apathy. In addition older populations are often more likely to suffer from physical complaints such as arthritis and be dependent on pensions, which also limits their pursuits of new experiences rather than apathy symptoms. The CPA thus illustrated that only half of the items expected to load onto the cognitive apathy factor did load onto it. The reason that the other items did not load onto the factor as expected may be because the items are conceptually more related to affective and behavioural apathy than cognitive apathy. In addition many of these items are vulnerable to socio-economic, language and age influences which can compromise the accuracy with which the informant or patient answers the items. Hence it is shown that the AES is not effective in tapping into the cognitive sub-domain of Apathy and is susceptible to various limitations which must first be addressed in order to be effective in detecting and tapping into cognitive apathy.

The results of the PCA thus indicate that only about half of the expected items load onto the factors they were expected to. In addition some items are vulnerable to other influences and are either poorly worded or conceptually flawed. Consequently, our findings support the statement that the AES was shown to have a three-factor structure and roughly

half the items loaded onto these factors as expected. However the number of items that loaded differently than expected were vulnerable to external influences and possibly flawed leads to the conclusion that the AES is not effective in tapping into the three sub-domains of apathy.

Limitations and Future Directions of the Present Study

The primary limitation of this study is that it was based on archival data collection. Hence, we had to utilise the measures that are used at the GSH/IAA Memory Clinic, even though some were not wholly suitable for the purposes of the present study. Take for instance the CSDD variable. The CSDD was not a suitable measure to correlate the AES measure of affective apathy with because its primary function is to measure depression. As stated previously apathy and depression might have overlapping symptomatology, but they are distinctive neuropsychiatric disorders. In the study not all correlations reached moderate correlations of .4 and thus the sample size was not consistently large enough to detect the effects that were investigated. A bigger sample size is needed to strengthen the effects we expected to detect in the relationship between the variables, especially where the results neared significance. Finally, the informant version of the AES that was used in the present study could have been compromised as some informants reported that they did not always live with the affected individuals. Hence their knowledge of the affected individual may be limited.

Future studies exploring the AES may wish to replicate the correlational aspect of this study on a more heterogeneous sample group. This study focused primarily on AD patients because of the higher incidence of apathy in this clinical sample. As the AES was developed with a heterogeneous sample of patients including various dementias, TBI's, strokes as well as healthy controls, a more heterogeneous sample may show other patterns of results or strengthen the argument put forth by this study. Another suggestion for future studies would be to further investigate and perhaps address the limitations of the AES found in this study and hence attempt to revise and improve the AES so that its more effective at distinguishing and tapping into the affective, behavioural and cognitive sub-domains of apathy.

Conclusion

Based on the results of this study the AES was found to be an ineffective measure of the multi-dimensionality of apathy. Apathy is increasingly being recognised as a multidimensional disorder which can be fractionated into affective, behavioural and cognitive subdomains. Distinguishing the three subdomains of apathy potentially has great value in informing treatment and research approaches. The AES is the most widely used measure of apathy but this study showed that while the AES is able to distinguish between the different subdomains of apathy it is not effective in tapping into them. Correlational results indicated that affective AES scores were not significantly correlated to the CSDD. However, affective AES scores were correlated significantly to one item in the CDSS which is conceptually similar to affective apathy symptoms. This suggests that although apathy and depression scales may have items that are sensitive to both disorders, they are distinctive neuropsychiatric disorders. Behavioural apathy as measured by the AES was partially correlated to the ADLs, particularly the instrumental ADLs. The cognitive AES scores was significantly correlated with the TMT A and B, although these results indicated that the affective AES score was contributing to some of the variance, thus indicating that the three sub-domains are not necessarily mutually exclusive.

These correlational results indicated that the AES is effective in distinguishing the affective, behavioural and cognitive sub-domains of apathy. The principle component factor analysis results demonstrated again that the AES is effective in distinguishing between the affective, behavioural and cognitive apathy sub-domains. However these results indicated that the items on the AES did not load according to expectations, thus illustrating that the AES is not effective in tapping into the sub-domains. The AES states that certain items are expected to load onto three factors pertaining to the three sub-domains. However our results indicated that only about half of the items loaded as expected, the other items were found to be conceptually different from their associated sub-domain. Taken together the findings of this study indicate that the AES is an ineffective measure for apathy because it failed to show adequate ability in tapping into the three subdomains of apathy. While this study was limited by archival data and the measures used by the memory clinic future studies should consider replicating this study on a more heterogeneous sample and perhaps attempt to revise and address the shortcomings found in the AES so that an effective AES may be produced. This would make a tremendous contribution to the treatment and research approaches pertaining to apathy as a multidimensional disorder.

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Appendix A
Letter of Ethical Approval



UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • Facsimile [021] 406 6411
e-mail: preaward@curie.uct.ac.za

04 April 2007

REC REF: 152/2007

Dr S Kalula
Geriatric Medicine

Dear Dr Kalula

PROJECT TITLE: APPLICATION FOR BLANKET ETHICAL APPROVAL FOR MEMORY CLINIC DATA.

Thank you for your letter to the Research Ethics Committee dated 23rd March 2007.

I have pleasure in informing you that the Ethics Committee has formally approved the above mentioned study.

Please inform the Committee of each study being performed.

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

M. Blockman

PROF M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

lemjedi

Appendix B:

Apathy Evaluation Scale (AES)

Apathy Evaluation Scale (Informant)

Name: _____ Date: ___/___/___

Informant's Name: _____ Relationship: _____

For each statement, circle the answer that best describes the subject's thoughts, feelings, and activity in the past 4 weeks.

1. **S/he is interested in things.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
2. **S/he gets things done during the day.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
3. **Getting things started on his/her own is important to him/her.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
4. **S/he is interested in having new experiences.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
5. **S/he is interested in learning new things.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
6. **S/he puts little effort into anything.**
NOT AT ALL (1) SLIGHTLY (2) SOMEWHAT (3) A LOT (4)
7. **S/he approaches life with intensity.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
8. **Seeing a job through to the end is important to him/her.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
9. **S/he spends time doing things that interest him/her.**
NOT AT ALL (4) SLIGHTLY (3) SOMEWHAT (2) A LOT (1)
10. **Someone has to tell him/her what to do each day.**
NOT AT ALL (1) SLIGHTLY (2) SOMEWHAT (3) A LOT (4)
11. **S/he is less concerned about her/his problems than s/he should be.**
NOT AT ALL SLIGHTLY SOMEWHAT A LOT

- | | | | | |
|--|----------|----------|-------|-----|
| | (1) | (2) | (3) | (4) |
| 12. S/he has friends. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |
| 13. Getting together with friends is important to him/her. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |
| 14. When something good happens, s/he gets excited. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |
| 15. S/he has an accurate understanding of her/his problems. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |
| 16. Getting things done during the day is important to her/him. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |
| 17. S/he has initiative. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |
| 18. S/he has motivation. | | | | |
| NOT AT ALL | SLIGHTLY | SOMEWHAT | A LOT | |
| (4) | (3) | (2) | | (1) |

The Apathy Evaluation Scale was developed by Robert S. Marin, M.D. Development and validation studies are described in RS Marin, RC Biedrzycki, S Firinciogullari: "Reliability and Validity of the Apathy Evaluation Scale," *Psychiatry Research*, 38:143-162, 1991.

Total score

Appendix C

Cornell Scale for Depression in Dementia (CSDD)

N2 Cornell Scale for Depression

Instruction: Tick the appropriate box for each item.

	Unable to evaluate (U)	Absent (0)	Mild or intermittent (1)	Severe (2)
A. Mood-related signs				
1 Anxiety (anxious expression, ruminations, worrying)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2 Sadness (sad expression, sad voice, tearfulness)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 Lack of reactivity to pleasant events	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4 Irritability (easily annoyed, short-tempered)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
B. Behavioural disturbances				
5 Agitation (restlessness, hand-wringing, hair pulling)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6 Retardation (slow movements / speech / reaction)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7 Multiple physical complaints (score 0 if GI symptoms only)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8 Loss of interest (less involved in usual activities; score only if change occurred acutely, i.e. in less than one month)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
C. Physical signs				
9 Appetite loss (eating less than usual)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10 Weight loss (score 2 if greater than 2 kilos in one month)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11 Lack of energy (fatigues easily, unable to sustain activities; score only if change occurred acutely, i.e. in less than one month)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Unable to evaluate (U)	Absent (0)	Mild or intermittent (1)	Severe (2)
D. Cyclic functions				
12 Diurnal variation of mood (symptoms worse in the morning)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13 Difficulty falling asleep (later than usual for this individual)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14 Multiple awakenings during sleep	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15 Early morning awakening (earlier than usual for this individual)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
E. Ideational disturbance				
16 Suicide (feels life is not worth living, has suicidal wishes, or makes suicide attempts)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17 Poor self-esteem (self-blame, self deprecation, feelings of failure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
18 Pessimism (anticipation of the worst)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
19 Mood-congruent delusions (delusions of poverty, illness or loss)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Score: Add the number received for each item.

Score < 6: Absence of depressive symptoms

Score >10: Probable major depression

Score >18: Definite major depression

Maximum Score: 38

Total unable to evaluate

Appendix D

Bristol Activities of Daily Living Scale

Bristol Activities of Daily Living Scale (modified)

Instruction: Circle the response that best describes the patient's level of ability to perform that activity. Only one box should be marked for each activity. Where in doubt, choose the level of ability which represents the patient's average performance over the past two weeks.

1. Food

a Selects and prepares food	0
b Able to prepare food only if ingredients are set out	1
c Able to prepare food only if shown step by step	2
d Unable to prepare food	3
e Not applicable	0

2. Eating

a Eats as previously	0
b Eats appropriately if food is made manageable and/or uses a spoon	1
c Needs someone to help guide food to mouth	2
d Needs to be fed	3
e Not applicable	0

3. Drink

a Able to make tea/coffee as previously	0
b Able to make tea/coffee only if ingredients are set out	1
c Able to make tea/coffee only if shown step by step	2
d Unable to make tea/coffee	3
e Not applicable	0

4. Dressing

a Dresses as previously	0
b Puts clothes on incorrectly or inappropriately	1
c Unable to dress self but moves limbs to assist	2
d Has to be dressed	3
e Not applicable	0

5. Hygiene

a Washes self as previously	0
-----------------------------	---

b Able to wash self if given soap, towel and water	1
c Able to wash self but needs help	2
d Has to be washed	3
e Not applicable	0

6. Teeth

a Cleans teeth as previously	0
b Cleans teeth only if given water and toothpaste or gargle	1
c Able to clean teeth but needs help	2
d Unable to clean teeth	3
e Not applicable	0

7. Toilet

A Uses toilet as previously	0
B Able to use toilet (or bucket) if helped	1
C Incontinent of urine	2
d Incontinent of urine and faeces	3
e Not applicable	0

8. Transfers

a Able to get in/out of a chair as previously	0
b Able to get in a chair but needs help to get out	1
c Needs help getting in/out of a chair	2
d Has to be lifted in/out a chair	3
e Not applicable	0

9. Mobility

a Walks independently	0
b Walks with assistance, i.e. furniture, arm for support	1
c Uses aid to walk, i.e. cane, frame	2
d Unable to walk	3
e Not applicable	0

10. Orientation – Time

a Fully orientated to time/day/date, etc.	0
b Unaware of time/day/date but seems unconcerned	1
c Repeatedly asks the time/day/date	2
d Mixes up night and day	3
e Not applicable	0

11. Orientation – Space

a Fully orientated to surroundings	0
b Orientated to familiar surroundings only	1
c Gets lost in home, needs reminding where toilet is	2
d Does not recognise own home	3
e Not applicable	0

12. Communication

a Able to hold appropriate conversation	0
b Understands others and tries to respond verbally with gestures	1
c Can make self-understood but has difficulty understanding others	2
d Does not respond to or communicate with others	3
e Not applicable	0

13. Telephone

a Uses telephone appropriately	0
b Uses telephone with help	1
c Answers telephone but does not make calls	2
d Unable/unwilling to use telephone	3
e Not applicable	0

14. Housework/gardening

a Able to do housework/gardening to previous standard	0
b Able to do housework/gardening but not to previous standard	1
c Limited participation in housework/gardening	2
d Unwilling/unable to participate in previous housework/gardening activities	3
e Not applicable	0

15. Shopping

a Shops to previous standard	0
b Only able to shop for 1 or 2 items without a list	1
c Unable to shop alone, but participates when accompanied	2
d Unable to participate in shopping even when accompanied	3
e Not applicable	0

16. Finances

a Manages own finances as previously	0
b Recognises money values and can sign name	1
c Does not recognise money values but can sign name	2
d Unable to sign name or recognise money values	3
e Not applicable	0

17. Transport

a Able to drive, cycle or use public transport independently	0
b Unable to drive but uses public transport, bike, etc.	1
c Unable to use public transport alone	2
d Unable or unwilling to use public transport even when accompanied	3
e Not applicable	0

Score:

Add encircled numbers for 17 activity domains

Maximum Score: 51**Total "not applicable" activities**