Apathy: An Ignored Neuropsychiatric Syndrome in South Africa

Steven Harding

Department of Psychology

University of Cape Town

Abstract

Apathy is a common feature of brain disorders, yet is often confused with depression and ignored by clinicians. This situation is problematic because apathy is associated with several adverse outcomes, including caregiver distress and decreased treatment adherence. This study investigated the prevalence of apathy and depression in 10 outpatients (7 women, 3 men, mean age = 63.7 years) at a South African memory clinic using the Apathy Evaluation Scale and the Cornell Scale for Depression in Dementia. Half of the patients had apathy, yet only 2 patients had both apathy and depression, and three patients had depression only. Apathy is dissociable from depression and should be screened for and treated in brain-damaged individuals.

Apathy is possibly the most frequently-occurring feature of brain disorders (Chase, 2011; Ishii, Weintraub, & Mervis, 2009). It is present in approximately 50% of all dementia patients, 30% of stroke patients, and over 60% of traumatic brain injury (TBI) sufferers (van Reekum, Stuss, & Ostrander, 2005). This last statistic is especially relevant to the South African context, where assaults and road accidents contribute to the approximately 90 thousand new cases of TBI annually (Levin, 2004; National Institute for Occupational Health, 2011). Apathy is also common in people with HIV, where the virus itself damages neural circuits of motivation (Hoare et al., 2010; Joska, Hoare, Stein, & Flisher, 2011). Currently, at least 5 million South Africans are HIV-positive (Joska et al., 2011). Apathy exacerbates the burden of associated disorders, and is associated with lower quality of life, greater caregiver distress, and lower adherence to medical treatments (Butterfield, Cimino, Oelke, Hauser, & Sanchez-Ramos, 2010; Marin, 1991; Rickles, 2010).

Despite these facts, apathy rarely features in neuropsychology textbooks, and is not listed as a distinct condition in any major diagnostic manual (Mulin et al., 2011). One likely cause of this situation is that many clinicians regard apathy as only a symptom of depression (Levy & Dubois, 2006; Stuss, Van Reekum, & Murphy, 2000), despite the distinct nature of these two disorders (Levy et al., 1998; Marin, 1991; Withall, Brodaty, Altendorf, & Sachdev, 2011).

This study sought to provide further evidence for the dissociable nature of apathy and depression, and the importance of recognising apathy in clinical settings, especially in South Africa. Because of the relatively unknown and misunderstood status of apathy, also included here is a broad overview of the syndrome.

### Apathy: A Broad Overview

The word apathy stems from the Greek *apatheia,* a term used by the Stoics to describe someone who was free from the passions, or *pathos*. In thinking that these strong emotions interfered with rational thought, they deemed apathy a desirable trait. Similar usage of the word continued during the Renaissance, especially among the humanist writers. However, from the 19th century, the term apathy assumed a negative connotation, used to denote mental or physical unresponsiveness (Chase, 2011; Starkstein, Petracca, Chemerinski, & Kremer, 2001). In its current use, apathy is commonly a pejorative synonym for indifference, particularly when describing someone's attitude towards certain societal matters, such as politics (Robert, Mulin, Malléa, & David, 2010).

Within psychology and psychiatry, apathy traditionally featured only as a poorly-defined adjective within the diagnostic criteria of other disorders, such as depression and schizophrenia (e.g. Andreasen, 1980; Greenson, 1949). However, this situation changed after 1990 with the conceptualisation of apathy as a discrete diagnostic entity.

**Definition**

The original neuropsychiatric definition of apathy is from Marin (1990), who conceptualised apathy as a disorder of motivation, evidenced by diminished goal-directed behaviour, cognition, and associated emotions. Where these deficits occur because of impairments in consciousness or intellect or are due to emotional distress, apathy is a symptom of another disorder; otherwise, it is a distinct syndrome (Marin, 1991).

Although the core of this definition is accepted by apathy researchers (Mulin et al., 2011), some dispute various elements of it. Specifically, some (e.g. Starkstein et al., 2001; van Reekum et al., 2005) note that *motivation* is a psychological construct that is not directly measurable, and instead refer to apathy in purely behavioural terms. However, Marin was aware of this limitation, and noted that one could only infer a patient's motivation through observable behaviours (see Marin, 1990). Others (e.g. Stuss et al., 2000) question the usefulness in distinguishing between apathy as a symptom and a syndrome, because the causes of apathy (discussed below) usually cause impairment in other domains. Reflecting this last criticism, studies rarely distinguish between apathy as a syndrome versus a symptom.

**Diagnostic Criteria**

The diagnostic criteria for apathy are closely linked to its definition. Marin (1991) originally proposed such criteria, which were subsequently used inconsistently in literature, causing several authors to call for a standardised construct of apathy (Starkstein et al., 2001). Recently, this call has been answered with a task force proposing a set of criteria that may become the accepted standard (Robert et al., 2009), which have since been validated in a sample of patients with Parkinson's disease (Drijgers, Kathy Dujardin, Reijnders, Defebvre, & Leentjens, 2010). Here, for a diagnosis of apathy, evidence of diminished motivation must be present for at least 4 weeks, along with impairment in at least two domains of apathy (goal-directed behaviour, cognition, and emotions) that cause impaired functioning. Additionally, these symptoms must not be due to physical or motor disabilities, or be due to impaired consciousness or drug use. With these criteria, the omission of Marin's exclusion criteria of intellectual and emotional impairment reflects the broader conceptualisation of apathy already used in the literature (Sagen et al., 2010).

The possible inclusion of apathy in the next edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) is the subject of continued debate (Chase, 2011).

**Measurement**

Despite the existence of diagnostic criteria, apathy is most commonly diagnosed using apathy scales, of which at least 15 exist. Two scales occur most frequently in the literature (Clarke et al., 2011).

The Apathy Evaluation Scale (AES; Marin et al., 1991) was developed alongside the original definition of apathy, and exists in clinician (AES-C), informant (AES-I), and self-rated (AES-S) versions. In all versions of the scale, the rater indicates the accuracy of 18 statements related to apathetic thoughts, feelings, and behaviour, on a 4-point Likert scale (see Appendix A). The original validity study (Marin et al., 1991) showed the scale to be valid and reliable in a sample of patients with stroke, probable Alzheimer's disease, major depression, and healthy adults. In subsequent studies, the AES-I showed the greatest sensitivity, and the AES-S showed the worst (Clarke et al., 2011, 2007). This is to be expected, as apathetic patients often show little insight into their apathy (Marin & Wilkosz, 2005).

The Neuropsychiatric Inventory (NPI; Cummings et al., 1994), a commonly used measure of 12 domains of functioning in brain damage patients, contains an apathy subscale. Because of its prominence, the NPI is included in many apathy studies, even though the AES has superior psychometric properties (Clarke et al., 2011). The NPI in its entirety does show good reliability, however, and its apathy subscale shows statistically significant convergent validity with the AES-I. Many official translations of the NPI exist, including Afrikaans (MAPI Research Trust, personal communication, March 22, 2011).

In addition to general apathy scales, several population-specific scales show good reliability and validity. These include the Dementia Apathy Interview and Rating (DAIR; Strauss & Sperry, 2002), the Positive and Negative Syndrome Scale (PANSS) for schizophrenia patients (Kay, Fiszbein, & Opler, 1987), and the Frontal System Behavior Scale (FrSBe; formerly the Frontal Lobe Personality Scale) for those with frontotemporal damage (Grace, Stout, & Malloy, 1999). These scales may be preferable to general apathy scales when specific disease impairments hinder routine assessment (Clarke et al., 2011).

**Prevalence**

There is strong evidence for the high prevalence of apathy in brain-damaged patients.

Table 1 shows the prevalence rates of apathy as reported in the most comprehensive meta-analysis of its type to date (van Reekum et al., 2005). Prevalence rates differ greatly—partly because of the differences in measurement used across study, but also because of inherent population characteristics. In particular, participants at different degrees of disease severity are likely to show different levels of apathy severity (Benoit et al., 2008). This confound is rarely controlled for, mainly because prevalence data is usually a secondary concern for the studies in which it is reported.

Table 1

*Prevalence of apathy across various patient populations*

| Disorder | *n* | Prevalence range | Point prevalence |
| --- | --- | --- | --- |
| TBI | 210 | 46-71 | 61 |
| AD | 999 | 37-81 | 60 |
| Frontal lesion | 68 | 12-89 | 60 |
| Basal ganglia disorders[a] | 589 | 12-90 | 40 |
| Stroke | 190 | 23-57 | 35 |
| HIV | 246 | 29-50 | 35 |
| VD | 145 | - | 34 |
| Lewy Body dementia | 36 | - | 23 |

*Note.* TBI = traumatic brain injury; AD = Alzheimer's disease; VD = vascular dementia; Data from "Apathy: Why care?" by R. van Reekum, D. T. Stuss, and L. Ostrander, 2005, *The Journal of Neuropsychiatry and Clinical Neurosciences, 17,* 7-19.
[a]Including Parkinson's disease.

One recent study (Mulin et al., 2011) sought to assess the prevalence of apathy using the newly-proposed diagnostic criteria (Robert et al., 2009). Using a sample of 306 patients from 6 countries, the associated disorders and apathy prevalence rates were: Alzheimer's disease (AD; 55%), mixed dementia (70%), mild cognitive impairment (43%), Parkinson's disease (27%), and schizophrenia (53%). These rates are consistent with the trend seen in Table 1, falling within the reported prevalence ranges.

To my knowledge, only one study has examined the presence of apathy in a South African population: Hoare et al. (2010) found a 50% rate of apathy in a small sample (n = 30) of HIV-infected individuals.

**Neural Correlates and Explanatory Models**

The prevalence rates of apathy are informative not only of the widespread nature of the syndrome, but also of its probable neural correlates. Above, it is evident that disorders affecting the frontal-subcortical system are likely to be associated with apathy. This system as a whole runs from the anterior cingulate cortex to the ventral striatum, the globus pallidus (a structure of the basal ganglia), the thalamas, and back to the anterior cingulate cortex. Because it is associated with motivation, damage at any point of this system could theoretically cause apathy symptoms (Drijgers, Verhey, Leentjens, Köhler, & Aalten, 2011; Tekin & Cummings, 2002).

Evidence from imaging studies with AD patients supports the above hypothesis. Apathy is correlated with abnormal perfusion of the frontal cortex and anterior cingulate cortex, as well as a lower density of gray matter in the anterior cingulate cortex, orbitofrontal cortex, and areas of the dorsolateral prefrontal cortex. Regarding subcortical structures, atrophy of the striatum  occurs early in AD, possibly explaining the early onset of apathy in the disease (Benoit et al., 2008; Drijgers et al., 2011; Robert et al., 2010) .

Similar correlates exist for other patient populations. In HIV patients, apathy is associated with damage to the basal ganglia and anterior cingulate cortex (Hoare et al., 2010; Paul et al., 2005). Parkinson's disease is characterised by a disruption of the basal ganglia, particularly the substantia nigra, which results in reduced dopamine production (Bogart, 2011).

Dopamine plays a key role in the development of apathy, as it is involved in two of three neurotransmitter pathways relevant to the syndrome. First, the meso-cortico-limbic dopaminergic pathway, which runs from the ventral tegmentum, through the anterior cingulate, to anterior cortical regions, is involved in affective processing. Second, the nigro-striatal dopaminergic pathway, which runs from the substantia nigra to the striatum, is likely involved in selecting and initiating goal-directed actions. Lastly, the cortical cholinergic pathway, which runs from the basal nucleus to the frontal cortex and other regions, is most likely involved in cognitive aspects of motivation. These three pathways thus correspond to the three domains of apathy: affective, behavioural, and cognitive (Ishii et al., 2009; Robert et al., 2010).

**SEEKING system.** Readers familiar with the work of Jaak Panksepp (Panksepp, 1998) will recognise an overlap between the areas and networks implicated above— particularly the meso-cortico-limbic pathway—and the SEEKING emotional system. This system exists in all mammals, and is responsible for generating interest in the external world. Within this framework, apathy could arguably be conceptualised as a disorder of the

SEEKING system. It is unfortunate, however, that none of the apathy literature cited in this paper makes any mention of Panksepp's research—especially because research into emotional systems is providing promising new insights into psychopathology (Panksepp & Watt, 2011; Zellner, Watt, Solms, & Panksepp, in press).

**Treatment**

Understanding the neural correlates of apathy opens up possibilities for its treatment. Although there are currently no officially approved pharmacological treatments, several lines of investigation are showing some promise. Consistent with the pathways implicated above, anecdotal evidence and several case studies report success with dopaminergic agonists, acetylcholinesterase inhibitors, and atypical antipsychotics (Chase, 2011; Roth, Flashman, & McAllister, 2007). However, there is still an urgent need for credible pharmacological trials for apathy treatment, as the few trials that do exist (e.g. Corcoran, Wong, & Keane, 2004; Marangell, Johnson, Kertz, Zboyan, & Martinez, 2002) lack adequate sample sizes, randomisation and control groups.

Besides medical approaches, several authors have identified possible psychological interventions for apathy. A recent review identified 28 studies using such interventions (Lane-Brown and Tate, 2009). The most common interventions described were: cognitive interventions, those exploring the effect of multisensory environments, structured behavioural interventions, and music therapy. For those with severe impairments, such as patients with late-stage dementia, music therapy showed positive results. For those with milder impairments, cognitive interventions showed positive results. Here too, though, there is a need for additional scientific research, especially since pseudoscientific and untested therapies are capable of gaining undue popularity (Lilienfeld, 2011). Also, given the high cost of psychological therapies, there is a need for cost-effective treatments for apathy, particularly for local contexts, in light of apathy's associated outcomes.

**Associated Outcomes**

Apathy is correlated with several adverse outcomes, including worsened health, faster disease progression, and decreased occupational functioning. However, here it would be wrong to suggest (as some do; Chase, 2011) a simple explanatory model, where apathy causes these outcomes. Not only is it more logical to assume that worsened health causes increased apathy in some cases, it is can also be uninformative to suppose the reverse. That is, identifying apathy as the simple cause of the above outcomes does not aid rehabilitation efforts, and can be tautological (where "decreased occupational functioning" is nearly

identical to "decreased goal-oriented behaviours"). This approach is likely to leave some sceptical of the value of apathy as a construct.

What is useful information, however, is the fact that apathy is associated with increased distress in caregivers, even when holding level of disease progression constant (Butterfield et al., 2010). In addition, apathy is associated with poor treatment adherence, and increased burden of the associated disorder (Rickles, 2010). This information is not tautological, and is understandable in light of apathetic patient characteristics. For instance, caregivers may be frustrated when apathetic patients fail to complete basic tasks for themselves, even though they are physically capable of doing so—behaviour that is easily misconstrued as defiant. Similarly, caregivers may feel alarmed when patients show little concern about their illness or other problems. Apathetic patients are less likely to adhere to treatments because of this lack of concern, coupled with diminished overall motivation (Chase, 2011; Ishii et al., 2009). With these two outcomes in mind, the above associations, including worsened health, become more understandable.

Given the high prevalence of apathy in HIV patients, and the high incidence of HIV infection in South Africa, the above outcomes are especially relevant. HIV treatment regimens require considerable commitment from patients, as do the regimens for associated illnesses, such as tuberculosis (Joska et al., 2011). This is also true for the physical rehabilitation involved in TBI, as well as the caregiver burden of dementias in South Africa (Hinkin, Castellon, Atkinson, & Goodkin, 2001).

### Apathy and Similar Disorders

Despite the above evidence for it being a distinct syndrome, with dissociable neural correlates and specific adverse associated outcomes, many clinicians still do not acknowledge apathy (Mulin et al., 2011). There are at least two reasons for this situation.

The first reason relates to the presentation of apathy and its historical antecedents. Apathy symptoms are similar to the negative symptoms of schizophrenia (Brown & Pluck, 2000), although negative symptoms have a more complex etiology. Within schizophrenia treatment and research, positive symptoms (including hallucinations and delusions) were more striking and more problematic for caregivers than negative symptoms. This fact is highlighted by the fact that frontal lobotomies, which induced apathy symptoms through deliberate crude lesions to the frontal cortex, were once used as treatment for mental illness (Brown & Pluck, 2000). The same is likely true within other patient populations, especially in institutional settings: Those who do not cause trouble through deliberate non-compliance are less likely to be noticed or be a problem to carers (Ishii et al., 2009). However, as noted

above, apathetic patients *can* be a greater burden to caregivers in certain situations, so this cannot be the only explanation.

The second reason for apathy's lack of recognition is its relation to other disorders. Apathy is not the only disorder of diminished motivation. Specifically, abulia, derived from the Greek *aboulia*, meaning "non-will" is best characterised as a more severe form of apathy, in which a patient lacks *all* goal-directed behaviour. (Akinetic mutism is in turn a worse form of abulia, characterised by a complete lack of movement and speech.) Also similar to apathy, demoralisation refers to a psychological reaction to external stressors (Marin, 1990; Marin & Wilkosz, 2005). Confusion between these definitions may have hindered progress in apathy research. However, the disorder with which apathy is most commonly conflated is depression.

**Apathy and Depression**

In simple terms, apathy is a disorder of motivation, and depression is a disorder of low mood. The fact that apathy is often mistaken for depression is partly understandable; at least three of the nine possible symptoms of major depressive disorder (of which only five are needed for a diagnosis) involve motivation. These are: diminished interest or pleasure in daily activities, fatigue, and slowed movement. (American Psychiatric Association, 2000). In addition, depression is often common in the same disorders that are associated with apathy (Tomlinson, Grimsrud, Stein, Williams, & Myer, 2009).

However, three lines of strong evidence exist to support the distinct nature of the two disorders. First, depression and apathy do not correlate within associated disorders. Table B1 (Appendix B) shows the prevalence rates of apathy and depression reported by several studies. As with the overall prevalence rates of apathy (Table 1, above), the prevalence rates differ across studies. However, all studies listed report patients who had only apathy, or only depression. In most cases, these patients outnumber those who have both apathy and depression. More concrete evidence comes from studies that directly investigated the relationship between depression and apathy. Soon after the conceptualisation of apathy, Marin and his colleagues demonstrated that only small, nonsignificant correlations existed between the apathy and depression scores of a sample of brain-damaged patients—and these correlations were due to an overlap of some items on the depression and apathy scales used (Marin, Firinciogullari, & Biedrzycki, 1993). Subsequent researchers also failed to identify a statistically significant correlation between apathy and depression (e.g. Levy et al., 1998; Marin, Firinciogullari, & Biedrzycki, 1994).

Second, apathy and depression respond differently to pharmacological treatments within the same individuals. As mentioned above, apathy shows some response to dopaminergic agonists, acetylcholinesterase inhibitors, and, to a lesser extent, atypical antipsychotics. However, only the last of these is useful in treating major depression, which is most often treated with selective serotonin reuptake inhibitors (Chase, 2011; Cuijpers, van Straten, Warmerdam, & Andersson, 2009).

Third, the clinical features of apathy and depression are distinct. Depression is variously associated with anxiety, hallucinations, and irritability—apathy is not. Apathetic patients usually do not show concern over their symptoms, but depressed patients often exhibit great distress (Levy et al., 1998; Marin, 1990).

Despite this evidence, not all clinicians are convinced of the existence of apathy or the utility of its diagnosis. One survey found that half of the British psychiatrists and neurologists interviewed did not differentiate depression from disorders of motivation (Vijayaraghavan, Krishnamoorthy, Brown, & Trimble, 2002). In South Africa, the head of neurology in a local state hospital recently echoed similar sentiments—claiming that apathy is only a feature of depression (P. Njomboro, personal communication, 7 June 2011).

Some research supports these dissenting views. For instance, one study, which originally sought to investigate apathy and depression in a clinical setting, concluded that apathy was not a useful research tool, and excluded it from final analysis (Glenn, O'Neil-Pirozzi, Goldstein, Burke & Jacob, 2001). In addition, a recent prevalence study found depression to be present in almost all (94%) apathetic patients (Mulin et al., 2011).

**Clinical implications.** It should be clear by now, I hope, that disagreements regarding apathy have important, real-world consequences. Three particularly pertinent areas for concern in South Africa are as follows:

1. Apathetic patients misdiagnosed as depressed may be prescribed antidepressant medication that not only does little to alleviate their symptoms, but also causes further harm through its side-effects (Ishii et al., 2009). Patients who are not on medical aid have to carry the burden of this expense themselves, which can cost up to a quarter of their monthly earnings (N. Yorke, personal communication, 15 August 2011).

2. Apathetic patients are much less likely to adhere to medication than other patients (Butterfield et al., 2010). A failure to recognise which patients are apathetic constitutes a failure to recognise which patients require greater attention regarding adherence. This is applicable in both inpatient and outpatient settings. In the former,

nurses and other staff can assist in ensuring adherence, and in the latter, family members and caregivers can provide support.

3. Caregivers and family members who understand why patients are displaying apathetic behaviour are less likely to be distressed than those who are not afforded this explanation (Drago et al., 2010). Thus, clinicians who do not acknowledge and diagnose apathy indirectly allow for increased caregiver distress.

For these reasons, this study sought to assess the presence of apathy and depression in a sample of South African outpatients.

## Aims and Specific Hypotheses

This study had two major interrelated aims. First, it sought to highlight the importance and relevance of apathy syndrome in South Africa. This aim is partially accomplished through the above review, but also through the second aim: to investigate the prevalence of apathy, and its correlation with depression, in a local sample of brain-damaged individuals.

Thus, my hypotheses were:

- Both apathy and depression would be present in a small local sample of memory clinic patients. .
- Apathy would be dissociable from depression, with some patients showing apathy symptoms in the absence of depression, and vice versa.

Several other initial hypotheses involving the correlation of depression and apathy scores were abandoned once it became apparent that the sample size would be too small for meaningful statistical analyses.

## Method

### Participants

This study used data provided by caregivers of 10 consecutive eligible outpatients (7 women, 3 men, $M_{age}$ = 63.7 years, age range: 55-78 years) who underwent neuropsychological assessment at the Institute for Ageing in Africa (IAA) Memory Clinic between July and October 2011. Time constraints and difficulties securing access to participants limited the size of the sample, as the intended size was 50. All patients had subjective memory impairments, and a medical practitioner had referred them to the clinic because of these impairments. At the time of assessment, 4 had probable AD, 2 had alcohol-related memory impairment, 1 had probable frontotemporal dementia, and 1 had mild cognitive impairment. The diagnoses of the remaining participants were unavailable at the time of data collection.

For inclusion in the study, an English or Afrikaans-speaking caregiver had to accompany each patient. The presence of a caregiver is a requirement of the IAA Memory Clinic, and I am only fluent in English and Afrikaans. This language requirement did not exclude any patients from participating, but one patient arrived at the clinic alone and could not participate in the study.

Participants received no compensation and participated voluntarily. They were treated in accordance with the ethical guidelines of the Health Professions Council of South Africa (Health Professions Council of South Africa, 2007) and the University of Cape Town (University of Cape Town, 2006). The University of Cape Town Faculty of Health Sciences ethics committee granted ethical approval for the study (reference 102/2011; see Appendix C).

**Measures**

**Apathy scale.** Apathy was measured using the AES-I, because of its superior psychometric properties (see above). A score of 38 and above, of a possible 72, indicates apathy syndrome. Although the AES-C has been used in a South African sample (Hoare et al., 2010), no local studies have examined the psychometric properties of any apathy scales.

**Depression scale.** Depression was measuring using the Cornell Scale for Depression in Dementia (CSDD; Alexopoulos, Abrams, Young, & Shamoian, 1988a; see Appendix C) The CSSD consists of 19 items, which are completed by a clinician based on the responses of either a caregiver or the patient. Of a possible 38 points, a score above 10 indicates probable major depression, and a score above 18 indicates definite major depression. The minimum score is 0. Although the scale is designed specifically for patients with dementia, it shows good reliability and validity in normal and clinical populations (Alexopoulos, Abrams, Young, & Shamoian, 1988b)**.** However, to my knowledge, no studies have examined its psychometric properties in South African populations.

**Procedure**

The CSSD is part of the routine assessment at the IAA Memory Clinic, and a qualified neuropsychologist or suitably-trained neuropsychology student collected this data. (More details about the clinic are available in Kalula et al., 2010.) My supervisor and I administered the apathy scale, strictly adhering to its administration guidelines (Marin et al., 1991). As a further measure of validity, I first observed three instances of this administration before administering the scale myself.

In all instances for the apathy scale, patients' caregivers were interviewed in the absence of the patient, in order to reduce bias, as caregivers may be unwilling to answer some items honestly in the presence of the patient  (Marin et al., 1991)**.** However, this was not possible for some instances with the CSSD, where some caregivers provided responses in the presence of patients. Because the memory clinic is housed in a teaching hospital, observers were present in varying numbers during the interview process. This may have influenced the answers given by the caregivers, and at least one patient expressed concern about the presence of observers.

For both scales, raters read the scale items to the caregivers. This action is not strictly necessary for the AES-I, but doing so allowed any reading difficulties of the participants to be avoided.

## Results

Table 2 shows the depression and apathy scores of the sample, as well as the patients' diagnoses.

Table 2

*Apathy and Depression Scores*

| Patient | Diagnosis | AES-I | CSDD |
|---------|-----------|-------|------|
| L. R. | - | 34 | $11^b$ |
| A. S. | AD | 31 | $13^b$ |
| S. A. | FTD | $52^a$ | 9 |
| T. F | MCI | 33 | $16^b$ |
| A. C | Alcohol dementia | $63^a$ | $13^b$ |
| J. P. | AD | $69^a$ | 3 |
| M. W. | AD | $44^a$ | $20^c$ |
| P. A. | - | 25 | 7 |
| M. Z. | - | 37 | 9 |
| D. M. | AD | $49^a$ | 5 |

*Note.* AD = Alzheimer's disease, FTD = frontotemporal dementia, MCI = mild cognitive impairment. Initials have been modified to preserve anonymity.
[c]Score indicates clinically significant apathy. [b]Score indicates probable major depression. [c]Score indicates definite major depression.

Across all participants, the mean score on the AES was 43.7 ($SD = 14.4$) and the mean score on the CSDD was 10.6 ($SD = 5.1$). Five patients had apathy, and 5 patients had probable depression. However, only 2 patients had both apathy and depression.

Although the small sample size limits the usefulness of statistical analyses, I ran correlations between the apathy and depression scores (in a manner similar to Marin et al., 1993) to check for any significant results, using IBM SPSS 19 software. Table 3 shows the correlations of individual AES-I items with the total CSDD scores, and with the total AES-I scores. Note that I have reworded the AES-I items in the negative to reflect the actual direction of the correlations. (A higher score on AES-I items indicates greater apathy, thus a high score on item 1, "s/he is interested in things", would indicate that the patient is *not* interested in things).

Table 3

*Correlation of AES-I Items with total scores*

| Item | CSDD | AES-I |
|---|---|---|
| 1. Not interested in things | -.18 | .32 |
| 2. Does not get things done | .20 | .64* |
| 3. Starting things is unimportant | -.50 | .86** |
| 4. Not interested in having new experiences | -.69* | .50 |
| 5. Not interested in learning new things | -.61 | .57 |
| 6. Puts little effort into anything | .06 | .62 |
| 7. Does not approach life with intensity | -.18 | .57 |
| 8. Seeing a job through is unimportant | -.15 | .76* |
| 9. Spends little time doing things of interest | -.08 | .55 |
| 10. Must be told what to do each day | .52 | .19 |
| 11. Lack of concern about problems | -.20 | .73* |
| 12. Has no friends | -.37 | .62 |
| 13. Getting together with friends is unimportant | -.38 | .78** |
| 14. Does not get excited when something good happens | -.45 | .88** |
| 15. Has inaccurate understanding of problems | .08 | .78** |
| 16. Getting things done during the day is unimportant | -.52 | .86** |
| 17. Has little initiative | .07 | .76* |
| 18. Has little motivation | -.06 | .65* |

*Note.* Table shows Spearman correlations of individual items of the informant-rated Apathy Evaluation Scale (AES-I) with total scores of the Cornell Scale for Depression in Dementia (CSDD) and the total scores of the AES-I. AES-I items have been reworded in the negative.

*$p < .05$. ** $p < .01$

The Spearman correlation between total AES-I scores and total CSDD scores was nonsignificant ($r = -.28$, $p = .42$). Table 4 shows the correlations of individual CSDD items with the total AES-I scores, and the total CSDD scores.

Table 4

*Correlation of CSDD Items with total scores*

| Item | AES-I | CSDD |
|---|---|---|
| 1. Anxiety | -.60 | .58 |
| 2. Sadness | -.62 | .43 |
| 3. Lack of reactivity to pleasant events | -.29 | .40 |
| 4. Irritability | -.13 | .67* |
| 5. Agitation | .24 | .35 |
| 6. Retardation of movement | -.35 | .00 |
| 7. Multiple physical complaints | -.17 | .05 |
| 8. Loss of interest | .16 | .62 |
| 9. Appetite loss | -.14 | .14 |
| 10. Weight loss | .14 | -.17 |
| 11. Lack of energy | .31 | .58 |
| 12. Diurnal variation of mood | .04 | .20 |
| 13. Difficulty falling asleep | .04 | .67* |
| 14. Multiple awakenings during sleep | .01 | .63* |
| 15. Early morning awakening | -.70* | .68* |
| 16. Suicidal ideation | - | - |
| 17. Low self-esteem | -.22 | .33 |
| 18. Pessimism | .11 | .06 |
| 19. Delusions | .34 | .56 |

*Note.* Table shows Spearman correlations of individual items of the Cornell Scale for Depression in Dementia (CSDD) with total scores of the informant-rated Apathy Evaluation Scale (AES-I) and the total scores of the CSDD.

**Discussion**

As predicted, apathy and depression were present and dissociable in the patients: Apathy and depression were comorbid in 2 patients, but 3 patients had apathy only, and 3 had depression only. Thus, apathy is present and dissociable from depression in South Africa. Also as expected, most of the correlations returned nonsignificant results, most likely because of the small sample size.

However, some items did show significant correlations. Item 4 on the AES-I ("s/he is not interested in having new experiences") was negatively correlated with total depression scores. One likely interpretation of this result is that, consistent with existing evidence, many depressed patients do not show apathy symptoms. However, several caregivers also alluded that the old age of the patients played a large role in their interest in new experiences. Here, it is unclear whether some of these responses may have reflected the normative beliefs of the caregivers rather than the nature of the patients.

On the CSDD, item 15 (early morning awakening) showed a significant negative correlation with total apathy scores. This corresponds with the frequent occurrence of hypersomnia in apathetic patients (Ishii et al., 2009).

The correlations of individual items and scores on the same scale give an indication of which symptoms were most frequent in the sample. Of particular interest, item 15 ("has an inaccurate understanding of his/her problems") showed a large, positive correlation, as did item item 16 ("getting things done during the day is unimportant"). I argue that the high frequency of these symptoms in the sample would correspond to a lower level of treatment adherence in these patients, as suggested by existing evidence (Butterfield et al., 2010). Also worthy of mention, item 13 ("getting together with friends is unimportant") showed a strong positive correlation with AES-I scores. This could suggest that the apathetic patients have a lower level of social support. Because social support can aid physical and psychological health (Hyde, Gorka, Manuck, & Hariri, 2011; Uchino, 2006), this possibility deserves further investigation.

**Limitations and Future Directions**

Admittedly, this study faced several important limitations. The most obvious of these, as already mentioned, is the small sample size included. This limitation resulted from time restraints, as well as difficulties in accessing patient populations. However, future studies can overcome this limitation if the AES-I is included in routine assessments of brain-damaged

patients. At this point, I hope the reader would agree that such an inclusion should form part of assessments regardless of any secondary research interests involved. The NPI (described above) is already used in many neuropsychological assessments, and can serve as a convenient measure of apathy for time-stressed assessments. However, it is necessary for clinicians to recognise that the apathy subscale of the NPI denotes a syndrome distinct from depression, and is worthy of particular attention (Ishii et al., 2009). In settings where time is less constrained, and in patient populations where the incidence of apathy is likely to be high, I recommend the use of either the AES-I or AES-C, because of their superior psychometric properties (Clarke et al., 2011).

The second limitation present was the use of multiple raters, as well as the presence of observers during test administration. Unfortunately, the last of these limitations is not easily overcome, particularly in academic hospitals and interdisciplinary clinics. However, through the use of a single rater, in the future it should be possible to establish sufficient rapport with the caregiver that any concerns about observers will not influence responses (Leach, 2005).

The third limitation is common to almost all neuropsychological tests in South Africa—a lack of local norms and validity studies, and test translations. Efforts to remedy this situation regarding tests other than the AES-I are ongoing (Kalula et al., 2010). However, they are time and resource intensive. I argue that the clinical importance of apathy should outweigh and reservations surrounding test validity until validity studies are feasible. However, translations of apathy scales are necessary. In my data collection, I had to spontaneously translate some AES-I items into Afrikaans, which may have influenced the results as my translations may have been partially inaccurate. An Afrikaans version of the NPI exists, but other languages are also needed for both the NPI and the AES. In addition, there is a need for clinicians who can speak multiple South African languages.

Thus, apathy was dissociable from depression in a local sample, and was prevalent in half of the patients sampled here. Based on international prevalence rates, it is likely that other local patients have similar prevalence of apathy. However, this possibility is under-explored in local contexts, despite the adverse outcomes associated with apathy. To ensure the best possible well-being of brain-damaged patients—that is, for clinicians to uphold their ethical obligations—it is necessary for clinicians to acknowledge and screen for the existence of apathy.

Appendix A

The Apathy Evaluation Scale (Informant Version; Marin et al., 1991)

## Apathy Evaluation Scale (Informant-female)

Name: _____     Date: ___/___/___

Informant's Name: _____     Relationship:_____

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

1.    She is interested in things.

          NOT AT ALL SLIGHTLY          SOMEWHAT A LOT

2.    She gets things done during the day.

          NOT AT ALL SLIGHTLY          SOMEWHAT          A LOT

3.    Getting things started on her own is important to her.

          NOT AT ALL SLIGHTLY          SOMEWHAT          A LOT

4.    She is interested in having new experiences.

          NOT AT ALL          SLIGHTLY          SOMEWHAT          A LOT

5.    She is interested in learning new things.

          NOT AT ALL SLIGHTLY          SOMEWHAT          A LOT

6.    She puts little effort into anything.

          NOT AL ALL          SLIGHTLY          SOMEWHAT          A LOT

7.    She approaches life with intensity.

          NOT AT ALL SLIGHTLY          SOMEWHAT          A LOT

8.    Seeing a job through to the end is important to her.

          NOT AT ALL SLIGHTLY          SOMEWHAT          A LOT

9.    She spends time doing things that interest her.

          NOT AT ALL SLIGHTLY          SOMEWHAT          A LOT

10.    Someone has to tell her what to do each day.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

11.    She is less concerned about her problems than she should be.

      NOT AT ALL SLIGHTLY        SOMEWHAT      A LOT

12.    She has friends.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

13.    Getting together with friends is important to her.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

14.    When something good happens, she gets excited.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

15.    She has an accurate understanding of her problems.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

16.    Getting things done during the day is important to her.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

17.    She has initiative.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

18.    She has motivation.

      NOT AT ALL SLIGHTLY        SOMEWHAT A LOT

Appendix B

Table B1

*Prevalence of Apathy and Depression in Previous Studies*

| Citation | *n* | Measures | | Prevalence (%) | | |
| --- | --- | --- | --- | --- | --- | --- |
| | | Apathy | Depression | Apathy Only | Depression only | Both |
| AD Patients | | | | | | |
| Benoit et al. (2008) | 686 | NPI | NPI | 30 | 8 | 12 |
| Starkstein et al. (2009) | 79 | AS | HamD | 18 | 19 | 13 |
| Starkstein, Ingram, Garau, & Mizrahi (2005) | 150 | Structured interview | HamD | 7 | 31 | 12 |
| TBI Patients | | | | | | |
| Kant, Duffy, & Pivovarnik (1998) | 83 | AES-S | BDI | 10 | 10 | 50 |
| Lane-Brown & Tate (2009) | 34 | AES-I | DASS | 32 | 13 | 35 |
| PD patients | | | | | | |
| Isella et al. (2002) | 30 | AES-S | GDS | 33 | 44 | 26 |
| Starkstein et al. (2009) | 164 | AS | Clinical interview | 5 | 33 | 26 |
| Pedersen , Larsen, Alves,  Aarsland (2009) | 232 | UPDRS subscale | MADRS | 15.5 | - | 11 |
| HIV patients | | | | | | |
| Rabkin et al. (2000) | 133 | AES-S | HamD | 10.5 | 3 | 1.5 |
| Tate et al. (2003) | 45 | AES-S | CMDI | 26 | 80 | |
| Stroke patients | | | | | | |
| Brodaty, Sachdev, Withall, Altendorf, Valenzuela, & Lorentz (2005) | 167 | AES-S | HamD | 29 | 7.9 | 3.5 |
| Starkstein, Fedoroff, Price, Leiguarda, & Robinson (1993) | 80 | AS | HamD | 9 | 18 | 9 |
| Withall, Brodaty, Altendorf, & Sachdev (2011) | 106 | AS | NPI | 6.6 | 3.8 | 21.7 |

*Note*. AD = Alzheimer's disease, TBI = traumatic brain injury, PD = Parkinson's disease,  NPI = Neuropsychiatric Inventory, AS = Apathy Scale, HamD = Hamilton Depression Scale, AES = Apathy Evaluation Scale (-I = informant, -S = self-rated), DASS = Depression Anxiety Stress Scale, GDS = General Depression Scale, UPDRS = Unified Parkinson's Disease Rating Scale, MADRS = Montgomery-Asberg Depression Rating Scale.

Appendix C

UNIVERSITY OF CAPE TOWN

**Faculty of Health Sciences**
**Human Research Ethics Committee**
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6626 • Facsimile [021] 406 6411
**e-mail:** shuretta.thomas@uct.ac.za

15 April 2011

HREC REF: 102/2011

Dr P Njomboro
Psychology
Upper Campus

Dear Dr Njomboro

**PROJECT TITLE: THE NEUROPSYCHIATRY OF APATHY.**

Thank you for your thoughtful and comprehensive response to the issues raised by the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the Human Research Ethics Committee has **formally approved** the above-mentioned study.

**Approval is granted for one year till the 30 April 2012.**

Please submit an annual progress report (FHS016) if the research continues beyond the expiry date. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file.

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

**Please quote the HREC REF in all your correspondence.**

Yours sincerely

A/PROF MARC BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

Appendix D

The Cornell Scale for Depression in Dementia (Alexopoulos, Abrams, Young, &

Shamoian, 1988a)

**Cornell Scale for Depression in Dementia**

Name_____    Age _____    Sex _____    Date _____

Inpatient                           Nursing Home Resident                           Outpatient

**Scoring System**

A = unable to evaluate          0 = absent          1 = mild or intermittent          2 = severe

Ratings should be based on symptoms and signs occurring during the week prior to interview. No score
should be given in symptoms result from physical disability or illness.

### A. Mood-Related Signs

| | | | | |
|---|---|---|---|---|
| 1. Anxiety: anxious expression, ruminations, worrying | a | 0 | 1 | 2 |
| 2. Sadness: sad expression, sad voice, tearfulness | a | 0 | 1 | 2 |
| 3. Lack of reactivity to pleasant events | a | 0 | 1 | 2 |
| 4. Irritability: easily annoyed, short-tempered | a | 0 | 1 | 2 |

### B. Behavioral Disturbance

| | | | | |
|---|---|---|---|---|
| 5. Agitation: restlessness, handwringing, hairpulling | a | 0 | 1 | 2 |
| 6. Retardation: slow movement, slow speech, slow reactions | a | 0 | 1 | 2 |
| 7. Multiple physical complaints (score 0 if GI symptoms only) | a | 0 | 1 | 2 |
| 8. Loss of interest: less involved in usual activities (score only if change occurred acutely, i.e. in less than 1 month) | a | 0 | 1 | 2 |

### C. Physical Signs

| | | | | |
|---|---|---|---|---|
| 9. Appetite loss: eating less than usual | a | 0 | 1 | 2 |
| 10. Weight loss (score 2 if greater than 5 lb. in 1 month) | a | 0 | 1 | 2 |
| 11. Lack of energy: fatigues easily, unable to sustain activities (score only if change occurred acutely, i.e., in less than 1 month) | a | 0 | 1 | 2 |

### D. Cyclic Functions

| | | | | |
|---|---|---|---|---|
| 12. Diurnal variation of mood: symptoms worse in the morning | a | 0 | 1 | 2 |
| 13. Difficulty falling asleep: later than usual for this individual | a | 0 | 1 | 2 |
| 14. Multiple awakenings during sleep | a | 0 | 1 | 2 |
| 15. Early morning awakening: earlier than usual for this individual | a | 0 | 1 | 2 |

### E. Ideational Disturbance

| | | | | |
|---|---|---|---|---|
| 16. Suicide: feels life is not worth living, has suicidal wishes, or makes suicide attempt | a | 0 | 1 | 2 |
| 17. Poor self esteem: self-blame, self-depreciation, feelings of failure | a | 0 | 1 | 2 |
| 18. Pessimism: anticipation of the worst | a | 0 | 1 | 2 |
| 19. Mood congruent delusions: delusions of poverty, illness, or loss | a | 0 | 1 | 2 |

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Acknowledgements

**Declaration**

1. I know that plagiarism is wrong. Plagiarism is to use another's work and pretend that it is one's own.

2. I have used the APA (6th ed.) convention for citation and referencing. Each contribution to, and quotation in, this essay from the work(s) of other people has been attributed, and has been cited and referenced.

3. This dissertation is my own work.

4. I have not allowed, and will not allow, anyone to copy my work with the intention of passing it off as his or her own work.

Signature _____