Conceptualization of Apathy symptoms in clinical practice

Tlholego Lekhutlile- LKHTLH001

Applied Cognitive Science and Experimental Neuropsychology Laboratory

Department of Psychology

University of Cape Town

Supervisor: Dr Progress Njomboro

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Abstract

Apathy is widely common in various neuropsychiatric, neurodegenerative and medical conditions and is associated with negative health outcomes. Although, this clinical syndrome is prevalent and associated with negative health outcomes, it is still poorly understood by clinicians and it is not formally recognized as a distinct diagnostic category in major classification manuals for mental disorders. Most clinicians are reluctant to treat apathy as a unique clinical syndrome and are unable to distinguish it from other related disorders such as depression. Using the Delphi approach this study aimed to: 1) establish how well clinicians could identify apathy symptoms, 2) establish if clinicians could distinguish apathy symptoms from depressive anxiety and fatigue symptoms and finally 3) to investigate whether academic clinicians differ from clinicians in their level of awareness of apathy symptoms. A total of 18 clinicians in the fields of neuropsychology, general medicine, neurology, clinical psychology and psychiatry participated in this study. All participants were administered a questionnaire that asked them to identify apathy symptoms from a total of 18 symptom description that included symptoms of apathy, depression, anxiety, and chronic fatigue. We found that apathy symptoms are poorly understood among clinicians and are frequently misidentified as depressive symptoms. Although overall, participants were poor at identifying symptoms of apathy, academic clinicians were significantly better at recognizing these apathy symptoms than clinicians who only did clinical practice The findings from this study suggests that more effort should be put in raising awareness of apathy symptoms among clinicians, particularly highlighting their differences from symptoms of depression.

Keywords: Apathy, Depression, Fatigue, Anxiety

Apathy or reduced motivation is one of the most frequent neuropsychiatric disorders following neurological change (Chase 2011; van Reekum, Stuss, Donald, & Ostrender, 2005). The disorder is also prevalent in some psychiatric, psychological and medical conditions. These disorders include Alzheimer's disease (AD), Vascular dementia (VaD), HIV/AIDS and affective illness (Clark et al., 2011; Starkstein, Ingram, Garau, & Mizrahi, 2005; Tagariello, Girardi, & Amore, 2009). Apathy is also common in disorders that involve pathology of the subcortical circuitry such as Huntington's and Parkinsons' diseases (for a review, see Ishii, Weintraub, James, & Mervis, 2009). Prevalence rates for apathy in most of these disorders are quite high. For instance, prevalence rates for apathy in traumatic brain injury (TBI) patients range from 60 % to 71 % across several studies (Andersson, Krogstad & Finset, 1999; Kant, Duffy, & Pivovarnik, 1998; van Reekum et al., 2005). In stroke, apathy has been reported in as high as 60 % of the patients (Starkstein et al., 2005). Evidence from other studies involving patients with Alzheimer's disease and others with focal frontal lesion show that the prevalence rate for apathy ranges from 60% to 80% in these disorders (e.g., Starkstein, Jorge, Mizrahi, & Robinson, 2006; Clark et al., 2011).

Marin (1990) is credited with coining the term apathy, to relate to observable affective, behavioral and cognitive deficits whose underlying cause is lack of motivation. According to Marin (1990), key aspects of apathy involve diminished goal directed behavior, which is operationalized as lack of effort and/ or initiation, and is evidenced by dependence on others to structure activities (Marin 1991). Another related feature is reduced goal directed cognition, which entails decreased enthusiasm to acquire new sets of skills or seek novel experiences, and also loss of insight and worry about one's functional status. There is also a reduced level of goal related emotions manifesting as inability to show emotional responsiveness to good or bad life events, and flat or unchanging affect. According to Marin (1991) these deficits should not be explained by emotional distress, retarded level of consciousness, or impairment in intellectual functioning. For a diagnosis of apathy, Marin (1991) proposes that the patient should present with one or more symptoms involving loss of goal oriented behavior, emotions and cognition (see also Starkstein, 2000; Robert et al., 2009; van Reekum et al. 2005).

Although the role of lack of motivation in apathy has been recently queried (e.g., Levy & Dubois, 2006) Marin's view remains largely dominant. Levy and Dubois (2006)'s alternative view conceptualizes apathy in terms of quantifiable reductions in self-generated voluntary and purposeful acts that has a neurological basis. According to this view, apathy is seen as a result of a pathology in the prefrontal cortex-basal ganglia circuitry, a system

generally known to be responsible for generating and controlling goal directed behavior (Levy & Dubois, 2006). These authors also propose that apathy is a pathology related to deficits in the activation of behavior.

Recently, a task force proposed a standard criteria for the diagnosis of apathy (Robert et al., 2009). The task force proposed that for a diagnosis of apathy, there should be loss of motivation for a duration not less than four weeks, together with corresponding impairments in any two of the major subdomains of apathy, namely; goal directed behavior, goal directed cognition and emotions. The deficits should cause significant impairment to a patient's general functioning and should not be attributable to physical disability and substance abuse. In a follow up study, Mulin et al. (2011) found that patients who met the apathy diagnostic score on the Neuropsychiatric Inventory (NPI) also met the proposed diagnostic criteria for apathy formulated by Robert and colleagues (2009).

Apathy is associated with a considerable decline in cognitive abilities (Ishii et al., 2009; Landes, Sperry, & Strauss, 2005). Several studies have shown a strong relationship between apathy symptoms and cognitive decline in conditions including Alzheimer's disease, schizophrenia, depression, and stroke (Starkstein et al., 2005; Starkstein, et al., 2006; Ready, Ott, Grace, & Cahn-Weiner, 2003). Apathy is also associated with problems related to activities of daily living (ADLs) and consequently results in significant caregiver burden and distress due to the patients' failure to independently meet their functional needs (Ishii et al., 2009; Starkstein et al., 2006). These functional deficits also manifest in negative behaviors such as poor dietary choices or lack of concern with personal hygiene (Butterfield, Cimino, Oelke, Hauser, & Sanchez-Ramos, 2010; Ishii et al., 2009). Additionally, apathy is also a reliable predictor of poor disease prognosis and worse illness outcomes (Clark et al., 2011; Ishii et al., 2009).

Despite the overwhelming evidence that apathy is a common neuropsychiatric outcome in most brain disorders, and is associated with negative health outcomes, the disorder remains poorly understood among both researchers and clinicians. For instance, there is a general lack of consensus on the conceptualization of apathy itself, and also on the composition of its symptoms (Leentjens et al., 2008). Apathy is also not formally recognized as a distinct syndrome like other disorders such as depression. For this reason apathy is not well defined in major diagnostic and disease classification systems such as the International Classification of Diseases (ICD 10) and the Diagnostic and Statistical Manual for Mental Disorders (DSM-5). In the DSM-5, apathy is only mentioned in the context of other syndromes, and also as part of personality alterations attributable to a medical condition

whereas the term is absent in the International Classification of Diseases (ICD 10). This is partly explained by the fact that apathy has traditionally been viewed as a symptom of other disorders such as depression, anxiety, and fatigue or as part of the negative symptoms spectrum in schizophrenia (Cochrane et al., 2015; Leentjens et al., 2008; Sagen et al., 2010). Similarly, apathy has also been confused with other disorders of goal directed behaviour such as abulia, akinesia and athymia. Although these other disorders have lack of spontaneity and lack of purposeful action as their common denominator, it is not yet clear whether they differ with apathy merely in terms of symptom severity or whether they have different underlying neural mechanisms (Vijayaraghavan, Krishnamoorthy, Brown, & Trimble, 2002).

To date, apathy is most commonly confused with depression, and traditionally, apathy has always been conceptualized as a symptom of depression. This is also reflected in most instruments that measure depression having specific items that relate to apathy (e.g., the Hamilton depression rating scale; Hamilton, 1976). One reason for this confusion is that depression and apathy have shared symptomatology, such as anhedonia, loss of interest, and diminished levels of activity (Levy et al., 1998; Starkstein et al., 2005). These symptoms may be part of depressive symptoms but may also result from lack of motivation which is a key marker of apathy (see Marin, 1991). In addition, depression is often comorbid with apathy in various disorders such as stroke, fronto temporal dementia, progressive supranuclear palsy and Parkinson's disease (Levy et al., 1998; Sagen et al., 2010). The confusion regarding the nosological position of apathy and the failure to differentiate it from depression can however have negative clinical consequences and health costs. For example, patients with apathy who are misdiagnosed with depression can end up being enrolled in depression pharmaceutical interventions. This has been shown to worsen their condition (see Fava, Graves, Benazzi, 2006; Hoehn-Saric, Lipsey, & Mc Leod, 1990; Wongpakaran, N., van Reekum, Wongpakaran T., & Clarke, 2007).

Over the past 10 to 15 years, several lines of research have emerged showing that although apathy and depression have shared symptomatology, they are in fact separate clinical conditions with distinct clinical features. For instance, depression is usually marked by negatively biased thoughts, emotional distress, loss of hope and suicidal ideation. On the other hand apathy is essentially a disorder that is marked by pathological motivational drive and lack of goal directed activity (Levy et al., 1998; Njomboro & Deb, 2012; Starkstein et al., 2005). Depression can also be characterized by symptoms such as hallucinations, anxiety and irritability but these symptoms don't constitute the clinical definition of apathy (Levy et al., 1998). There is also evidence showing that depressed patients are generally distressed by

their symptoms whereas apathetic patients are not overly concerned about their apathy state (Levy et al., 1998; Marin, 1996). Pharmacological studies on depression and apathy also suggest that these two conditions are neurochemically distinct. For example, dopaminergic agonist and acetylcholinesterase inhibitors are usually used in treating apathy and they have been shown to produce promising results in abating apathy symptoms (Chase, 2011; Gauthier, et al., 2002; van Reekum et al., 2005). On the contrary, these agents are not useful treatment options for depression, which is mostly treated with selective serotonin reuptake inhibitors, or with anti-psychotics in certain instances (Chase, 2011). Furthermore, brain imaging and lesion studies also suggest that depression and apathy involve different regions of the brain and that they also have distinct underlying neural involvement. For example, apathy is related to a dysfunction of frontal cortical structures such as the orbito prefrontal cortex, anterior cingulate cortex and the middle temporal regions, while depression involves dysfunction of frontal- striatal and limbic circuits (Landes, Sperry, Strauss, & Geldmacher, 2001; Njomboro & Deb, 2012).

Apart from being confused with depression, apathy can also be misidentified as a symptom of anxiety or fatigue (Bogdanova & Croni-Golomb, 2012; Cochrane et al., 2015; Ishi et al., 2009). In the context of anxiety, this confusion may be due to anxiety having overlapping symptoms with depression (which in turn has overlapping symptoms with apathy). This confusion has been shown in conditions such as Parkinson's disease, where anxiety is also often associated with depression (Bogdanova & Croni-Golomb, 2012). Nonetheless, there is wealth of evidence showing that apathy and anxiety have different neural correlates. For instance, unlike apathy, anxiety is associated with the left hemisphere involvement (Bogdanova & Croni-Golomb, 2012). Fatigue on the other hand is a disorder marked by an overwhelming sense of tiredness, lack of energy and feelings of exhaustion (Cochrane et al., 2015). This condition can easily be confused with apathy in the sense that a patient who suffers from chronic fatigue is less likely to be productive, and also engages in limited goal directed activity, just as is seen in apathy (Marin, 1991). Some studies have shown close associations between apathy and fatigue in some disorders (e.g., Cochrane et al., 2015). However, apathy and fatigue are distinct conditions, with different neural substrates (Chaudhuri & Behan, 2000).

The confusion around the nosological position of apathy has meant that research into the condition has been difficult. As a result there is no standard pharmacological intervention for apathy symptoms. However, some studies using both socio-environmental interventions and pharmacological treatments have yielded promising results. For instance, randomized

controlled trials have shown that acetylcholinesterase inhibitors such as donepezil, galantamine and rivastigmine reduces apathy symptoms in AD patients (Gauthier, et al., 2002; Tariot et al., 2001). Other studies have shown that dopaminergic drugs such as amantadine and bromocriptine also significantly abate apathy symptoms (van Reekum et al., 2005; Campbell & Duff, 1997). However, there are yet to be controlled trials for these agents. Other possible psychological treatment modalities have been suggested for the treatment of apathy. These interventions include cognitive behavioral therapy and music therapy (Ishii et al., 2009). However, there is no evidence showing that cognitive behavioral therapy and music therapy have been empirically validated.

The current literature suggest that apathy is a distinct neuropsychiatric syndrome with specific underlying neural substrates, adverse health outcomes and specific treatment options, and that this syndrome is dissociable from other seemingly related conditions such as depression, anxiety and chronic fatigue. Despite this evidence, many clinicians are still hesitant to recognize apathy as a distinct condition and are also unable to differentiate it from a related family of disorders in which goal directed activity is impaired (Vijayaraghavan et al., 2002). Research that surveys how clinicians and researchers conceptualize apathy symptoms is important in relation to other neuropsychiatric conditions. This research is particularly important in South Africa and neighboring countries. There is evidence that clinicians in countries such as South Africa and Botswana are more likely to encounter patients with apathy or who are susceptible to develop it at some stage. For instance, it is reported that about 5 million people in South Africa are living with HIV/AIDS (Joska, Hoare, Stein, & Flisher, 2011) and the estimated prevalence rate of HIV/AIDS in Botswana is around 27 % (Stover, Fidzani, Molomo, Moeti, & Musuka, 2008). Apathy is one of the most prevalent disorders in HIV/AIDS (Clark et al., 2011). In addition there is evidence that South Africa has one of the highest incidences of road traffic accidents in the world and about ninety thousand cases of traumatic brain injury in South Africa are accounted for by these accidents (National Institute for Occupational Health, 2011). Furthermore, other causes of acquired brain damage, such as violence and assaults, are also common (Levin, 2004; National Institute for Occupational Health, 2011). Apathy is also one of the most frequent neuropsychiatric disorders in patients with brain damage (van Reekum et al., 2005). It is therefore important to investigate how clinicians in these countries conceptualize apathy symptoms. The outcome of such an enquiry will help assess the level of appreciation of apathy symptoms and also help inform the diagnosis of apathy and the planning of treatment approaches. On that basis, this study aimed to: 1) establish clinicians' awareness of apathy

symptoms, 2) to establish if clinicians can differentiate apathy symptoms from depression symptoms and finally 3) to investigate whether academics differ with clinicians in their awareness of apathy symptoms. Based on the available literature (e.g., Vijayaraghavan, et al., 2002) and on anecdotal evidence, I hypothesize that the participants will be less aware of apathy symptoms. I also hypothesize that participants will misidentify apathy symptoms as depression symptom dimensions. Lastly, I hypothesise that academics will be more likely to have a correct conceptualisation of apathy symptoms than clinicians because there has been lots of research and literature on apathy in the last 10 years.

Methods

Design and setting

In this study a cross sectional survey was used to investigate whether clinicians could identify apathy symptoms against symptoms of other disorders that apathy is commonly confused with. The study is an initial step to a bigger study that is using the Delphi approach to collect views on apathy symptoms and ultimately come up with a consensus position on these symptoms as well as a scale to measure them. The Delphi approach is a systematic way of collecting data about a particular issue from a pool of experts in a particular area of interest and is widely used in research across different fields (Fish & Osborn, 1992). The approach is most suitable for studies that aim to develop an agreement on a topic that is surrounded by different positions (Fish & Osborn, 1992; Vijayaraghavan, et al., 2002). On that basis, the Delphi technique is more appropriate for this study given the current lack of consensus on the conceptualisation of apathy among researchers and clinicians. Based on this theoretical framework of the Delphi approach, participants were selected on the basis of their expertise and experience with neuropsychiatric symptoms. They were selected using convenient sampling in Botswana and South Africa.

The Apathy scale covered behavioral, cognitive and emotional subdivisions of apathy symptoms. The questionnaires sampled whether the items in the questionnaire reflected apathy, depression, fatigue and anxiety.

Participants

Participants for this study were drawn from a pool of experts in clinical fields that are more likely to deal with patients with apathy symptoms. These included neuropsychology, general medicine, neurology, clinical psychology and psychiatry. Participants were selected based on their expertise and experience. Invitations to participate in the study were sent to

more than a hundred clinicians, and a total of 18 participants took part in the study. The literature suggest that a sample of 18 experts is sufficient to generate consensus on studies of this nature Delbecq, van de Ven, & Gustafson, 1975; Hasson, Keeney & Mc Kenna, 2000). The sample size in studies using the delphi technique is not based on statistical power, but rather on expertise and experience (Hsu & Standford, 2007). All participants had at least one year post qualification and most of them were in clinical practice (See table 1 below).

Table 1. Demographics

Area of expertise	Academia		Clinical practice		Both		Total	
	N	%	N	%	N	%	N	%
Clinical psychology	2	50	1	25	1	25	4	22.2
Medicine	0	0	9	90	1	10	10	55.6
Neuropsychology	0	0	0	0	1	100	1	5.6
Psychiatric nursing	0	0	3	100	0	100	3	16.7
Total	2	11.1	13	2.2	3	16.7	18	100

The sample comprised 10 (55.6 %) medical doctors, 4 (22.2%) clinical psychologists, 3 (16.7%) psychiatric nurses and 1 (5.6%) neuropsychologist. These professional were either in clinical practice, academia or both clinical practice and academia. Majority of the participants were in clinical practice (72.2%). Participants who were in both academia and clinical practice made 16.7% of the total sample. The least was academia, which made only 11.1% of the total sample. Most of the participants (50%) have been clinicians for years ranging from 1 to 5. They were followed by clinicians who worked for a period ranging from 6 to 10 years (27.8%). 11. 1% of the participants have been in their respective fields for 11 to 15 years. Around 11% of the participants worked for more than 16 years.

Measures

The data was collected using a Delphi questionnaire which was developed using sampled items from scales that assess apathy, depression, fatigue and anxiety. The survey questionnaire was developed from all the 18 items on the Apathy Evaluation Scale (AES; Marin, Biedrzycki, & Firinciogullari, 1991) and one item from the Neuro-Psychiatric Inventory (NPI; Cummings et al., 1994) and some from the Lille Apathy Rating Scale

(LARS; Sockeel et al., 2006). The AES items were chosen because the scale is the most widely used measure of apathy and has demonstrated good psychometric qualities across clinical samples such as stroke, Alzheimer's disease and major depression (see Marin et al., 1991 for a detailed review). Selection of which apathy items to include from the NPI and LARS was based on current conceptualization of apathy in recent literature that we deemed not sufficiently covered by the AES. The questionnaire also included 11 items from the Beck's Depression Inventory II (Beck, Steer, & Brown, 1996), and 7 fatigue items from the brief self-rated fatigue measure (Michielsen, De Vries, & Van Heck, 2003). In addition, 5 anxiety items were sampled from Beck's Anxiety Inventory (Beck & Steer, 1990). In total, the questionnaire had 56 items excluding items for demographic information (see Appendix 1, see also appendix 2 for where which item was adopted from). The questionnare was estimated to take between 10 and 15 minutes to complete. Most studies using the delphi technique make use of an unstructured questionnaire in the initial phase (Hsu & Standford, 2007; Proctor & Hunt, 1994). I however used structured questionnaire in the inial phase because there is evidence supporting the use of strucured questionnaires in the first phase of Delphi survey particularly when the information is readily accesible from the literature (Kerlinger, 1973).

Procedure

An inivitation to participate in the study together with a Microsoft word electronic copy of the questionnare and a link to its google forms version were sent to emails of potential participants (see Appendix 1). The participant had to decide whether an item belonged to apathy, depression, fatigue or anxiety or a combination of these clinical conditions. The questionnaire was electronically distributed among clinicians and academics in the faculty of Health Sciences and the Psychology department at the University of Cape Town, and the Psychology department at University of Botswana . We also invited clinicians in four hospitals in Botswana namely, Selebi Phikwe Government Hospital, Scottish Livingston hospital, Sbrana Psychiatric Hospital and Princess Marina Referral Hospital to participate in the study. All the Participants gave informed consent and ethics approval for the study was granted by the Faculty of Humanities at the University of Cape Town (see Appendix 1 for the consent and ethics Information)

Statistical analysis

Participants' apathy score was based on the total number of apathy items that the participants correctly identified. Apathy items which were identified by the participants as

symptomatic of both apathy and another condition (depression, fatigue and anxiety) were excluded in computing total apathy score. These items were excluded because previous research on apathy items on the apathy evaluation scale have shown that these items relate more to apathy than those other conditions (see Chase, 2011; Marin et al., 1991; Clarke et al., 2007). The total possible score for apathy was 18 and the least was 0. The Depression score was the total number of correctly identified depression items from the questionnaire. The highest possible score for depression was 11. Anxiety and fatigue total scores were also the total number of correctly identified items belonging to the two syndromes. The possible total scores for anxiety and fatigue were 5 and 7 respectively. If each of the items was correctly identified by 70% of the responded or more, we concluded that clinicians had a correct conceptualization of that symptom dimension in relation to the disorder it was symptomatic for. Other researchers using the Delphi technique have also suggested that a 70% consensus or more should be used in deciding which symptoms are familiar to participants (e.g., Hsu & Standford, 2007; Proctor & Hunt, 1994). However, some researchers have suggested that the level of consensus should be set at 80% (e.g., Hasson, Keeney and Mc Kenna, 2000).Of interest to the study was how many apathy items were correctly identified by 70% or more of the participants. Although the main focus of the study was on apathy symptoms, the same approach was adopted for depressive, anxiety and fatigue symptoms. In addition, a percentage of how many apathy items were misidentified was also computed. Independent samples t-tests were also performed to investigate whether clinicians and academics differed in recognition of the symptoms. The analysis was carried out using Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 22.

Results

The results show that the participants had a poor conceptualization of apathy. The average apathy score was low (M= 5.67, SD= 4.00) out of the possible score of 18. In addition all apathy items had an identification rate that was below 70%. Table 2 below shows identification rates for all apathy symptom dimensions, with those with higher recognition rates at the top of the table.

Table 2. Responses to symptoms of Apathy

Symptoms	Apathy	
	N	%
The patient no longer has self-initiative.	11	61.1
The patient no longer has self-motivation.	10	55.6
The patient no longer shows interest in things.	7	38.9
The patient no longer puts effort into anything.	7	38.9
The patient is no longer interested in learning new things.	7	38.9
The patient no longer gets things done during the day.	5	27.8
The patient needs to be told by someone what to do each day.	5	27.8
The patient no longer places importance in getting things started on his/her own.	5	27.8
The patient no longer has friends.	5	27.8
The patient is no longer concerned about personal problems.	5	27.8
The patient no longer places importance on doing a job and seeing it through to the end.	6	22.2
The patient no longer places importance on getting things done during the day.	4	22.2
The patient is no longer interested in having new experiences.	4	22.2
The patient no longer gets excited when something good happens.	3	16.7
The patient no longer spends time on personal interests.	3	16.7
The patient no longer approaches life with intensity.	3	16.7
The patient no longer has an accurate understanding of personal problems.	2	11.1
The patient no longer places importance on getting together with friends.	2	11.1

Some apathy symptoms were misidentified as depressive symptoms. For instance two apathy items relating to lack of insight and lack of interest in social relations had a

response rate above the 70% cut off, indicating that most participants conceptualized these symptoms as part of depressive symptoms. Table 3 gives the percentages of participants who misidentified apathy symptoms as symptoms of depression.

Table 3. Rate of Apathy items misidentified with depression

Symptoms	Depression	
	N	%
The patient no longer has an accurate understanding of personal problems.	13	72.2
The patient no longer places importance on getting together with friends.	13	72.2
The patient is no longer concerned about personal problems.	12	66.7
The patient no longer has friends.	9	50.0
The patient no longer gets excited when something good happens.	7	38.9
Patient no longer places importance on getting things done during the day.	7	38.9
The patient is no longer interested in having new experiences.	7	38.9
The patient no longer places importance on doing a job and seeing it through to the end.	6	33.3
Patient no longer places importance in getting things started on his/her own.	6	33.3
The patient no longer spends time on personal interests.	6	33.3
The patient no longer shows interest in things.	5	27.8
The patient needs to be told by someone what to do each day.	5	27.8
The patient is no longer interested in learning new things.	4	22.2
The patient no longer puts effort into anything.	3	16.7
The patient no longer has self-initiative.	2	11.1
The patient no longer gets things done during the day.	2	11.1
The patient no longer approaches life with intensity.	2	11.1
The patient no longer has self-motivation.	1	5.6

Across participants, the average depression score was high (M=8.94, SD= 1.39; Max =11). In addition, 80 % of depression items had an identification rate of more than 70%. For instance all the participants (100%) correctly identified suicidal thoughts and wishes poor self-esteem as symptoms of depression. In addition, over 90% of the respondents correctly identified sadness and having feelings of worthlessness as symptoms of depression only. Table 4 shows the percent identification rates for depressive symptoms. None of the depression items had a misidentification rate of more than 15%.

Table 4. Responses to depression items

Statement	Depression		Apathy	
	N	%	N	%
The patient has suicidal thoughts and wishes.	18	100	0	0.0
The patient blames self a lot.	18	100	0	0.0
The patient is sad and unhappy most of the time.	17	94.4	0	0.0
The patient expresses feelings of being worthless.	17	94.4	1	5.6
The patient cries more often than before.	16	88.9	0	0.0
The patient has lost appetite	15	83.3	1	5.5
The patient says the future if hopeless.	15	83.3	1	5.6
The patient has become more irritable and easily gets annoyed.	14	77.8	0	0.0
The patient has become restless.	12	66.7	0	0.0
The patient no longer shows pleasure from previously enjoyed activities.	10	55.6	1	5.6
The patient has become indecisive.	9	50.0	2	11.1

An independent samples t-test was performed to compare recognition rate for apathy between clinicians who were also academics and those who only did clinical work. Academic clinicians had a higher recognition rate for apathy symptoms (M= 10.20, SD= 2.05) than clinicians (M= 3.92, SD= 3.07). This difference was statistically significant (t (18, 16) = -4.19, p< 0.001). In addition, a dependent samples t-test was also performed to compare recognition rates of the participants for apathy and depression. This statistical test was also performed to compare recognition rates of the participants for apathy and fatigue and also for apathy and anxiety. By comparing depression and apathy scores, we found that participants recognized depression items better (M= 8.94, SD= 1.39) than apathy items (M= 5.67, p= 0.008). This difference was statistically significant (t (18, 17) = -.3.024, p= 0.008). The participants were better at recognizing apathy (M= 5.67, SD= 4.00) than fatigue (M= 2.56, SD= 1.46). The difference was statistically significant (t (18, 17) = 3.95, p= 0.001).We also found that participants were also better at recognizing apathy items (M= 5.67, SD= 4.00) than anxiety (M= 1.50, SD= 1.10). The difference between the recognition rate of the participants for apathy and depression was statistically significant (t (18, 17) = 5.56, p<0.001).

Discussion

The purpose of this study was to establish how well apathy symptoms were understood among clinicians. We also wanted to establish if clinicians could distinguish apathy symptoms from those of depression, anxiety, and chronic fatigue. Finally, we also investigated whether academic clinicians differ with non-academic clinicians in their awareness of apathy symptoms capture the current conceptualization of apathy symptoms. The results indicate that overall apathy symptoms are poorly understood. Both academic and non-academic clinicians were poor at identifying apathy symptoms. The identification rate for all apathy items was below the baseline rate proposed by Hsu and colleagues (2007).

Furthermore, a significant number of apathy symptoms were misidentified as relating to depression. The poor understanding of apathy symptoms reported in this study is consistent with results from previous studies (e.g., Vijayaraghavan, et al., 2002). Part of the problem is that despite recent efforts to create diagnostic criteria for apathy (e.g., Robert et al., 2009), the disorder remains largely ill-defined and poorly conceptualized by both researchers and clinicians, and its nosological position is still a subject of debate (Chase, 2011, Leentjens et al., 2008; Vijayaraghavan, et al., 2002). Apathy is also not formally recognised as a unique clinical syndrome and until recently, rarely featured in neuroscience, neuropsychology and mental health textbooks (Chase, 2011).

The confusion between apathy and depressive symptoms shown in this study might also be due to the fact that apathy has traditionally been treated as a symptom of depression. This is further confounded by the reality that quite often, apathy and depression have high cormorbidity in most neurological disorders. In addition, apathy forms part of diagnostic criteria in some assessment measures for depression (Leentjes et al., 2008; Levy & Dubois, 2006; Marin 1991; Starkstein, 2000). Over the years research has however shown that symptoms of apathy are distinct from symptoms of depression, both in their neurochemical substrates and clinical profiles. For instance, lack of concern for one's status, diminished level of activity and lack of interest have historically been seen as symptoms of depression but have now been found to relate to apathy than depression (Marin, 1991; Njomboro & Deb, 2012; Robert et al., 2009; Starkstein, 2005).

On the other hand identification of depressive symptoms was good. The recognition rate for depressive symptoms was higher than that for apathy items. This is partly explained by the fact that depression is recognized as a unique clinical syndrome and has received considerable scholarly and clinical attention (Leentjes et al., 2008; Levy et al., 1998). Depression is also well defined in major disease classification manuals such as the diagnostic and statistical manual for mental disorders, firth edition (American Psychology association, 2013). Most researchers and clinicians are therefore more likely to be familiar with depression and its symptom profile. On that basis it is unlikely that depressive symptoms can be confused with symptoms apathy.

Although, the results of this study indicate that both academic clinicians and clinicians doing only clinical poorly conceptualize apathy symptoms, academic clinicians had a relatively better conceptualization of apathy symptoms than clinicians in clinical practice only. This result might be explained by the fact that apathy has predominantly been a research concept and clinical practice usually lags behind research (Chase, 2011). Research output on apathy, its neuropathology and treatment has grown rapidly (e.g., Gauthier, et al., 2002; Levy & Dubois, 2006; van Reekum et al., 2005) but it is yet to be formally recognized as a diagnostic category in major classification manuals such as ICD-10 and DSM-5. It is as such understandable why experts in clinical practice seem to have a poor conceptualization of apathy compared to academics. Academics are likely to be knowledgeable with latest empirical advances in their respective areas than clinicians.

Nonetheless, apathy items had a higher recognition rate when compared to anxiety and fatigue items. This result is surprising because one would assume that anxiety and fatigue symptoms will be more recognizable than apathy symptoms because the nosological

positions of anxiety and fatigue are not questionable. Clinicians will as such be more aware of these symptoms than apathy symptoms.

In summary, the results of this study mean that clinicians may be missing apathy symptoms and misdiagnosing apathy as depression, thereby giving wrong treatments that have negative side effects on patients and huge costs on the health delivery system.

Conclusion

It is now recognized that apathy has deleterious consequences on general health and interpersonal relationships. However, it is still poorly understood in clinical practice and mostly treated as a symptom of depression. The confusion between apathy and depression can have serious clinical implications as apathy patients can be misdiagnosed with depression and prescribed depression medication. Wrong medication and erroneous treatment modalities may worsen apathy symptoms. The lack of a consensus on the clinical definition of apathy has also limited research advances in this area, particularly research on treatment approaches. It is therefore vital for apathy to be recognized as a unique clinical condition with specific etiology. Development of a clear conceptual and clinical definition for apathy will also help in its diagnosis and possible treatment options. Efforts should be made to have apathy included in disease classification manuals as a distinct clinical condition. Given the negative outcomes associated with apathy it will be important to educate clinicians on apathy and its symptom composition.

Limitations

The results of this study should be discussed in the context of some limitations. Firstly, the time frame with which this study was undertaken was a limitation. It required more time particularly because it was embedded within the Delphi approach which is known to be time consuming. Owing to this limited time, I did not have the time to undertake the second round of the Delphi approach. It was proposed that the second questionnaire will be developed which will consist of the items that 70% of the participant believed that they reflect apathy symptoms. The questionnaire would have then be resent to the participants for reevaluation. However, I did not proceed to this second phase because of time limitation. However, the study is informative since it has managed to show how apathy is conceptualized in clinical practice.

Secondly, I had a relatively small sample size. The sample size was small possibly because my target population was a generally busy population; as such I had to give them

more time to respond to the questionnaire. Unfortunately, I didn't have that time. I however, don't think this limitation will necessarily affect my results negatively because studies utilizing the Delphi technique are not based on statistical power but on expertise and experience. Lastly, the majority of the participants in this study were medical doctors. It is possible that the results generally reflect their understanding of apathy not other experts underrepresented in this study.

Despite these limitations, this study had strengths. It was the first of its kind in South Africa. It has therefore laid the ground for future research on this area. It has provided valuable information on how apathy is conceptualized in clinical practice. This information has the potential to inform future research on apathy and also inform the diagnosis and treatment of apathy. In addition, this study is likely to shed some light on the distinctiveness of apathy, adding to what has been previously found in many years of research on this subject.

Recommendations

I recommend that follow up research should be conducted on this subject using a large sample and with additional rounds of the Delphi technique. Additional rounds will help to establish a consensus on which symptoms reflect apathy. I also recommend that future research should strive to get a fairly equal number of experts in this area, so that the results don't seem to reflect views of a certain profession.

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I acknowledge the contribution and support I was given by my supervisor, Dr Progress Njomboro for the entire duration of this study. Many thanks also to Professor Collin Tredoux and Michelle. Special thanks also to Kerapetse Keabile, who assisted with data collection in Botswana. Department of staff training and development at the University of Botswana funded this research. Lastly, I thank my participants for their participation.

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Appendix 1

Conceptualization of neuropsychiatric syndromes among clinicians

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You are being invited to take part in a study on symptoms of Depression, Apathy, Fatigue and Anxiety. Your participation in this study is important because we hope the information you provide will help define these conditions and also inform their management. Participation is voluntary and if you choose to stop participating at any point of the survey you are free to do so. However, it will be very valuable to us if you complete the questionnaire. The information you provide will not be associated with your name in any way and it will be treated with utmost confidentiality. There are no known risks associated with participation in this study.

If you need further information about your participation you can contact Dr Progress Njomboro (Progress.Njomboro@uct.ac.za) or Tlholego Lekhutlile for the outcome of the study at **LKHTLH001@myuct.ac.za or on +27 60 7322 537.**

Please fill in all items on this questionnaire by **clicking on the box next to your preferred answer.**

Before continuing please consent to taking part in this study by clicking **Agree** below.

I consent to participate in this study.

☐ Agree

☐ Disagree

What is your area of expertise?

☐ Neuropsychology

☐ Neuropsychiatry

☐ Psychiatry

☐ Neurology

☐ Medicine

☐ Clinical Psychology

☐ Psychiatric Nursing

☐ Clinical Social work

Other: _____

2. **For how long have you worked as a clinician?**

☐ 1-5 years

☐ 6-10 years

☐ 11-15 years

☐ 16-20 years

☐ More than 20 years

3. Which sector are you working in?

☐ Clinical practice

☐ Academia

☐ Both clinical practice and academia

Other_____.

4. How knowledgeable are you about symptoms of Depression?

☐ Very knowledgeable

☐ Fairly knowledgeable

☐ Not knowledgeable

5. How knowledgeable are you about symptoms of Apathy?

☐ Very knowledgeable

☐ Fairly knowledgeable

☐ Not knowledgeable

6. How knowledgeable are you with symptoms of Anxiety?

☐ Very knowledgeable

☐ Fairly knowledgeable

☐ Not knowledgeable

7. How knowledgeable are you about symptoms of fatigue?

☐ Very knowledgeable

☐ Fairly knowledgeable

☐ Not knowledgeable

Items 8 to 63 describe common neuropsychiatric symptoms. Please indicate whether these symptoms belong to Apathy, Depression, Anxiety or Fatigue.

8. The patient no longer has self-motivation.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

9. The patient has lost weight.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

10. The patient no longer has an accurate understanding of personal problems.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

11. The patient no longer has self-initiative.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

12. The patient gets tired very quickly.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

13. The patient has become more oppositional and hard to handle.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

14. The patient no longer expresses emotion in the voice or on the face.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

15. The patient has lost appetite.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

16. The patient has suicidal thoughts and wishes.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

17. The patient leaves tasks unfinished and is not concerned about it.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

18. The patient no longer gets things done during the day.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

19. The patient no longer engages in previous activities and hobbies.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

20. The patient no longer seeks the company of others.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

21. The patient no longer attends meetings or social events.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigu

22. The patient no longer shows interest in things.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

23. The patient has become restless.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

24. The patient has become more passive and compliant.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

25. The patient no longer places importance on doing a job and seeing it through to the end.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

26. The patient sleeps most of the time.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

27. The patient no longer puts effort into anything.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

28. The patient frequently forgets to do tasks and chores.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

29. The patient no longer gets excited when something good happens.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

30. The patient gets easily distracted when doing tasks.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

31. The patient no longer attends to personal hygiene unless told to do so by someone.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

32. The patient has little energy to finish through simple tasks.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

33. The patient blames self a lot.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

34. The patient has become slower in movement, speech and reactions.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

35. The patient no longer places importance on getting together with friends.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

36. The patient cries more often than before.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

37. The patient is no longer interested in learning new things.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

38. The patient is indifferent to both pleasant and unpleasant events.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

39. The patient gets excited for no apparent reason.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

40. The patient needs to be told by someone what to do each day.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

41. The patient no longer starts a conversation unless spoken to first.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

42. The patient no longer enquires about friends and loved ones.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

43. The patient no longer places importance in getting things started on his/her own.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

44. The patient is sad and unhappy most of the time.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

45. The patient no longer spends time on personal interests.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

46. The patient seems neither happy nor sad.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

47. The patient worries about trivial things.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

48. The patient no longer talks about future goals or plans.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

49. The patient has become more irritable and easily gets annoyed.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

50. The patient says the future if hopeless.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

51. The patient leaves tasks unfinished and is not concerned about it.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

52. The patient is sad and unhappy most of the time.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

53. The patient has become indecisive.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigu

54. The patient complains of exhaustion.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

55. The patient no longer shows pleasure from previously enjoyed activities.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

56. The patient no longer has friends.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

57. The patient no longer approaches life with intensity.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

58. The patient is no longer concerned about personal problems.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

59. The patient no longer places importance on getting things done during the day.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

60. The patient expresses feelings of being worthless.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

61. The patient has problems with concentration.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

62. The patient no longer expresses affection towards loved ones.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

63. The patient is no longer interested in having new experiences.

☐ Apathy

☐ Depression

☐ Anxiety

☐ Fatigue

Thank you for your participation.

Appendix 2

The patient no longer has self-motivation (AES).

The patient no longer has an accurate understanding of personal problems (AES).

The patient no longer has self-initiative (AES).

The patient no longer gets things done during the day (AES).

The patient no longer shows interest in things (AES).

The patient no longer places importance on doing a job and seeing it through to the end (AES).

The patient no longer puts effort into anything (AES).

The patient no longer gets excited when something good happens (AES).

The patient no longer places importance on getting together with friends (AES).

The patient is no longer interested in learning new things (AES).

The patient needs to be told by someone what to do each day (AES).

The patient no longer places importance in getting things started on his/her own (AES).

The patient no longer spends time on personal interests (AES).

The patient no longer has friends (AES).

The patient no longer approaches life with intensity (AES).

The patient is no longer concerned about personal problems (AES).

The patient no longer places importance on getting things done during the day (AES).

The patient is no longer interested in having new experiences (AES).

The patient has problems with concentration (Brief self-rated fatigue measure).

The patient sleeps most of the time (Brief self-rated fatigue measure).

The patient complains of exhaustion (Brief self-rated fatigue measure).

The patient gets tired very quickly (Brief self-rated fatigue measure).

The patient has little energy to finish through simple tasks (Brief self-rated fatigue measure).

The patient worries about trivial things (Brief self-rated fatigue measure).

The patient has lost weight (Brief self-rated fatigue measure).

The patient no longer engages in previous activities and hobbies (Beck's anxiety inventory).

The patient frequently forgets to do tasks and chores (Beck's anxiety inventory).

The patient gets easily distracted when doing tasks (Beck's anxiety inventory).

The patient gets excited for no apparent reason (Beck's anxiety inventory).

The patient gets excited for no apparent reason (Beck's anxiety inventory).

The patient has lost appetite (BDI- II).

The patient has suicidal thoughts and wishes (BDI- II).

The patient has become restless (BDI- II).

The patient blames self a lot (BDI- II).

The patient cries more often than before(BDI- II).

The patient is sad and unhappy most of the time (BDI- II).

The patient has become more irritable and easily gets annoyed (BDI- II).

The patient says the future if hopeless (BDI- II).

The patient has become indecisive (BDI- II).

The patient no longer shows pleasure from previously enjoyed activities (BDI- II).

The patient expresses feelings of being worthless (BDI- II).