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A Correlational Study of Apathy and Depression in Parkinson's Disease

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Abstract

Common psychiatric traits in patients with Parkinson's disease (PD) include apathy (diminished motivation with a lack of caring) and depression (sadness with a sense of facing overwhelming challenges). Past research studies of the relationships between apathy and depression in PD have resulted in conflicting conclusions. In this study 121 patients with idiopathic Parkinson's disease were recruited during attendance at an outpatient interdisciplinary clinic (mean age = 72.6 years, $SD = 8.6$). Each completed the Apathy Scale (AS) and the Beck Depression Inventory II (BDI-II). The primary data analysis was a Pearson correlation between the AS and an 18-item apathy-corrected BDI-II score (questions 4, 12, and 15 of the BDI-II are arguably related to apathy and were therefore removed). The result was statistically significant ($r = .44$), but this correlation also indicates that most of the variance in the two variables is not shared. The correlation between the AS and the entire BDI-II was only slightly stronger, ($r = .49$). A secondary analysis using the recommended cut-off scores for each assessment indicated that 32 (26%) had both apathy and depression, 17 (14%) had depression only, 36 (30%) had apathy only, and 36 (30%) had neither. Results were similar using an apathy-adjusted cut-off score for the BDI-II. In conclusion, apathy and depression appear correlated with each other, but one of these psychiatric characteristics often appears without the other, when using standard cut-off scores or when adjusting for apathy-related items in the BDI-II. The profession of occupational therapy, based on enhancing occupational participation, should address separate yet potentially coordinated interventions for both apathy and depression.

Parkinson's disease is a progressive degenerative disease of the basal ganglia (Melnick, 1995). It is the second most prevalent neurological disease in America (Christensen, 2005). The four cardinal features of PD are resting tremor, rigidity, bradykinesia, and postural impairment (Gaudet, 2002). There are also common cognitive and psychiatric features seen in patients with PD (Barbas, 2006) as well as other common non-motor symptoms such as autonomic dysfunction, sensory symptoms, and pain (Poewe, 2008). The etiology of this disease is unknown although several causes have been suggested, such as viral infection, environmental factors, and genetics (Melnick, 1995). Diagnosis of PD is best determined through clinical criteria; however, confirmation of the disease is only determined post-mortem (de Lau & Breteler, 2006).

Common psychiatric and affective changes in patients with PD include apathy, depression, anxiety, (Barbas, 2006) cognitive dysfunction and dementia, psychosis, and sleep disorders (Poewe, 2008). This study focuses on apathy and depression. Apathy is defined by Marin (p. 22, 1990) as "diminished motivation not attributable to diminished level of consciousness, cognitive impairment, or emotional distress." Depression is known as one of the most recognizable psychiatric features in PD and may occur at any stage of the disease (Ferreri, Agbokou, & Gauthier, 2006). It is defined by Comer (p. 158, 2002) as "a low, sad state in which life seems dark and its challenges overwhelming." Although symptoms of depression may vary from person to person, some common symptoms include emotional (e.g., sad, anxious), motivational (e.g., initiative), behavioral (e.g., inactive), cognitive (e.g., negative views of self), and physical changes (e.g., headaches, weight loss or gain) (Comer, 2002). Slaughter, Slaughter, Nichols, Holmes, and Martens (2001) found that approximately one of three patients with PD experience depression at some point during the course of their disease. This study also stated that the onset of depression could be associated with reaction to

PD symptoms, more likely at early onset, and neurochemical changes, more likely later on in the course of the disease. Barbas (2006) found similar findings of depression associated with PD and stated that depression could be associated with factors such as reaction to illness. A controversy is that apathy is sometimes considered a feature of depression. For example, in the study by Slaughter et al. (2001), apathy is included as a clinical manifestation of depression in PD. Barbas (2006) also mentions apathy in relationship to PD, but lists apathy as a separate affective change from depression.

According to Ferrerri et al. (2006), it is often difficult to differentiate apathy from depression. Seven previous research studies have examined apathy and depression in patients with Parkinson's disease (Starkstein, Mayberg, Preziosi, Andrezejewski, Leiguarda, & Robinson, 1992; Levy, Cummings, Fairbanks, Masterman, Miller, Craig, Paulsen, & Litvan, 1998; Isella, Melzi, Grimaldi, Iurlaro, Piolti, Ferrarese, Frattola, & Appollonio, 2002; Pluck & Brown, 2002; Kirsch-Darrow, Fernandez, Marsiske, Okun, & Bowers, 2006; Dujardin, Sockeel, Devos, Delliaux, Krystkowiak, Destee, & Defebvre, 2007; Pedersen, Larsen, Alves, & Aarsland, 2008). See Table 1 for a summary of all seven studies' results in terms of the relationships between apathy and depression.

Starkstein et al. (1992) studied 50 participants diagnosed with PD. The Present State Examination (PSE) and DSM-III were used to diagnosis major or minor depression. Apathy was assessed using the 14-item Apathy Scale (AS). This study found that 15 (30%) of the participants had apathy and depression, 13 (26%) depression only, 6 (12%) apathy only, and 16 (32%) neither. Hence 38% of the subjects had one of the disorders without the other.

Levy et al. (1998) studied 40 participants diagnosed with PD. The Neuropsychiatric Inventory (NPI) was used to assess both apathy and depression (each has its own subscale). This study found that 11 (28%) of the participants had apathy and depression, 11 (28%)

depression only, 2 (5%) apathy only, and 16 (40%) neither. This was one of the few studies in which the correlation between apathy and depression was computed; it reported a significant, but weak correlation ($r = .34$).

Isella et al. (2002) studied 30 participants diagnosed with PD. The 30-item Geriatric Depression Scale (GDS) was used to assess depression. The 14-item AS was used to assess apathy. This study found 14 (47%) had apathy and depression, 4 (13%) had depression only, 7 (23%) had apathy only, and 5 (17%) had neither.

Pluck and Brown's (2002) study involved 45 participants with PD. The Hospital Anxiety and Depression Scale (HADS) and the Beck Depression Inventory (BDI) were used to assess depression. The original 18-item Apathy Evaluation Scale (AES) assessed apathy using both the clinical and self-report versions. According to the HADS, only 2 of 45 (4%) participants with PD were depressed. The BDI resulted in much different results: 43% of the participants were assessed to have depression. The clinical version of the AES found 17 (37.7%) participants apathetic and the self-report version found a similar amount, 36%, apathetic. The authors also reported out of the 17 apathetic participants 44% (approximately 7 participants) were also considered depressed according to the BDI. Based on the results of the BDI and the clinical version of the AES it can be concluded that 7 (16%) of participants had both apathy and depression, 12 (27%) had depression only, 10 (22%) had apathy only, and 16 (36%) had neither apathy nor depression.

A study by Kirsch-Darrow et al. (2006) involved 80 participants with PD. The BDI and the Center for Epidemiologic Studies – Depression Scale (CES-D) were used to assess depression. The 14-item AS was used to assess apathy. Using the BDI and AS scores, the study found that 18 (23%) of the participants were both apathetic and depressed, 3 (4%) had depression alone, 23 (29%) had apathy alone, and 36 (45%) had neither. The scores from the

CES-D were not analyzed in relation to the AS, but it was reported that depression was present in 31% of the participants.

Dujardin et al. (2007) examined 159 participants with PD. Each participant was separated into one of three groups: stable PD (i.e., nondemented with stabilized symptoms; $n = 47$), fluctuating PD (i.e., nondemented with severe symptoms; $n = 73$), and PD with dementia ($n = 39$). Fifty-eight healthy controls were matched according to age and education level. Apathy was assessed using the Lille Apathy Rating Scale (LARS). Depression was assessed using the Montgomery and Asberg Depression Rating Scale (MADRS). This study found that 51 (32%) of PD participants and 1 (2%) control participant were apathetic. Apathy was most common in the PD participants with dementia (56%). Overall for the PD subjects, 31 (19%) had both apathy and depression, 9 (6%) had depression only, 20 (13%) had apathy only, and 99 (62%) had neither apathy nor depression.

The most recent study by Pedersen et al. (2008) included 232 participants diagnosed with PD. Major depression was assessed by semi structured interviews according to the DSM-III and minor depression was determined by the MADRS. Participants with both major and mild depression were considered depressed in this study. Apathy was assessed using a validated motivation/initiative item of the UPDRS section I with a cut-off score of less than or equal to two. This study found 88 (38%) of the participants apathetic, 48 (21%) participants had both apathy and depression, 21 (9%) had depression only, 36 (16%) had apathy only, and 122 (53%) had neither apathy nor depression (the sum does not add up to 232 because 5 subjects had missing values on the depression measure, 4 of whom had apathy). The authors noted that 11 of the 88 apathetic participants (5% of the entire sample) presented apathy independent of depression, dementia, cognitive impairments, and use of antidepressants and

antipsychotics. A problem with this study is that a single UPDRS item is a questionable measure of apathy.

In summary, some of these seven studies reported that apathy often appears separate from depression; others reported that apathy was seldom reported separately from depression. Differences among studies could be due to various factors. The studies used different depression assessments, which may account for some of the variance in depression scores found among the participants with PD. Another factor could be that some of the depression assessments contain questions related to apathy, which could have had an effect on the reported relationship between apathy and depression in PD. For example a factor analysis of the Geriatric Depression Scale completed by Adams, Matto, and Sanders (2004) identified five subdivisions of the GDS, including apathy as one of the five divisions.

In this study, Robert Marin's modified Apathy Scale (AS) will be used to assess apathy. This AS, with 14 items, was used in three out of the seven previous studies where apathy and depression were evaluated in patients with Parkinson's disease. It is a recommended assessment to screen for apathy and to assess severity of apathy in individuals with PD (Leentjens, Dujardin, Marsh, Martinez-Martin, Richard, Starkstein, Weintraub, Sampaio, Poewe, Rascol, Stebbings, & Goetz, 2008).

This study will use the Beck Depression Inventory (BDI-II) to assess depression. Versions of the Beck Depression Inventory were used in two out of the seven studies of apathy and depression. The BDI-II is considered to have excellent reliability and validity in patients with Parkinson's disease (Levin, Llabre, & Weiner, 1998). One criticism of the BDI-II is that it contains three items that are arguably related to apathy. In Dujardin et al.'s (2007) study involving apathy characteristics in PD, she mentions that symptoms of apathy include "reduced interest and participation in the main activities of daily life, a lack of initiative, a

trend toward early withdrawal from initiated activities, indifference, and flattening affect” (p.778). These language describing these symptoms is similar to questions 4 (loss of pleasure), 12 (loss of interest), and 15 (loss of energy) found in the BDI-II. Therefore, the three apathy related questions in the BDI-II (questions 4, 12, and 15) will not be included in the total score for the main analyses so that the scores will only reflect the questions specific to depression (i.e., sadness, pessimism, self-dislike, suicidal thoughts or wishes, etc.) However, in a secondary analysis, all questions in both tests will be included so that traditional cut-off scores can be used.

This study is the next step in determining the relationships between apathy and depression in PD. The main research question deals with the correlation of apathy and depression in PD, after apathy-related items are taken out of the BDI-II. Analysis of cut-off scores will supplement the correlational analysis. Descriptively, it will be important to determine the rate at which depression can appear without apathy, and vice versa.

Method

Participants

This study included 121 participants from the Parkinson’s Disease Interdisciplinary Clinic at the University of Toledo Health Science Campus. All participants had a diagnosis of idiopathic PD as determined by a board-certified neurologist specializing in movement disorders. The mean age of the participants was 72.6 years ($SD = 8.6$). The mean years since diagnosis of PD was 6.6 ($SD = 6.4$).

Instruments

The instruments used were the 21-item BDI-II, an apathy-corrected 18-item version of the BDI-II, and the 14-item AS. An earlier version of the Beck Depression Inventory was used in two out of the seven previous studies of apathy and depression. The most recent

version, the BDI-II, is considered to have excellent reliability and validity in patients with Parkinson's disease (Levin et al., 1998) and is considered to be the most widely used self-report depression scale in PD research (Pluck & Brown, 2002). It has been criticized, however, for its use of somatic items (e.g. hypokinesia, psychomotor retardation) that are similar to symptoms of PD (Leentjens, Verhey, Luijckz, & Troost, 2000). Another previously mentioned criticism of the BDI-II is that it contains three items that are arguably related to apathy. These items are #4 (loss of pleasure), #12 (loss of interest), and #15 (loss of energy). Removal of these three items creates the apathy-corrected 18-item version of the BDI-II used in this study.

Visser, Leentjens, Marinus, Stiggelbout, and van Hilten (2006) recommended a cut-off score of 13/14 for the 21-item BDI-II after completing a reliability and validity study of the BDI-II in patients with PD. This means a score of 13 or less will indicate no depression, while a score of 14 or above will indicate depression. For the 18-item apathy-corrected version of the BDI-II, a cut-off score of 12 was chosen based on the same ratio used for the recommended cut-off of the BDI-II (i.e., $14/21 = 2/3$; $12/18 = 2/3$).

The 14-item AS was used in three out of the seven previous studies. A review of apathy scales in PD by Leentjens et al. (2008) reported the AS to be of "good face validity, internal consistency, interrater, and test-retest reliability" (p.6). In measuring apathy in PD, the 14-item AES was also found to be both reliable and valid (Starkstein et al., 1992). The AS is a recommended assessment to screen for apathy and to assess severity of apathy in individuals with PD (Leentjens et al., 2008). The items on the AS are specific to apathy, with items oriented to a lack of interest in learning new things, a lack of concern about condition, indifference, and needing a push to get started on things. A cut-off score of 13/14 is typically used for the 14-item AES (Starkstein et al., 1992). This means a score of 13 or less will

indicate no apathy and a score of 14 or higher will indicate depression.

Procedure

The BDI-II and the AS are instruments that are routinely used in the Parkinson's Disease Interdisciplinary Clinic during admittance to the clinic along with other paperwork typically completed. The data were first entered routinely into a clinical database together with other assessments. Staff at the University of Toledo Center for Clinical Research then de-identified the database by generating random identification codes to create a researchable file open to approved investigators. The University of Toledo Institutional Review Board determined that analysis of the de-identified data did not involve human subjects' research, according to IRB definitions.

Results

Of 121 BDI-II and AS assessments a few items were left blank on both assessments. On the BDI-II three participants left two scores blank, and eleven participants left one score blank; for the AS one participant left three scores blank, two participants left two scores blank, and six participants left one score blank. In order to compensate for missing data for an individual, the average score of the completed entries (for both the BDI-II and AS) was inserted into the missing spots.

The primary data analysis was a Pearson correlation between apathy and depression using the AS and the 18-item apathy-corrected BDI-II score. The result was statistically significant ($r = .44$), but this correlation also indicates that most of the variance in the two variables is not shared, with a coefficient of alienation equal to 81.7%. The correlation between the AS and the entire 21-item BDI-II was only slightly stronger, $r = .49$.

Secondary analyses examined the relationships between apathy and depression when cut-off scores were used to indicate whether or not the person had the disorder. Using the

recommended cut-off scores for the full versions of both assessments, we found that 32 (26%) had both apathy and depression, 17 (14%) had depression only, 36 (30%) had apathy only, and 36 (30%) had neither. Using a cut-off score of 12 for the 18-item apathy-corrected BDI-II, we found that 29 (24%) participants had both apathy and depression, 15 (12%) had depression only, 39 (32%) had apathy only, and 38 (31%) had neither apathy nor depression. See Table 1 for cross break comparisons to the seven previous studies on apathy and depression in PD.

Discussion

The focus of this study was to examine the relationship between apathy and depression in patients with PD. After examining the analyses of the continuous and categorical data of both the AS and BDI-II (minus the items related to apathy) and the AS and BDI-II (using all testing items), it is clear that there is a relationship between apathy and depression. Both Pearson correlations (between the AS and the standard BDI-II and between the AS and the apathy-modified BDI-II) were statistically significant ($p < .05$).

Although there is a relationship between apathy and depression, it is important to note that attributes can be correlated without being the same thing. Minich (2008) completed a meta-analysis on five of the previously mentioned studies (Starkstein et al., 1992; Levy et al., 1998; Isella et al., 2002; Pluck & Brown, 2002; Kirsch-Darrow et al., 2006); her conclusion was that “apathy and depression are not the same thing” (p. 15).

The cross breaks in Table 1 make it clear that apathy and depression can occur separately from one another. The total percentage of participants with apathy but not with depression across all studies (including this study) is 23% (140 out of 605 participants), and the total percentage of participants with depression only (not apathy) is 15% (90 out of 605 participants). Hence, across all studies, more persons with PD had one or the other (38%) than

had both: 29% (176 out of 605 participants). Therefore, apathy and depression can and do appear separately from each other at high rates, at least according to the various measures and cut-offs used in the different studies.

When comparing the results of this study (using the recommended cut-off score of the complete BDI-II and the AS) to the results of the seven prior studies, we find that this study's results has the highest number of participants with apathy only; falls close to mid-range with number of participants with depression only and number of participants with both apathy and depression (demonstrating that the percentages are not outliers); and has one of the lowest percentages of participants with neither apathy nor depression (second to Isella et al.'s 2002 study). See Table 2 for a comparison of results across the eight studies. While the percentage of participants with apathy is the highest in the current study, it does not lie far from the other studies (i.e, Pluck & Brown, 2002, found 22% with apathy only, Isella et al., 2002, found 23%, and Kirsch-Darrow et al., 2006, found 29%). The same can be reported for the results of participants with neither apathy nor depression (i.e., Isella et al., 2002, reported 17%, Starkstein et al., 1992, reported 32%, and Pluck et al., 2002, reported 36%). An explanation for the relatively high apathy-alone numbers (30%) might be the use of the AS, in that the study that came closest (29%, by Kirsch-Darrow et al., 2006) also used the AS as opposed to other possible measures of apathy.

It is interesting to note that results of the correlations and cross breaks were similar regardless of whether items related to apathy in the BDI-II were included or not. The three items included in the BDI-II related to apathy did not seem to alter the outcome of the study. This is important for future studies that are considering dismissing the BDI-II due to its inclusion of items related to apathy.

A few limitations can be noted in this study. One limitation involved the missing data in both AS and BDI-II assessments. While the amount of missing data was minimal, it is always better not to make assumptions about the data. The decision was made to include the subjects with some missing data in order to give the most complete picture of the results as possible. A second limitation was the lack of control over the administration of the assessments. Because the assessments were given by nurses and volunteer staff, it was difficult to know exactly how the assessments were administered to the participants. Although this is noted as a limitation, this data collection method was also the most naturalistic method for data collection without the typical problems encountered when administering informed consent. The use of a de-identified database resulting from routine clinical practice decreases possible bias that might occur because of subjects' perceptions of participating in a research project.

This study is important to the practice of occupational therapy, a practice that places a high level of importance on personal motivation and goal-oriented interventions to gain functional independence. Understanding whether or not the individual is apathetic, depressed, both apathetic and depressed, or neither apathetic nor depressed will affect the approach to intervention when working with that individual. A specific model of practice to decrease apathy is needed in the profession of occupational therapy. Future research studies may want to focus on the evidence-based intervention approaches to working with individuals with PD who have apathy and/or depression.

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Table 1. Summary of Studies Investigating the Presence and Absence of Apathy and Depression in PD.

<u>First Author</u> <u>(Year)</u>	<u>N</u>	<u>Apathy</u> <u>Instrument(s)</u>	<u>Depression</u> <u>Instrument(s)</u>		<u>No Apathy</u>	<u>Apathy</u>
Starkstein (1992)	50	AS (14 item)	PSE and DSM-III	<u>No Depression</u> <u>Depression</u>	16 (32%) 13 (26%)	6 (12%) 15 (30%)
Levy (1998)	40	NPI Subscale	NPI Subscale	<u>No Depression</u> <u>Depression</u>	16 (40%) 11 (28%)	2 (5%) 11(28%)
Isella (2002)	30	AS (14 item)	GDS	<u>No Depression</u> <u>Depression</u>	5 (17%) 4 (13%)	7 (23%) 14(47%)
Pluck (2002)	45	AES (18 item)	BDI	<u>No Depression</u> <u>Depression</u>	16 (36%) 12 (27%)	10 (22%) 7 (16%)
Kirsch-Darrow (2006)	80	AS (14 item)	BDI	<u>No Depression</u> <u>Depression</u>	36 (45%) 3 (4%)	23 (29%) 18 (23%)
Dujardin (2007)	159	LARS	MADRS	<u>No Depression</u> <u>Depression</u>	99 (62%) 9 (6%)	20 (13%) 31 (19%)
Pedersen (2008)	232	UPDRS section I	DSM-III MADRS	<u>No Depression</u> <u>Depression</u>	122 (53%) 21 (9%)	36 (16%) 48 (21%)
Hill (2009)	121	AS (14 item)	BDI-II Standard	<u>No Depression</u> <u>Depression</u>	36 (30%) 17 (14%)	36 (30%) 32 (26%)
		AS (14 item)	BDI-II (18 item)	<u>No Depression</u> <u>Depression</u>	38 (31%) 15 (12%)	39 (32%) 29 (24%)

Table 2. Comparison of Results Across Studies

	No Apathy				Apathy			
	<u>Seven Prior Studies</u>			<u>This</u>	<u>Seven Prior Studies</u>			<u>This</u>
	Range	<i>M</i>	<i>SD</i>	<u>Study</u>	Range	<i>M</i>	<i>SD</i>	<u>Study</u>
No Depression	17 - 62%	41%	13.5%	30%	5 - 29%	17%	7.5%	30%
Depression	4 - 28%	16%	9.8%	14%	16 - 47%	25%	9.7%	26%