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The Negative Impact of Apathy in Parkinson's Disease

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1. Introduction

Apathy is one of the most common neuropsychiatric complications of neurodegenerative disorders such as Alzheimer (AD) and Parkinson disease (PD). Apathy can be broadly defined as a clinical syndrome characterised by a change from baseline in three key domains: level of interest, level of initiative and emotional reactivity. It is one of the most under-diagnosed and poorly managed aspects of the neurodegenerative disorders. In PD particularly, the consequences of apathy may be significant and may impact negatively on long-term prognosis, exacerbate the motor and physical aspects of the disease, add to carer burden and stress, be associated with greater functional decline and disability, and impair quality of life (QOL). This chapter will outline these various outcomes and their relation to apathy in PD.

2. Background to apathy in PD

The prevalence of apathy in PD has been reported as ranging from about 17% to over 40% (Pluck and Brown, 2002). This wide range is likely a result of differences in populations studied (e.g. community versus clinic), types of apathy rating scales used, and discrepancies in, or lack of, the use of validated diagnostic criteria. In a cross-sectional validation study of newly proposed diagnostic criteria for apathy, the frequency of apathy in the PD subgroup was 27% (Mulin et al., 2011).

The definition of apathy has evolved over the past few years as the multi-dimensional nature of the syndrome is increasingly being recognised. A common conceptualisation of apathy, as proposed by Starkstein et al. (2001) among others, is that it constitutes a lack or reduction of goal-directed behaviour, as manifested in the dimensions of: (1) loss of or diminished initiative; (2) loss of or diminished interest; and (3) diminished or blunted emotions. The syndrome of apathy, while very common in neurodegenerative disorders, may also occur in other medical, neurologic or psychiatric conditions. The diagnostic criteria for apathy have followed the definition. Most recently, an international task force proposed a new set of criteria which have now been validated in several conditions, including AD and PD (Robert et al. 2009; Mulin et al., 2010). According to these criteria, a diagnosis of apathy can be made in the presence of four or more weeks of a loss of or reduction in motivation in at least two of three proposed apathy dimensions of emotional reactivity, interest and initiative. This change in behaviour should be sufficient to cause clinically significant impairment in functioning in various spheres.

Aside from diagnostic criteria, apathy can also be rated using a number of different validated apathy rating scales. These scales were reviewed by the Movement Disorder Society (MDS) and the recommendation for PD was that the Apathy Scale (AS) (Starkstein et al., 1992) or the Apathy Evaluation Scale (AES; clinician version, AES-C) (Marin, 1991) were the most robust scales for use in PD (Leentjens et al., 2008). PD-specific apathy rating scales which have recently been developed include the Apathy Inventory (AI) (Robert al., 2002), which can be either patient- or informant-rated, as well as the Lille Apathy Scale (LARS) (Sockeel et al., 2006). The LARS is a 33-item scale comprised of nine domains underscoring the apathy syndrome. Scores can range from an optimal score (no apathy) of +36 to the most severe score of -36, and the cut-off score for moderate apathy is -16. Principal component analysis of data derived from a study of 159 PD participants (51 with apathy as per the LARS cut-off) revealed a four-factor solution describing apathy dimensions. These were: intellectual curiosity, action initiation, emotion and self-awareness (Dujardin et al., 2007). Gallagher et al. (2008) used the LARS to determine how useful the Unified Parkinson's Disease Rating Scale, Part I (UPDRS) (Fahn & Elton, 1987) is as an apathy screening and diagnostic instrument by rating both scales in 74 PD sufferers. Using the LARS cut-off, 20% of the sample had apathy and they found that the UPDRS apathy item was sensitive (73%) in detecting apathy in PD but did not have sufficient diagnostic quality. Finally, the apathy domain of the informant-based Neuropsychiatric Inventory (NPI) (Cummings et al., 1994), has also been validated for identifying apathy, as either a "present/absent", or in terms of magnitude (frequency x severity). On this scale, a domain score for magnitude of symptoms of ≥ 4 indicates "clinically significant" pathology although no clear cut-off score for apathy per se has been established. A clinician-rated version of the NPI (NPI-C) is currently being developed and may be useful in the assessment and diagnosis of apathy (de Medeiros et al., 2010).

The underlying pathophysiology of apathy is related to specific disease-related degenerative brain changes that impact on motivation, and possibly, reward pathways. In particular, deficits in the frontal-subcortical circuit involving the anterior cingulated cortex (ACC) are likely to result in an apathy syndrome, or in specific dimensions of the syndrome (Robert et al., 2009; Devinsky et al., 1995). Neurotransmitter deficits which may play a role in apathy include: dopamine, which is important in reward and motivation; serotonin (5-HT), which may also have a role in PD-related depression in PD; and acetylcholine, a key neurotransmitter whose loss is related to dementia in PD (Czernecki et al., 2002; Leentjens et al., 2006).

The syndrome of apathy may occur as a sole behavioural complication of PD, or, as is frequently the case, may be co-morbid with other psychiatric complications such as depression or anxiety (Pluck and Brown, 2002; Aarsland et al, 1999). In our own cross-sectional study of a sample of 99 PD participants without dementia, the proportion of the 26 participants with apathy (on AES-C) who also experienced moderate to severe depression (Hospital Anxiety and Depression Rating Scale (HADS), depression sub-score ≥ 11) was 45%, which was significantly higher than in the PD participants with no apathy. Furthermore, HADS anxiety ratings were also significantly higher in those with apathy compared to those with no apathy (Leroi et al., 2009). The co-occurrence of apathy and depression in PD may be a diagnostic challenge, however, it is important to distinguish these syndromes in order to ensure that management strategies for depression, which are commonly prescribed, do not worsen or leave apathy symptoms untreated. If properly validated scales for apathy and depression are used in the diagnosis, it is possible to parse out the diagnostic entities with a degree of accuracy (Marin et al., 1993; Dujardin et al., 2007).

3. Impact of apathy on prognosis in PD

The question of whether the presence of apathy in PD impacts on prognosis is an important one since it has implications for early and robust detection and management of apathy. Unfortunately, very few long-term prospective studies have examined this question and the handful of cross-sectional studies linking apathy to disease severity are not entirely adequate to address the question of causation. Nonetheless, a few shorter-term follow-up studies have been done, in PD as well as AD, and suggest that the presence of apathy may have negative implications for the disease course, particularly once dementia is already established. Apathy in PD may also as a risk factor for the conversion into dementia from the non-demented state (Starkstein et al., 2006; Robert et al., 2006a; Dujardin et al. 2009). One of the only PD studies to address this question longitudinally is a study of apathy in a cohort of 40 non-demented PD patients who were followed up for a median of 18 months. Those with apathy (n=20) had a higher rate of conversion to dementia in PD over this period compared to those who had no apathy (n=20) at the start of the study (Dujardin et al., 2009). These findings are consistent with a longer study in AD patients for up to four years which revealed that apathy sufferers had a more severe overall prognosis and declined more rapidly compared to those without apathy (Starkstein et al., 2006). Another study, of shorter duration, found that in those with apathy and the amnestic form of mild cognitive impairment (MCI) converted to dementia in AD at a higher rate after one year compared to those without apathy (Robert al., 2006a).

4. Impact of apathy on the physical aspects of PD

PD is primarily a movement disorder affecting gait, speed and flexibility of movement. As the disease progresses, these symptoms become worse rendering the PD sufferer less active and increasingly prone to the complications of immobility. Furthermore, other, non-motor aspects of the disease such as postural instability, swallowing difficulties, bladder and bowel problems, cognitive impairment and depression may also contribute to a greater disease burden and increase the risk of developing medical complications. If apathy is present as well, effects of both the motor and the non-motor aspects of the disease may be exaggerated. In particular, the apathy dimensions of lack of initiative and interest may result in the PD sufferer withdrawing from their usual physical activities and hobbies, including activities of daily living and becoming increasingly sedentary. This may exacerbate existing problems such as constipation, and may also lead to secondary physical complications including urinary and respiratory infections, deep vein thrombosis and increased frailty. Loss of appetite, weight loss and poor nutritional status may also be associated with the presence of apathy and these conditions also add risk of developing medical complications and hastening decline (Benoit et al, 2008).

5. Impact of apathy on cognitive function in PD

Cognitive impairment in PD can broadly be categorised into dopaminergically-driven executive-type cognitive changes, which appear early on in the course of the disease, and more widespread, cholinergically-driven dementia-type cognitive changes, which occur as the disease advances (Williams-Gray et al., 2007). Executive dysfunction, including impairments in planning, verbal fluency, working memory, and attention, may progress to

the point whereby functional abilities are affected. At this stage, it can be considered "mild cognitive impairment" (MCI) in PD. The more widespread cognitive impairments that lead to a full dementia syndrome typically appear after about 11 years of PD and may occur in over 80% of PD sufferers if they live with the disease for long enough (Hely et al., 2008).

A characteristic aspect of cognitive impairment in PD is "bradyphrenia", or slowness of thinking, which may be underscored by various aspects of the disease, including deficits in attention and interest, fatigue, slowness of thinking, poor persistence in tasks, mild memory problems, as well as apathy. Specifically, the lack of initiative and interest, which are key dimensions of PD-related apathy, may contribute to the development of bradyphrenia.

The cognitive changes that frequently accompany apathy syndromes are gradually being understood, however there have only been a few studies specifically examining this issue in PD. Whether these cognitive changes are the consequence or an impact of apathy, rather than apathy being a behavioural manifestation of the cognitive changes is not entirely clear (Duffy and Campbell, 1994). At best this relationship can be considered "bidirectional". Some of the studies examining cognitive changes in apathy in PD have used such tools as the Mini-mental State Exam (MMSE) (Folstein et al., 1975). The overall finding are that those with apathy are more cognitively impaired globally compared to those who do not have apathy (e.g. Landes et al., 2001; Starkstein et al., 2001, 2005; Aarsland et al., 2001; Senanarong et al., 2005). Studies using more specific neuropsychological test batteries reveal a strong association between apathy and frontal-type cognitive functions, even in the non-demented state. In our own cross-sectional study of a cohort of 99 non-demented PD sufferers, 46%of the variance predicting working memory impairment, an aspect of frontal-executive dysfunction, was accounted for by the presence of apathy, as well as older age and the presence of motor complications (Andrews et al., 2009). Working memory deficits in apathy in PD are of particular interest since both these functions may be underpinned by deficits in the ACC. In addition to working memory deficits, this same study also found significantly greater impairments in global cognitive impairment, as per the MMSE, as well as verbal fluency, even when accounting for differences in age, age on onset and duration of disease, and depression and anxiety. Interestingly, although attentional shift was initially worse in the apathy group, this difference was no longer evident once the co-variates were accounted for. These findings are supported by studies of cognitive impairment in AD and MCI, which have also found significantly worse word list learning, verbal fluency, set shifting and naming in those with apathy compared to those without apathy (Kuzis et al., 1999; Sperry et al., 2001; Robert et al., 2006b; McPherson et al., 2002; Pluck and Brown, 2002; Starkstein et al., 1992).

6. Impact of apathy on quality of life in PD

Measurements of the *subjective* experience of living with a chronic, neurodegenerative disease have increasingly become a focus of clinical and research interest in PD. The concept of "quality of life", or, more accurately, "health-related quality of life" (Hr-QOL) is a multidimensional construct embodying aspects of cognitive, emotional and physical functioning (Schrag, 2000). Several studies have used Hr-QOL scales to assess the impact of PD on individuals. These have shown that PD patients generally score lower than age-matched controls with other diseases and that key factors associated with poor Hr-QOL include depression, social isolation, physical functioning, sleep impairment, pain and discomfort, amongst other factors (Schrag, 2006). Depression in particular is an important factor determining Hr-QOL in PD, and this would suggest that a behavioural syndrome such as apathy, which is closely linked to depression, would also impact on this outcome.

6.1 PD study of apathy and quality of life

To date, one of the only studies directly examining the impact of apathy on Hr-QOL in PD is our own cross-sectional study of 97 non-demented community dwelling PD sufferers (Leroi et al., 2011a) who were assessed with the Parkinson's Disease Quality of Life Scale-8 item version (PDQ-8)(Jenkinson et al., 1997), which is a well-validated abbreviated version of the PDQ-39 (Peto et al., 1995). This study found that in those without frank dementia in PD, lower self-reported Hr-QOL was associated with *less* cognitive impairment and younger age, rather than the profile typical of those with apathy, namely, older age and more cognitive impairment (Leroi et al., 2011a). These findings can be explained in that the younger and more active the PD sufferer is, the greater the impact of a diagnosis of a chronic degenerative disease may be. In contrast, those who are older, no longer working, and who may have lower expectations of life, may be less affected in terms of HRQoL. Interestingly, these findings are supported by a study of AD sufferers in care homes who had apathy. It found that in those with apathy, self-reported QOL was lower in those with less cognitive impairment, based on MMSE scores (Gerritson et al., 2005).

Data from the PD study mentioned above (Leroi et al., 2011a) were further analysed in order to compare "low" and "high" Hr-QOL in PD using the median split method. The median score on the PDQ-8 was 20.8. Those who scored above this median (n=48) were considered as to have poorer Hr-QOL (higher PDQ-8 score is worse Hr-QOL), and those who scored below this median (n=51) were considered as having better Hr-QOL. Table 1 shows a comparison of the mean scores across various demographic and clinical factors. From this analysis, it was clear that "level of motivation" or apathy as determined by the AES-C score differed between the two groups, with significantly higher apathy scores (AES-C) in the "high" PDQ-8 group. This comparison also revealed that those who were in the "high" PDQ-8 group (worse Hr-QOL) were no different in age to the low group, but differed significantly on several disease variables, including the "high" group having younger onset of disease, longer duration and more motor complications, in the form of dyskinesias, "on/off" phenomena and dystonias. Psychiatrically, the two groups differed, with higher anxiety, depression and overall psychiatric burden scores, the latter as reflected by the NPI "total" score, in the "high" scoring group. Cognitively, the two groups did not differ on global cognition (MMSE total), attention (serial 7's; Trail Making Test-B), short-term memory (5 minute recall from the MMSE) or verbal fluency (FAS test), however, as is consistent with Leroi et al. (2011a), the "high" group were significantly better than the "low" group on measures of working memory (n-back).

The above findings, however, contrast with other studies in PD, in which more severe levels of cognitive impairment or dementia, depression, and more advanced disease stage are associated with worse levels of self-reported Hr-QOL (Schrag 2006). The impact of disease variables may depend on stage of disease, with advanced disease and the presence of dementia having a greater impact compared to early disease (Schrag 2006). Indeed, these are the conditions that are associated with more severe and more prevalent apathy syndromes. It is possible that the presence of dementia may alter the impact of apathy on self-reported Hr-QOL due to apathy's effect on insight and the ability to reflect on experiences affecting the self. Our own data found that in comparing PDQ-8 in a cohort of PD-apathy sufferers (NPI ≥ 4) without cognitive impairment (n=24) to those with PDD and apathy (n=9), the PDD group had worse Hr-QOL (mean PDQ-8 in PD, 23.26 (SD 9.51); mean PDQ-8 in PDD, 34.02 (SD 12.67); t=-2.64, p=.01).

Patient measures (n=99)	**Low PDQ-8 (better Hr-QOL) (n=51)**	**High PDQ-8 (worse Hr-QOL) (n=48)**	**Statistic (t test or Mann-Whitney U)**	**Significance (*p*-value)**
	Mean (SD)			
Apathy Evaluation Scale –Clinicians' version (total score)	26.92 (12.38)	33.30 (15.68)	-2.24	.03
Demographic factors:				
Age at assessment (years)	64.51 (9.67)	62.39 (11.46)	0.99	.33
Clinical factors:				
Unified PD Rating Scale: motor subscale	27.00 (12.10)	30.79 (11.40)	-1.55	.12
Unified PD Rating Scale: complications of therapy subscale	2.37 (2.56)	5.15 (3.48)	U=589.50	<.001
Duration of PD (months)	82.47 (52.35)	110.35(75.09)	-2.14	.04
Age of onset of motor symptoms	57.71 (11.05)	52.78 (11.83)	2.12	.04
Psychiatric measures:				
Hospital Anxiety & Depression Rating Scale- depression subscore	5.02 (3.56)	7.67 (3.65)	U=609.50	<.001
Hospital Anxiety & Depression Rating Scale- anxiety subscore	4.59 (3.62)	8.15 (4.38)	U=704.50	<.001
Neuropsychiatric Inventory total	8.12 (11.09)	15.13 (13.99)	U=743.50	.002
Cognitive measures:				
MMSE Serial sevens	4.27 (1.00)	4.09 (1.33)	0.79	.43
MMSE 5-minute recall	2.49 (0.83)	2.48 (0.86)	0.07	.95
Trails B error score	5.53 (9.31)	7.66 (10.39)	-1.05	.30
n-back	16.83 (3.51)	15.02 (3.62)	2.43	.02
FAS	40.84 (14.06)	41.17 (12.44)	-0.12	.90

Table 1. Comparison of high- and low-PDQ-8 groups across various demographic and clinical variables in the PD participant groups.

7. Impact of apathy on disability in PD

The notion of "disability" in PD is increasingly recognised as being important however there is almost no literature on the specific association between apathy and disability in PD. Disability, like quality of life or carer burden, is a multidimensional construct, likely underpinned by a variety of different factors, both generic and PD-specific. The general definition of "disability" as defined by the "Americans with Disabilities Act of 1990 is "a physical or mental impairment that substantially limits one or more major life activities" (http://www.ada.gov/cguide). With regards to PD, "disability" loosely refers to "functional impairment" and is most commonly associated with the core aspects of the disease, namely, severity of motor impairments (tremor, instability, rigidity, bradykinesia). Non-motor aspects of PD have also been shown to be key contributors to overall functional impairment, or disability. In particular, some studies have shown that the presence of or severity of depression is associated with increased disability (Weintraub et al., 2004; Holroyd et al., 2005). One of the most comprehensive studies on this topic was by Weintraub et al. (2004). This study found that using a bivariate analysis, the key associated features with disability were the presence of psychosis, depression (presence and severity), age, duration of PD, cognitive impairment, apathy, sleepiness and aspects of motor impairment. Assessing these factors with a multivariate analysis, 37% of the variance in UPDRS ADL score was accounted for by severity of depression and worsening cognition, and 54% of the variance in Schwab-England score was accounted for by the same two factors plus increasing severity of PD. The limitation of this study was that it was undertaken in a mostly male, veteran population in the USA and did not have a control group of comparable motor severity in PD. Hence, the generalisability to the general PD population is limited. To date there have been relatively few studies investigating the specific impact of apathy on disability in PD, however, it is likely that apathy-induced disability has a further impact by increasing carer burden and levels of distress.

7.1 PD study of apathy and disability

In PD, the most robust way to measure disability is using a PD-specific activities of daily living (ADL) scale from the UPDRS, as well as a more general disability scale, the Schwab-England scale (Schwab & England, 1969). Disability captures the notion that the ability to undertake ADL is an important measure of disease severity and may not be dependent on duration of disease or stage according to the Hoehn-Yahr scale. The UPDRS ADL subscale is a 13-item scale that rates degree of ability to carry out daily tasks such as dressing and using a cutlery on a scale of 0-4 per item. It has a range of 0-52, with higher scores indicating greater impairment. It was designed specifically for assessing those with a diagnosis of PD and encompasses such items as the ability to eat and drink, move, toilet, dress, undertake hygiene routines, and communicate. The Schwab-England scale rates ADL ability on a scale of 0-100% with 100% being completely independent and with no disability. This scale is a useful *global* measure of independence and performance on ADL.

Using the UPDRS ADL scale, as well as the Schwab-England scale, we undertook a cross-sectional study of 99 non-demented PD sufferers with apathy, as determined by the AES-C

(Leroi et al., 2011a). These participants were consecutively recruited from neurology clinics in the UK and all met criteria for idiopathic PD. We found that disability on these measures was significantly higher in those with both apathy and PD (n=26) compared to those without apathy and PD (n=73). Mean disability ratings are shown Table 2. Furthermore, apathy was strongly and significantly associated with higher levels of disability rated on both these scales (UPDRS-ADL, rho=0.36; p<0.001; Schwab-England, rho=-0.55; p<0.001). In a subsequent multivariate regression analysis, apathy, together with later stage of disease and more cognitive impairment, accounted for 56% (p<.001) of the variance predicting disability.

	Mean (SD)		
	Apathy (n=26)	**Control (n=73)**	**Statistic**
Unified PD Rating Scale: ADL subscale	18.23 (4.10)	13.35 (4.97)	t=4.50; p<.001
Schwab-England scale	63.46 (12.39)	82.00 (9.26)	t=-8.93; p<.001

Table 2. Disability ratings compared between the two non-demented PD groups: with and without apathy

Further analysis of these data using the median split method was undertaken to explore the relationship of various demographic and clinical (motor, psychiatric and cognitive) factors between those with *high* levels of disability (mean UPDRS ADL score equal to or above the median cut-off of 15; n=53) and those with *low* levels of disability (mean UPDRS ADL score below the median cut-off of 15; n=46). Table 3 shows the comparison between the two groups of the mean scores across various factors. The mean apathy score (AES-C) was significantly higher in the "high" disability group (p=.004) in spite of there being *no* significant difference in age and several disease variables such as duration of disease, age of onset and dopaminergic load. However, the more disabled group did have worse motor scores (higher UPDRS motor score)(p<.001), worse motor complications (higher UPDRS complications of therapy score)(p=.03), and more severe stage of disease (Hoehn-Yahr score)(p=.001).

Interestingly, and in contrast to previous findings in the literature, there was no difference between groups on level of self-rated depression and anxiety, as assessed by the HADS. With regards to cognitive variables, there was no difference in complex attention (serial 7's), and short-term memory (5 minute recall from the MMSE). In contrast, there was greater impairment in verbal fluency (FAS test)(p=.04) and time for attentional shift/visual scanning (Trail-making Test-B time)(p=.006) in the high disability group. Finally, as expected, this group was also significantly more impaired on working memory (n-back; p=.001). These findings underscore the significant impact that apathy and cognitive impairment have on disability in PD.

Participant measures (n=99)	**Low ADL Mean (SD) (n=53)**	**High ADL Mean (SD) (n=46)**	**Statistic (t test or Mann-Whitney U)**	**Significance (*p*-value)**
	Mean (SD)			
	Measure of motivation:			
Apathy Evaluation Scale-Clinicians' version	26.17 (12.07)	33.78 (15.63)	U=817.00	.004
	Demographic factor:			
Age at assessment (years)	62.04 (10.50)	64.65 (10.78)	t=-1.22	.23
	Disease factors:			
Unified PD Rating Scale: motor	24.00 (10.10)	34.47 (11.27)	t=-4.72	<.001
Unified PD Rating Scale: complications of therapy	2.92 (2.74)	4.48 (3.71)	U=917.00	.03
Duration of PD (months)	84.87 (59.96)	105.83 (69.61)	t=-1.61	.11
Age of onset of motor symptoms (years)	54.92 (11.41)	55.54 (12.03)	t=-0.26	.79
Hoehn-Yahr scale	2.09 (0.67)	2.55 (0.65)	t=-3.44	.001
Levodopa equivalent daily dose (mg)	798.19 (641.38)	821.10 (507.66)	U=1132.00	.54
	Psychiatric measures:			
Hospital Anxiety & Depression Scale: depression subscore	5.81 (4.13)	6.78 (3.37)	U=979.00	.12
Hospital Anxiety & Depression Scale: anxiety	6.73 (4.73)	5.76 (3.84)	U=1089.50	.45
	Cognitive measures:			
Mini-mental State Exam 5-minute recall	2.55 (0.77)	2.41 (0.91)	U=1133.00	.47
Trail Making Test-B time to complete (sec)	134.41 (86.64)	175.46 (88.31)	U=793.56	.006
Trail Making Test- B error score	5.12 (9.02)	7.89 (10.49)	U=956.50	.13
n-back	17.06 (3.38)	14.55 (3.55)	t=3.48	.001
FAS	43.47 (14.71)	38.22 (10.58)	t=2.01	.04

Table 3. Comparison of high- and low-disability (ADL) groups across various demographic and clinical variables in the PD participant groups.

8. Impact of apathy on carer burden in PD

Caring for someone with a chronic, prolonged and degenerative disorder such as PD can be associated with significant stress, strain and perceived burden in the carer. This is similar to the well-established effects that such caring may have on informal carers of any chronic and serious disease, and it has been shown that mortality of these carers is actually increased if emotional or mental strain results (Schulz and Beach, 1999). In PD, the complexity of the disease, which involves not only physical, but also cognitive and behavioural impairment, means that the caring role is even more challenging. Carers in PD have to be responsible for managing the household, the family finances, and other activities of daily living, as well as the physical care needs of the patient. These responsibilities generally increase as the disease progresses, and one study showed that while in the earlier stages of PD the carer performed an average of 11 care-related activities per day, in the later stages of PD, this increased to up to 30 per day (Carter et al., 1998). The manifestations of such carer burden in PD carers include depression, limitations in social life and low quality of life (Schrag et al., 2006).

Patient factors that have been shown to be associated with carer burden and stress include: severity of motor functioning; presence of mental dysfunction, particularly depression and cognitive impairment (Aarsland et al., 1999); and functional status (Martinez-Martin et al., 2007; Aarsland et al., 1999). However, the specific impact on carer burden of apathy has not been as well studied other than in those with significant cognitive impairment and dementia (Aarsland, 2007).

8.1 PD study of apathy and carer burden

Over the past few years, the issue of assessing carer burden and distress has been recognized as being much more complicated than previously appreciated. Since PD is a long-term condition which impacts on multiple facets of functioning, it follows that the effect on carers cannot be easily modelled. However, a simplified and commonly used method for assessing subjective carer burden is using a well-validated scale, the 29-item Zarit Burden Interview (Zarit et al., 1980). In this questionnaire, responses range from 0 (never) to 4 (nearly always) and it rates the impact on the carer's physical, emotional and socioeconomic status. Higher scores reflect greater carer burden. Our own study used a modified version (22-item) of this measure to examine the impact of apathy on carer burden in a cohort of 71 non-demented PD patients and their carers (Leroi et al., 2011b). The carers in this group were mostly male (60.6%) and had a mean age of 62.7 (SD 10.9) years. They had known the PD sufferer for a mean length of time of 39.8 (SD 14.4) years. The mean ZBI score in the group overall was 23.8 (SD 14.0) years. Apathy was defined in the PD sufferer as being a score of ≥14 on the modified Apathy Scale (Starkstein et al., 1992). Findings from this study revealed that carer burden in those with apathy was significantly greater compared to those without apathy (p=.004). This was supported by the finding of a strong correlation between level of apathy and carer burden (rho=0.41; p=<.001).

9. Conclusion

The discussion above has highlighted the significant negative impact that the presence of apathy can have in PD, whether or not dementia is present. In particular, apathy can have an adverse effect on prognosis of the disease, cognitive and physical functioning, quality of

life, disability and carer burden. However, this evidence has been gained mostly from cross-sectional studies which are limited in their ability to determine causality between apathy and these various outcomes. Longer, more detailed prospective studies are needed to examine these issues further in order to emphasize the need for more robust detection of and intervention into apathy in order to offset the negative outcomes.

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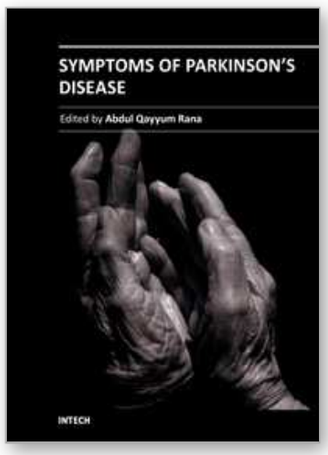

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This book about Parkinsonâ€™s disease provides a detailed account of various aspects of this complicated neurological condition. Although most of the important motor and non-motor symptoms of Parkinsonâ€™s disease have been discussed in this book, but in particular a detailed account has been provided about the most disabling symptoms such as dementia, depression, and other psychiatric as well as gastrointestinal symptoms. The mechanisms responsible for the development of these symptoms have also been discussed. Not only the clinicians may benefit from this book but also basic scientists can get enough information from the various chapters which have been written by well known faculty.

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