

Fatigue and Apathy in Individuals with Parkinson's Disease with and without Deep Brain Stimulation

Introduction

In recent years, non-motor symptoms of Parkinson's disease (PD) have received more attention, as these greatly affect quality of life for persons with Parkinson's disease (PWP), as well as their family and friends. Two poorly understood but common non-motor symptoms in PWP include fatigue and apathy. Each has separate effects on daily life.

Fatigue, a state of physical and/or mental tiredness, weakness, or exhaustion,¹ is common in the elderly as well as in those with chronic medical conditions, such as PD.² Reported prevalence of fatigue in PWP varies due to how researchers have defined fatigue, but ranges from 33-58%.^{2,3,4} Interestingly, fatigue has been shown to be more common in PWP (44-70% reported fatigue) than similarly matched peers (18-22%).^{5,6} Fewer studies have focused on fatigue and deep brain stimulation (DBS). Some studies, however, suggest that DBS as well as treatment with medications (e.g., levodopa) reduce fatigue in PWP.^{7,8}

Apathy, defined as general feelings of low motivation, lack of interest and effort, and indifference,^{9,10} is also common in PWP, with prevalence estimates ranging from 16-70%.^{11,12} Apathy seen in PD is linked to various areas in the brain that are also affected by PD.^{10,12,13} Studies looking at apathy in PWP that have undergone DBS report mixed results that suggest that some individuals with DBS experienced more apathy and some experienced less when compared to individuals with PD without DBS.¹⁴

Since fatigue and apathy are common in PD, it is important to take a close look at these symptoms, how they may relate to each other, and how they are impacting individuals with PD.

Objective

1. To examine the prevalence and characteristics of fatigue and apathy in PWP, particularly as it relates to those who have undergone DBS (**DBS group**) and those who have not had DBS (**Non-DBS group**).
2. To better understand how fatigue and apathy may manifest in **Early PD** versus **Advanced PD**.
3. To examine the relationship between other non-motor symptoms, specifically sleep, depression and anxiety, and fatigue and apathy.

Methods

The participants in this report included 205 individuals with PD who underwent DBS (**DBS group**) and 311 individuals with PD without DBS (**Non-DBS group**). Please see Table 1 for the demographic information. The participants were recruited from a variety of sources, and the data collected in this study represents individuals who either participated in previous surveys conducted by The Parkinson Alliance and were invited to participate in this

current survey; responded to study announcements in medical clinics around the country; found out about the study through their participation in local PD support groups; or responded to survey announcements located on The Parkinson Alliance website (www.parkinsonalliance.org) or our affiliate website devoted to DBS (www.dbs-stn.org). The participants either completed a paper-and-pencil survey or an on-line survey, depending on their preference.

Assessment Questionnaires: The participants in this study completed a Demographics questionnaire, questions related to other non-motor symptoms such as sleep, depression, and anxiety, The Parkinson Fatigue Scale, and the Apathy Scale.

The Demographic Questionnaire: This questionnaire included questions related to background information of the participants, questions related to symptoms of or related to fatigue and apathy (such as depression, anxiety, and sleep disturbance), and questions related to DBS for those who had undergone DBS therapy.

The Parkinson Fatigue Scale (PFS-16):¹⁵ The PFS-16 is a self-rated assessment designed to tap a single construct encompassing the physical aspects of fatigue in PD and its impact on daily function. The scale deliberately excludes emotional and cognitive features that may occur as part of the fatigue experienced but which may also occur independently in Parkinsonism. There were 16 items reflective of symptoms of fatigue. Example items include: 2. My life is restricted by fatigue. Item 4. Fatigue is one of my three worst symptoms.

Apathy Scale:¹⁶ This questionnaire is a self-rated assessment made up of 14 items related to apathy. The items tap into apathy as it relates to cognition, initiation, and general interest. Each item is formulated as a question (e.g., Question 12. Do you need a push to get started on things? Question 14. Would you consider yourself apathetic?).

Results

Table 1. Demographics and Clinical Features of the Sample

Variable	DBS (N=205)	Non-DBS (N=311)
How many years do you believe you have experienced apathy?		
Average Age in Years	64	69
Duration of PD in Years	16	8
Average Age of PD Onset *	49	62
Male	62%	62%
Female	38%	38%
Married	74%	78%
Living with Someone	86%	88%
Age at Time of DBS in Years (Range)	60	n/a
Duration since DBS in Years (Range)	5	n/a
DBS Target		
Subthalamic Nucleus (STN)	92%	n/a
Globus Pallidus interna (GPi)	5%	n/a
Thalamus	3%	n/a
Bilateral Stimulation	93%	n/a
Unilateral Stimulation	7%	n/a

* Denotes significant differences between the groups

Age and Duration of PD within the Two Groups:

- The majority of the participants were between the ages 50-69 (See Figure 1).
- About half of the participants in the **Non-DBS group** were between 50-69 years of age, with the other half predominantly being 70 years-old or older. Only a few participants were under the age of 50.
- The majority of the patients in the **DBS group** were between 50-69 years of age, with the remainder predominantly being 70-years-old or older. There were only a few participants that were younger than 50 years of age.
- There was a significant difference for duration of PD between the two groups (see Table 1 and Figure 2).
- The **DBS group** had PD for a longer duration than the **Non-DBS group**. For research purposes, the duration of PD was taken into consideration for all of the results reported below.

Figure 1. Age Categories for DBS and Non-DBS groups

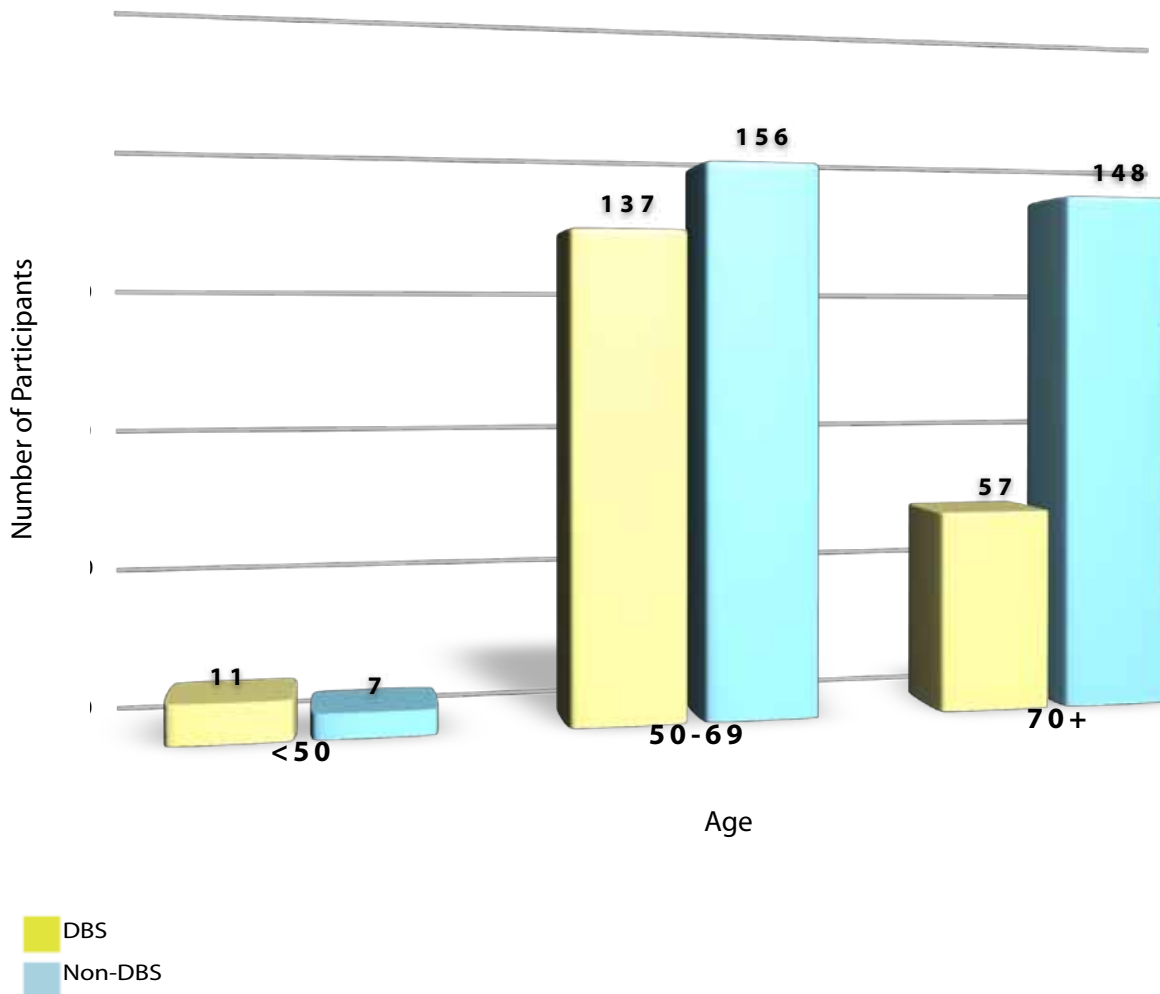
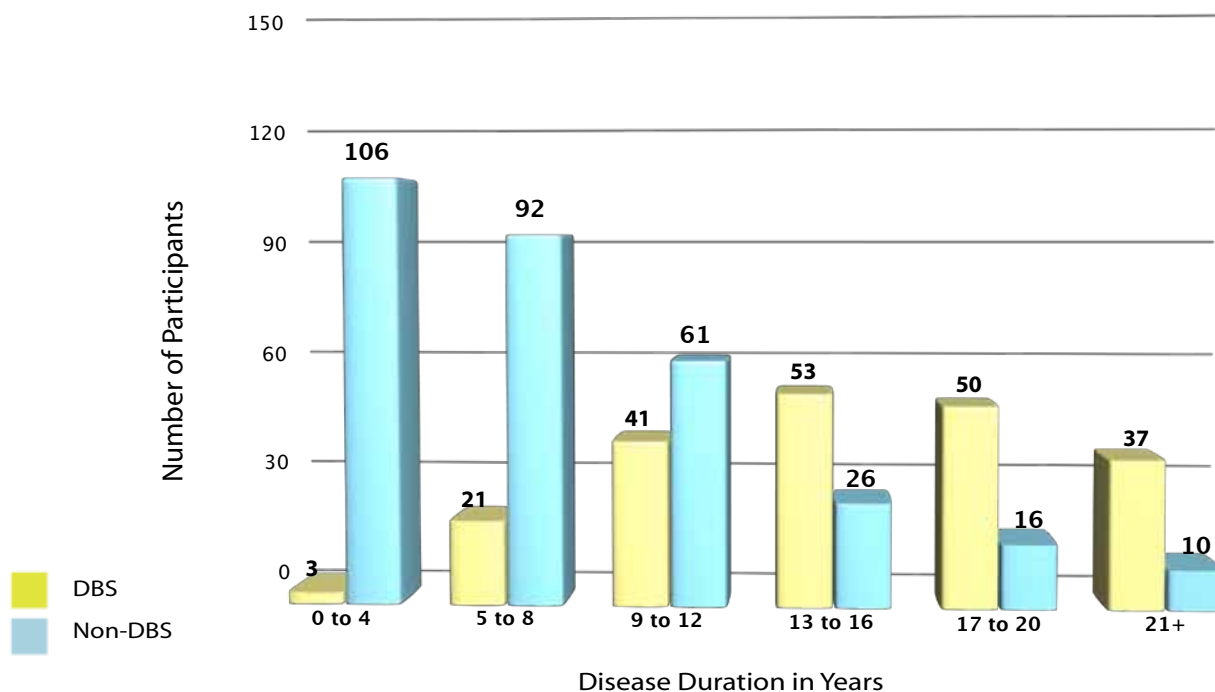


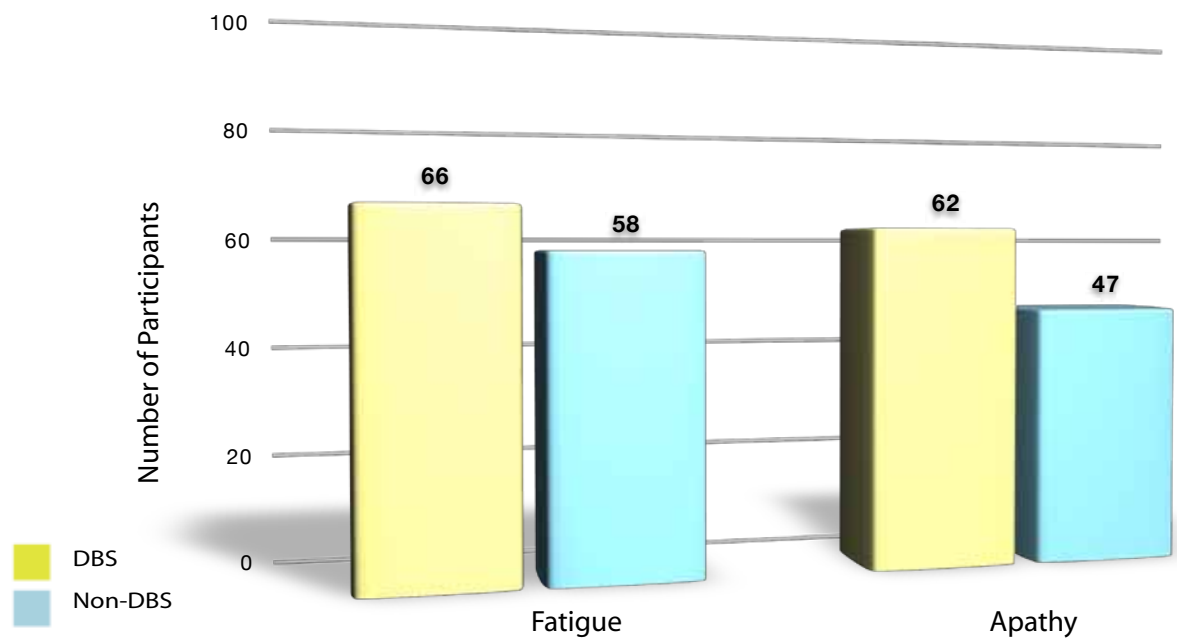
Figure 2. Disease Duration (in Years) for DBS and Non-DBS groups



Fatigue in Individuals with PD:

- For the total sample, when participants were simply asked “Do you experience Fatigue?” 73% of the participants (N=513) reported that they do experience fatigue.
 - 76% of the **DBS group** reported that they experienced fatigue.
 - 71% of the **Non-DBS group** reported that they experienced fatigue.
 - There was not a significant difference between the two groups in experiencing fatigue based on this question.
- The results from the Parkinson’s Disease Fatigue Scale also reflected significantly elevated levels of fatigue in this population (see Figure 3).
 - 66% of the **DBS group** and 58% of the **Non-DBS group** revealed clinically significant levels of fatigue.
 - The two groups were not significantly different from each other.
- The time of day where fatigue was most pronounced was similar for both the **DBS** and **Non-DBS groups**, with the greatest amount of fatigue occurring in the afternoon and the evening (see Table 2).
- The majority of PWP in both the **DBS** and **Non-DBS groups** (72% and 59%, respectively), had experienced fatigue for more than one year, and the fatigue was severe enough to interfere with day-to-day functions. After controlling for disease duration, the **DBS group** reported experiencing a debilitating level of fatigue for a significantly longer period of time when compared to the **Non-DBS group** (see Table 2).

Figure 3. Percentage of DBS and Non-DBS participants exhibiting clinically significant levels of Fatigue and Apathy



* There was a statistically significant difference between the DBS group and Non-DBS group as it relates to elevated levels of apathy

Table 2. Experience of Fatigue: The DBS and Non-DBS groups

Variable	DBS (N=204)	Non-DBS (N=309)
When do you experience the most fatigue?		
<i>Upon waking up in the morning</i>	3%	4%
<i>Mid to late morning</i>	11%	8%
<i>Afternoon</i>	36%	44%
<i>Evening</i>	25%	24%
<i>Most of the day or all day</i>	22%	14%
<i>Not applicable</i>	3%	6%
How many years do you believe that fatigue has interfered with day-to-day functions?		
<i>Less than 1</i>	8%	13%
<i>1 year</i>	12%	16%
<i>2 to 5 years</i>	42%	45%
<i>6 to 10 years</i>	19%	11%
<i>11 to 15 years</i>	5%	3%
<i>Greater than 15 years</i>	5%	<1%
<i>Not applicable</i>	9%	11%

Apathy in Individuals with PD:

- For the total sample, when participants were simply asked, “Do you experience apathy?” 49% of the participants (N=513) reported that they do experience apathy.
- When participants were simply asked “Do you experience apathy?” 56% of the **DBS group** reported that they had experienced apathy, while 45% of the **Non-DBS group** reported that they experienced apathy. Even after taking into consideration the duration of PD, significantly more individuals in the **DBS group** endorsed apathy than the **Non-DBS group**.
- The **DBS group** reported experiencing apathy for a significantly longer period of time as compared to the **Non-DBS group** (See Table 3).
- The Apathy Scale results confirmed that a significant portion of the participants experience apathy (See Figure 3).
 - 62% of the **DBS group** endorsed elevated levels of apathy.
 - 47% of the **Non-DBS group** endorsed elevated levels of apathy.
 - The level of apathy in the **DBS group** was significantly higher as compared to the **Non-DBS group**.

Table 3. Perception of Apathy: The DBS and Non-DBS groups

Variable	DBS (N=204)	Non-DBS (N=309)
How many years do you believe you have experienced apathy?		
<i>Less than 1</i>	10%	7%
<i>1 year</i>	11%	10%
<i>2 to 5 years</i>	29%	31%
<i>6 to 10 years*</i>	15%	5%
<i>11 to 15 years</i>	3%	2%
<i>Greater than 15 years</i>	3%	<1%
<i>Not applicable</i>	29%	44%

* Denotes the significant differences between the groups

Individuals experiencing BOTH Fatigue and Apathy:

- When participants were asked whether or not they experience fatigue and apathy, 39% (N=514) endorsed experiencing **both** fatigue and apathy.
- When looking at the responses on the Parkinson’s Disease Fatigue Scale and Apathy Scale, 44% (N=461) obtained scores that were clinically elevated for **both** fatigue and apathy.
- For the participants experiencing both fatigue and apathy, there was not a significant difference between the **DBS group** and the **Non-DBS group**.

Other Non-Motor Symptoms In Relation To Fatigue And Apathy:

Sleep Disturbance:

- This research found that fatigue and apathy are distinct experiences regardless of sleep quantity (how many hours a participant slept in one evening) or quality (intermittent waking in the evening). In other words, independent of sleep disturbance, fatigue and apathy were prevalent in PD.
- The **DBS group** reported longer cumulative sleep when compared to the **Non-DBS group**, which was statistically significant. The **DBS group** reported sleeping just over 7 hours per night cumulatively, while the **Non-DBS group** reported sleeping less than 7 hours of sleep cumulatively per evening.
- The **DBS group** and **Non-DBS group** were comparable on the duration of sleep they received without waking (approximately 4 ½ hours of sleep without waking).
- Many individuals in the **DBS group** and **Non-DBS group** reported taking naps, and the average duration of naps for both groups was approximately 1 hour.
- Sleep disorders were commonly reported and comparable for both the **DBS group** and **Non-DBS group**. Table 4 provides a list of sleep disorders that the participants indicated that they were experiencing.

Table 4. Sleep Disorders endorsed by the DBS and Non-DBS groups

Sleep Disorder	DBS (N=187)	Non-DBS (N=276)
<i>Sleep Apnea</i>	11%	15%
<i>REM Sleep Behavior Disorder</i>	5%	6%
<i>Excessive Daytime Sleepiness</i>	6%	7%
<i>Insomnia</i>	7%	8%
<i>Restless Leg Syndrome</i>	23%	17%

Depression and Anxiety:

Depression and anxiety are common in individuals with PD. Research has found that although psychological factors may contribute to the experience of fatigue and apathy,^{2,17} recent evidence has found that psychological factors alone do not explain the high prevalence of fatigue and apathy in PD.^{1,18,19}

- 46% of the **DBS group** indicated that they have received a diagnosis of depression, while 33% of the **Non-DBS group** indicated that they have received a diagnosis of depression.
- 31% and 25% of the **DBS group** and **Non-DBS group**, respectively, reported that they have received a diagnosis of anxiety.
- At the current time, the majority of both groups endorsed experiencing some level of perceived depression or anxiety, although the majority of both groups who endorsed at least some feelings of depression or anxiety characterized it as mild (See Table 5).
 - There was a statistically significant difference between the **DBS group** and **Non-DBS group** as it related to the experience of symptoms of depression, with more individuals in the **DBS group** endorsing mild

levels of depressive symptoms. Notably, the groups did not differ when considering report of moderate to severe symptoms of depression.

- There was not a statistically significant difference between the **DBS group** and **Non-DBS group** as it relates to the experience of symptoms of anxiety.
- Not surprisingly, symptoms of depression and anxiety did have a significant relationship with fatigue and apathy, but using statistical methods to take into account the impact of these symptoms on fatigue and apathy, depression and anxiety did not readily explain the prevalence of fatigue and apathy in PWP. Thus, fatigue and apathy appear to be experienced by individuals independent of psychological variables.

Table 5. Self-report Ratings of Depression and Anxiety: The DBS and Non-DBS groups

Variable	DBS (N=187)	Non-DBS (N=276)
Depression		
<i>None</i>	30%	47%
<i>Mild</i>	51%	35%
<i>Moderate</i>	18%	17%
<i>Severe</i>	<1%	1%
Anxiety		
<i>None</i>	43%	48%
<i>Mild</i>	36%	36%
<i>Moderate</i>	19%	14%
<i>Severe</i>	2%	2%

Younger versus Older PD Groups:

To look closer at the influence of age as it relates to fatigue and apathy, the participants were divided into a “**Younger PD group**” and an “**Older PD group**,” 50 to 69 years and 70 years and older, respectively.

Fatigue and Younger versus Older PD Groups:

- Overall, there was not a significant difference in fatigue between the **Younger PD group** and the **Older PD group** for those **with** and **without** DBS.
 - For the **Younger PD group**, 75% of the **DBS group** and 77% of the **Non-DBS group** indicated that they experienced fatigue, based on responding “yes” or “no” to the question “Do you experience Fatigue?”
 - There was not a significant difference between the groups.
 - For the **Older PD group**, 76% of the **DBS group** and 65% of the **Non-DBS group** endorsed experiencing fatigue on The Parkinson’s Disease Fatigue Scale, which was not significantly different from each other.
 - There was not a significant difference between the **Younger PD group** and the **Older PD group** for those **with** and **without** DBS on The Parkinson’s Fatigue Scale.
 - There were no significant gender differences in the experience of fatigue for either the **Younger PD**

group or the **Older PD group** for either the **DBS** or **Non-DBS groups**.

- The time of day **during** which fatigue was most pronounced was similar for both the **Younger group** and the **Older group**, which was reported to be predominantly in the afternoon and evening (See Table 6).
- For both the **Younger group** and the **Older group**, the most frequently endorsed duration that fatigue has interfered with day-to-day functions was 2 to 5 years, followed by 6 to 10 years.

Table 6. Experience of Fatigue: Younger and Old PD Groups

Variable	Younger PD Group		Older PD Group	
	DBS (N=145)	Non-DBS (N=154)	DBS (N=59)	Non-DBS (N=151)
When do you experience the most fatigue?				
<i>Upon waking up in the morning</i>	4%	5%	2%	3%
<i>Mid to late morning</i>	10%	6%	13%	10%
<i>Afternoon</i>	36%	47%	34%	43%
<i>Evening</i>	26%	27%	24%	20%
<i>Most of the day or all day</i>	21%	10%	24%	17%
<i>Not applicable</i>	3%	5%	3%	7%
What do you believe are the number of years that fatigue has interfered with day-to-day functions?				
<i>Less than 1</i>	7%	12%	10%	14%
<i>1 year</i>	12%	14%	9%	18%
<i>2 to 5 years</i>	39%	44%	51%	46%
<i>6 to 10 years</i>	20%	14%	15%	8%
<i>11 to 15 years</i>	6%	4%	5%	3%
<i>Greater than 15 years</i>	6%	1%	3%	0%
<i>Not applicable</i>	10%	11%	7%	11%

Apathy and Younger versus Older PD Groups:

- In the **Younger PD group**, 61% of those with **DBS** reported experiencing apathy, while 46% of the **Non-DBS group** experienced apathy, based on responding “yes” or “no” to the question “Do you experience apathy?”
 - There was a statistically significant difference between the two groups on this question.
- There was not a statistically significant difference in the report of apathy between the **DBS group** and **Non-DBS group** for the **Older PD group**, with reports of 44% and 45% of the **DBS group** and **Non-DBS group** reporting apathy, respectively.
- There was not a significant difference between the **Younger DBS group** and the **Older DBS group** on the Apathy Scale.
- There was a significant difference between the **Younger Non-DBS group** and the **Older Non-DBS group** on the Apathy Scale, with the **Older Non-DBS group** endorsing greater levels of apathy than the **Younger Non-DBS group**.

- Interestingly, when considering age, there was a significant difference between males and females in the **DBS group**.
 - **DBS group:**
 - In the **Younger PD group**, males endorsed more apathy than females, which was statistically significant.
 - Conversely, in the **Older PD group**, females endorsed more apathy than males, which was statistically significant.
 - **Non-DBS group**
 - There were no significant gender differences in the experience of apathy for either the **Younger PD group** or the **Older PD group**.
- There was not a statistically significant difference in the duration of apathy between the **DBS group** and **Non-DBS group** for the **Younger PD group** or the **Older PD group** (See Table 7).

Table 7. Perception of Apathy: Younger and Older PD Groups

Variable	Younger PD Group		Older PD Group	
	DBS (N=141)	Non-DBS (N=154)	DBS (N=42)	Non-DBS (N=149)
How many years do you believe you have experienced apathy?				
<i>Less than 1</i>	9%	7%	13%	7%
<i>1 year</i>	13%	7%	7%	14%
<i>2 to 5 years</i>	28%	32%	32%	30%
<i>6 to 10 years</i>	15%	5%	14%	6%
<i>11 to 15 years</i>	3%	2%	2%	1%
<i>Greater than 15 years</i>	3%	1%	3%	0%
<i>Not applicable</i>	29%	46%	29%	42%

Early versus Advanced PD:

To look closer at the influence of disease duration on fatigue and apathy, the participants in this study were divided into the groups **Early** versus **Advanced PD**. Previous research has found that in PD the mean time from symptom onset to development of motor complications was 6 years.^{20,21} Based on previous research, the participants in this study were divided into the groups **Early** versus **Advanced PD**, <6 years and 6+ years, respectively, to define a valid partition between early and advanced disease states.

Fatigue as it Relates to Early versus Advanced PD:

- PWP with **Advanced PD** experienced more fatigue than the **Early PD group**.
- When dividing the entire group (without dividing the participants into **DBS** and **Non-DBS groups**) into the **Early PD group** and the **Advanced DBS group**, 53% (n=135) of the **Early PD group** and 64% (n=387) of the **Advanced DBS group** were above the cutoff score on the Parkinson’s Disease Fatigue Scale. There was a statistically significant difference between the two groups.
- In the **Early PD group**, 70% of the **Non-DBS group** reported experiencing fatigue based on responding “yes” or “no” to the question “Do you experience fatigue?” The **DBS group** who were in the **Early PD**

group consisted of 5 participants. All 5 participants within the **DBS group** indicated that they experienced fatigue. Since there were so few individuals in the **DBS group** (N=5) within the **Early PD group**, analyses comparing fatigue in the **DBS group** to the fatigue in the **Non-DBS group** within this subset of “Early PD” were not conducted.

- In the **Advanced DBS group**, 75% of the **DBS participants** reported experiencing fatigue, and 71% of the **Non-DBS participants** experienced fatigue, which was not significantly different.
- The time of day during which fatigue was most pronounced was similar for both the **Early PD group** and the **Advanced DBS group**, which was reported to be predominantly in the afternoon and evening (See Table 6).
- For the **Early PD group**, the time of day during which fatigue was most pronounced was variable for the **DBS group** (again, there were few participants who were in this category).
- The majority of the **Non-DBS group** (52%) who were in the **Early PD group** indicated that the time of day during which fatigue was most pronounced was in the afternoon (See Table 8).
- For the **Advanced DBS group**, 36% and 25% of the **DBS group** reported that the time of day during which fatigue was most pronounced was in the afternoon and evening, respectively. Similarly, 39% and 29% of the **Non-DBS group** reported that the time of day during which fatigue was most pronounced was in the afternoon and evening, respectively (See Table 6).
- For the **Advanced DBS group**, the most frequently endorsed duration that fatigue has interfered with day-to-day functions was 2 to 5 years for both the **DBS** and **Non-DBS groups**.

Table 8. Perception of Fatigue: Early and Advanced PD Groups

Variable	Early PD		Advanced PD	
	DBS (N=5)	Non-DBS (N=125)	DBS (N=199)	Non-DBS (N=182)
When do you experience the most fatigue?				
<i>Upon waking up in the morning</i>	0%	5%	4%	3%
<i>Mid to late morning</i>	20%	9%	10%	7%
<i>Afternoon</i>	20%	52%	36%	39%
<i>Evening</i>	40%	16%	25%	29%
<i>Most of the day or all day</i>	20%	11%	22%	16%
<i>Not applicable</i>	0%	7%	3.0%	6%
How many years do you believe you have experienced fatigue that interferes with day-to-day functions?				
<i>Less than 1</i>	0%	18%	8%	9%
<i>1 year</i>	0%	17%	12%	16%
<i>2 to 5 years</i>	80%	45%	41%	44%
<i>6 to 10 years</i>	20%	5%	19%	15%
<i>11 to 15 years</i>	0%	2%	5%	4%
<i>Greater than 15 years</i>	0%	2%	5%	0%
<i>Not applicable</i>	0%	11%	10%	12%

Apathy as it Relates to Early versus Advanced PD:

- When dividing the entire group (without dividing the participants into DBS and **Non-DBS groups**) into the **Early PD group** and the **Advanced PD group**, 40% (of 135 participants) of the **Early PD group** and 56% (of 387 participants) of the **Advanced PD group** were above the cutoff score on the Apathy Scale. There was a statistically significant difference between the two groups, reflecting that the **Advanced PD group** experienced more apathy than the **Early PD group**, even when taking age into consideration.
- Since there were so few individuals in the **DBS group** (N=5) within the **Early PD group**, analyses comparing apathy in the **DBS group** to the apathy in the **Non-DBS group** within this subset of “Early PD” were not conducted. Notably, 3 out of 5 individuals (60%) in the **DBS group** within the **Early PD group** reported experiencing apathy. 40% of the **Non-DBS group** (n=126) within the **Early PD group** believed that they were experiencing apathy (See Table 9).
- When participants were simply asked “Do you experience Apathy?” in the **Advanced PD group**, 56% of the **DBS group** and 49% of the **Non-DBS group** indicated that they do experience apathy. There was not a statistically significant difference between groups.
- For the **Advanced PD group**, the most frequently endorsed duration that the participants have experienced apathy was 2 to 5 years for both the DBS and **Non-DBS groups** (see Table 9).

Table 9. Perception of experiencing Apathy: Early and Advanced PD Groups

Variable	Early PD		Advanced PD	
	DBS (N=5)	Non-DBS (N=126)	DBS (N=199)	Non-DBS (N=181)
How many years do you believe you have experienced apathy?				
<i>Less than 1</i>	20%	9%	10%	5%
<i>1 year</i>	20%	13%	11%	9%
<i>2 to 5 years</i>	60%	24%	28%	35%
<i>6 to 10 years</i>	0%	2%	15%	8%
<i>11 to 15 years</i>	0%	2%	3%	2%
<i>Greater than 15 years</i>	0%	0%	3%	1%
<i>Not applicable</i>	0%	50%	30%	40%

Conclusions

Fatigue and apathy are commonly reported by PWP and impact the daily lives of these individuals. The results of this study are discussed below in the context of the objectives of this report.

1. **We examined the prevalence and characteristics of fatigue and apathy in PWP, particularly as it relates to those who have undergone DBS (DBS group) and those who have not had DBS (Non-DBS group).**
 - Almost half of the PWP experience both fatigue and apathy, with the majority of the participants experiencing fatigue and almost half of the participants experiencing apathy, which is consistent with the high prevalence of fatigue and apathy documented in the PD literature.
 - Although there was not a difference for the experience of fatigue between the **DBS** and **Non-DBS groups**, there was a statistically significant difference in the experience of apathy between the groups. More individuals in the **DBS group** experienced apathy when compared to the **Non-DBS group**, and the **DBS group** also reported a longer duration of symptoms of apathy when compared to the **Non-DBS group**.
 - An international consortium of experts discussed the known possible effect of DBS (particularly of the STN) on verbal fluency/word-generation (which is sensitive to initiation deficits) and other aspects of executive functions (managing more complex information).²² There is a relationship with regard to the perceived lack of initiation in daily activity, not unlike symptoms of apathy, and poor performance on the aforementioned cognitive functions.²³ Thus, one may speculate that there is indeed a causal relationship between DBS and the symptoms of apathy.
 - As another possible explanation, Bronstein and colleagues pointed out that anti-parkinsonian medications are often reduced in DBS patients. This reduction in medication may also contribute in an increased level of apathy in DBS patients.
2. **We examined the prevalence of fatigue and apathy in Early PD versus Advanced PD and in participants classified as a Younger PD group versus an Older PD group.**
 - Duration of PD does appear to differentially impact the experience of fatigue and apathy in individuals with PD. Specifically, a greater number of individuals who have had PD for at least 6 years (Advanced PD) endorsed clinically significant levels of fatigue and apathy when compared to those individuals who have had PD for less than 6 years (Early PD). Thus, the longer individuals endure the course of PD, the increased likelihood that symptoms of fatigue and apathy may manifest in day-to-day activities.
 - Age (“**Younger PD group**” and “**Older PD group**”, 50 to 69 years and 70 years and older, respectively) was not a factor in the experience of apathy for the **DBS group**. In contrast, the **Older Non-DBS group** endorsed greater levels of apathy than the **Younger-Non-DBS group**.
3. **We examined the role of other non-motor symptoms, specifically sleep, depression and anxiety, on fatigue and apathy.**
 - Symptoms of depression and anxiety were found to have a significant relationship with fatigue and apathy, indicating that the more depression or anxiety a person experiences the greater the level of fatigue and apathy, with the converse also being true.
 - Although there were elevated levels of depression, anxiety, and sleep disturbance for both groups, fatigue and apathy were found to be independent symptoms for individuals with PD. In other words, depression,

anxiety, and sleep disturbance did not readily explain the experience of fatigue and apathy entirely. Thus, fatigue and apathy are distinct symptoms commonly experienced in PD, as they appear to be experienced by individuals independent of psychological variables and sleep disturbance.

Practical Implications

- Understanding the role of fatigue and apathy in the lives of individuals with PD can have a favorable impact on quality of life, vis-à-vis facilitating more therapeutic interaction.
- Fatigue was found to be most pronounced in the afternoon and evening for the **DBS** and **Non-DBS groups**, **Younger** and **Older PD groups**, and **Early** and **Advanced PD groups**.
 - Having knowledge and understanding as to when the patterns of fatigue and apathy present themselves has important practical implications.
 - For example, if individuals experience greater levels of fatigue and apathy in the afternoon and evening, engaging in any activities in the morning or early afternoon may lead to greater participation in cognitive and physical engagement (e.g., going to appointments, running errands, and other activities).
 - Additionally, the converse is also important such that increased assistance and support may be needed during times when fatigue and apathy are known to be more pronounced.
- Some treatment options for fatigue have included:²⁴
 - Discuss your symptoms of fatigue with your doctor.
 - Engage in regular exercise.
 - Anti-depressants may be of benefit for some patients. Although fatigue is not caused by depression, depression can worsen fatigue (or vice versa). Treating depression, if it is present, may assist in reducing the symptoms of fatigue.
 - Discuss your medication regimen with your doctor.
 - Discuss the possibility of medications that are known to help with alertness and increase activity.
- Strategies to improve difficulties with initiation may include.²⁵
 - Environmental cues or triggers for action, such as audible alarms, visual signs, or written calendars.
 - Verbal cues are often necessary.
 - Work with a neuropsychologist or psychologist who specializes in behavioral intervention to help build adaptive coping behaviors.
 - Anti-depressants may be of benefit for some patients. Although apathy can be independent of depression, depression can worsen apathy (or vice versa). Treating depression, if it is present, may assist in reducing the symptoms of apathy.

Closing Remarks

Both fatigue and apathy were apparent in many of the subgroups investigated, suggesting a continued need for additional research and understanding of these non-motor conditions. The effect of DBS on fatigue and apathy is not fully known, as DBS is still relatively in its infancy for PWP and researchers and clinicians continue to discover more about the impact of DBS on PWP.

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