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an affiliate of The Parkinson Alliance

Improving the Quality of Life
in the Parkinson's Community

Autonomic Symptoms in Parkinson's Disease

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INTRODUCTION

As many as two-thirds of patients with Parkinson's disease (PD) have signs and symptoms of autonomic dysfunction that may substantially impact their health-related quality of life[1,2]. The autonomic nervous system controls a number of functions in the body involving the cardiovascular system (i.e., blood pressure, heart rate.), digestion, urination, sexual arousal, thermo-regulation (i.e., managing temperature sensitivity), pupillary functions (i.e., light sensitivity), and swallowing. Thus, autonomic dysfunction, also called dysautonomia, refers to a complex array of symptoms that may manifest in, but are not limited to, the following:

- dizziness and fainting upon standing up because of a drop in blood pressure (orthostatic hypotension)
- inability to alter heart rate with exercise
- breathing difficulties
- sweating abnormalities, which could be either too much sweat or insufficient sweat
- digestion difficulties, such as constipation, diarrhea, bloating, loss of appetite, and difficulty swallowing
- urinary problems, such as difficulty starting urination, incontinence, and incomplete emptying of the bladder
- sexual problems such as erectile dysfunction in men and orgasmic difficulties in wome
- vision problems, such as light sensitivity and blurry vision

Dysautonomia often precedes the onset of motor symptoms in individuals with PD[3,4]. For example, gastrointestinal issues affect 70–80% of patients with PD, approximately half of whom report prominent constipation years before motor symptoms are apparent [2,5]. Autonomic disturbances also increase with age[6] and progression of disease[4], adversely impacting emotional well-being and quality of life[7].

Furthermore, PD treatments affect some aspects of autonomic functioning. In addition to a primary effect of PD neurological changes on autonomic function, levodopa, most antiparkinsonian medications, and deep brain stimulation (DBS) also impact autonomic functions[8]. Borgohain and colleagues[8] provide a nice review about effects of dopamine replacement therapy (DRT) and DBS on autonomic dysfunction. Based on their review, subthalamic (STN)-DBS may positively impact cardiovascular autonomic disturbances as evidenced by improved orthostatic hypotension through reduction of DRT. However, in general, the literature suggests that DBS may have variable effects on the cardiovascular autonomic dysfunction. There is also evidence suggesting that STN-DBS, in contrast to medical therapy, has a greater impact on improving gastrointestinal, urological and thermoregulatory symptoms more than medical therapy.

Halim and colleagues[9] found that 3 out of 11 patients undergoing STN-DBS reported improvement post-DBS in one or more symptoms of autonomic dysfunction. Notably, all three participants had early-onset PD, whereas the 8 individuals reporting no significant improvement had later-onset PD. Improvement was seen in sweating (thermoregulation), and/or bowel (gastrointestinal) and bladder (urinary) function. Other research has not found benefit from STN-DBS on autonomic dysfunction, reflecting an absence of differences between individuals with PD who have had DBS and those who are on optimal medical therapy alone (only medications)[10].

Despite a growing interest in the problem of autonomic dysfunction in PD, few studies have focused on autonomic dysfunction in PD, the "patient's perspective" about autonomic symptoms, and the relative differences between DBS and Non-DBS participants with respect to autonomic disturbances.

OBJECTIVE

1. To investigate the prevalence of autonomic dysfunction in a large sample of individuals with PD using the Scale for Outcomes in PD for Autonomic Symptoms (SCOPA-AUT).
2. To investigate the similarities and differences of self-reported autonomic dysfunction in individuals who have PD **with DBS** and **without DBS**.

METHODS

- Participants were recruited from previous participants in surveys conducted by The Parkinson Alliance (PA), advertisements at PD support groups, announcements in medical clinics, The PA website, or a DBS-focused affiliate website to The PA (DBS4PD.org).

- There were 1,489 individuals who participated in this survey, including 413 participants with PD who underwent **DBS** and 1,076 individuals with PD **without DBS** (**Non-DBS group**; see Table 1 for demographics). There was not a statistically significant difference on the SCOPA-AUT Total Score between DBS participants with STN and those with GPi targets. As such, all patients who had DBS of either the STN or GPi were included in the analyses.
- For both the DBS group and the Non-DBS group, 86% of the surveys were completed independently, whereas 14% of participants required writing assistance.
- Participants represented 50 states, with California (17%), Florida (12%), Arizona (11%), New Jersey (9%), Texas (8%), New York (8%), Colorado (5%), Pennsylvania (5%), Virginia (3%), and Michigan (2%) being the top 10 states that had the most participants. Geographical distribution was comparable between groups. There were 8 international participants.

Measures:

The Demographic Questionnaire and Questions Related to Autonomic Dysfunction:

The demographic questionnaire included questions related to background information and questions pertaining to blood pressure, swallowing, emotional well-being, the impact and/or restrictions that autonomic dysfunction has on social engagement, and quality of life.

Scale for Outcomes in PD for Autonomic Symptoms (SCOPA-AUT)[3]:

The Scale for Outcomes in PD for Autonomic Symptoms (SCOPA-AUT) is an instrument specifically designed to assess autonomic function in individuals with PD. The original measure is composed of 25 items, targeting the following domains: gastrointestinal; urinary; cardiovascular; thermoregulatory (e.g., managing temperature sensitivity); pupillomotor (light sensitivity); and sexual function (two items for men and two for women). Through the use of sophisticated analyses, Forjaz and colleagues[11] combined the sexual items for men and women, resulting in a total scale comprised of 23 items with the following breakdown of items per domain for this study:

- Swallowing (3 items)
- Gastrointestinal (4 items)
- Urinary (6 items)
- Cardiovascular (3 items)
- Thermoregulatory (4 items)
- Pupillomotor (1 item)
- Sexual Function (2 items)

The Hospital Anxiety and Depression Scale (HAD)[12, 13]:

The Hospital Anxiety and Depression Scale is a self-report rating scale designed to measure both anxiety and depression. It consists of two subscales, depression and anxiety. The HAD is scored by summing the ratings of 14 items to yield a total score, and by summing the ratings for the 7 items of each subscale to yield separate scores for anxiety and depression.

Factors to consider when interpreting the results:

- This study used a survey-based methodology. Generalizability of the results may be limited. Level of awareness of autonomic symptoms may be reduced, which may impact one's report of autonomic disturbance. Furthermore, participants have different surgeons and neurologists, which may result in diverse outcomes and management of symptoms.
- Sample sizes noted in the sections below may vary somewhat within specific groups (e.g., younger, older, early, advanced, DBS, Non-DBS etc.), since some individuals may not have responded to a specific question.

RESULTS

The summary of the demographic information for this study can be found in Table 1. The **Non-DBS group** was significantly older than the **DBS group (average 71 versus 66 years).** By contrast, the **DBS group** had a younger average age of PD diagnosis **(51 years)** than the **Non-DBS group (64 years)** and a longer duration of PD (see Table 1). Gender (male greater than female), marital status (majority being married), race (majority being White/Caucasian), and education (majority having higher education) were comparable between groups.

Table 1. Demographics and Clinical Features of the Sample

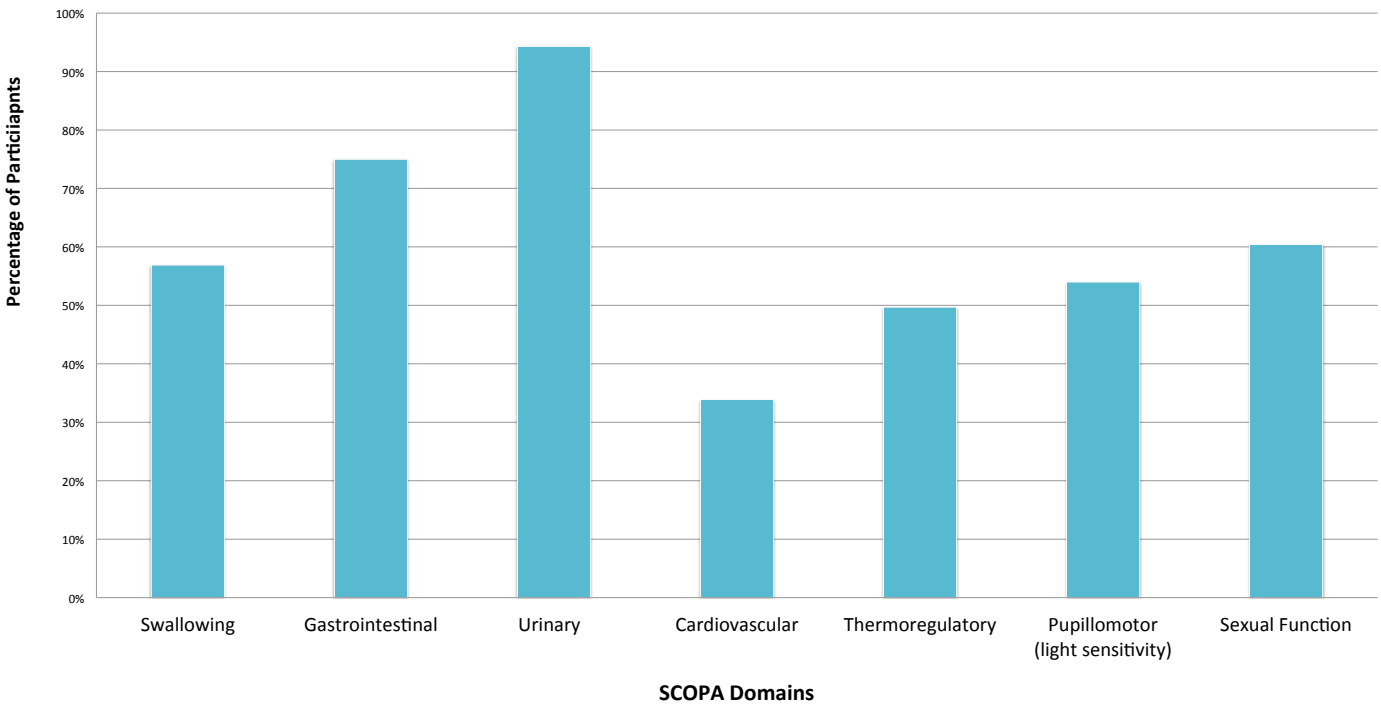
Variable	DBS (*n* =413)	Non-DBS (*n* =1076)
Average Age in Years (range)*	66 (37-87)	71 (31-97)
Duration of PD in Years (range)*	15 (1-45)	7 (0-58)
Average Age of PD Diagnosis (range)*	51 (27-75)	64 (27-90)
Average Age at Time of DBS in Years (range)	61 (31-85)	n/a
Average Duration since DBS in Years (range)	5 (0-25)	n/a
Bilateral Stimulation	86	n/a
Target		
STN	86%	n/a
GPi	11%	n/a
Thalamus	3%	n/a
Male	61%	56%
Female	39%	44%
Married	79%	78%
Race		
Caucasian	94%	95%
Latino/Hispanic	3%	3%
African American	<1%	<1%
Asian	2%	1%
Education		
<12 years	5%	4%
High School	8%	9%
Some College or Associate's Degree	24%	23%
College	24%	27%
Graduate/Advanced Degree	39%	36%
Dominant Hand		
Right	88%	88%
Left	11%	10%
Ambidextrous	2%	2%

*p<0.0001
n/a = not applicable

AUTONOMIC DYSFUNCTION IN PD: ALL PARTICIPANTS (N=1,489)

- Autonomic dysfunction was highly prevalent for the participants in this survey.
- The percentage of participants reporting at least one autonomic symptom within the respective domains of the SCOPA-AUT ranged from 50% to more than 90%. Of the numerous dysautonomic symptoms, the most frequently reported symptoms included urinary, gastrointestinal, and swallowing difficulties, followed by symptoms related to thermoregulatory dysfunction (managing temperature sensitivity), sexual dysfunction, cardiovascular issues, and pupillary dysfunction (light sensitivity).
- In order to better portray the significant prevalence of the most frequently experienced autonomic symptoms in individuals within this survey, Figure 1 illustrates the percentage of individuals who reported two or more autonomic symptoms per SCOPA-AUT domain; a substantial number reported significant autonomic dysfunction.
    - The most frequently reported symptoms involved urinary and gastrointestinal dysfunction.
        - 94% reported two or more Urinary items.
        - 75% reported two or more Gastrointestinal items.
        - Sexual dysfunction, followed by difficulties with swallowing, pupillomotor function (light sensitivity), thermoregulation (managing temperature sensitivity), and cardiovascular symptoms, are also highly experienced.

Figure 1. Percentage of PD Participants Reporting Two or More Autonomic Symptom Per SCOPA Domain (N= 1489)



* Notably, Pupillomotor (light sensitivity) is only comprised of one question/item in the domain, while all other domains have two or more questions/items.

Selected Symptoms Related to Autonomic Dysfunction:

Blood Pressure:

- 32% of the participants reported that they have high blood pressure; 57% reported they do not, and 11% were not sure.
- 18% of the participants reported that they had low blood pressure; 67% reported that they do not, and 15% were not sure.

Swallowing:

- 55% of the participants reported that they choke when swallowing **food** and/or **medications**.
  - As for frequency of having swallowing difficulties:
    - Sometimes: 47%
    - Often: 7%
    - Always: <1%
- 41 % reported having experienced choking on his/her **saliva**.
  - As for the frequency of experiencing choking on saliva:
    - Sometimes: 36%
    - Often: 5%
    - Always: <1%
- 50% of the participants reported that they experience **heartburn**.
  - As for the frequency of experiencing heatburn:
    - Sometimes: 38%
    - Often: 10%
    - Always: <1%

Emotional Well-being:

- Based on self-report ratings, participants rated their experience with depression and anxiety "in general" as either not at all, mild, moderate, or severe.

- Depression:
  - Not at all: 33%
  - Mild: 47%
  - Moderate: 18%
  - Severe: <2 %
- Anxiety:
  - Not at all: 25%
  - Mild: 49%
  - Moderate: 24%
  - Severe: <2%

- Approximately half of the participants indicated that they engage in repetitious/rhythmical movements/habits to reduce feelings of tension (e.g., moving your leg up and down; moving your foot around; tapping your hand on your lap or on the table; etc.):
  - Not at all: 48%
  - Sometimes: 37%
  - Often: 13%
  - Always: 1%
  - Not applicable: 1%

- Hospital Anxiety and Depression Scale (HAD):
  - The participants completed the HAD Scale, which is designed to assess numerous symptoms related to depression and anxiety, thus, providing an overall score for "Depression" and "Anxiety."
    - 26% of the participants were experiencing significant levels of depression.
    - 28% of the participants were experiencing significant levels of anxiety.

Impact of Autonomic Dysfunction on Social Involvement:

- Fifty-six percent of the participants in this study indicated that autonomic symptoms adversely impacted or restricted engagement in social activities.
  - Sometimes: 40%
  - Often: 12%
  - Always: 4%
  - Not applicable: 1%

AUTONOMIC DYSFUNCTION AS IT RELATES TO AGE AND DISEASE DURATION:

- Participants were divided into groups matched on age and disease duration.
  - Age: Age groups were divided into **Younger PD group** (ages 50-69) and **Older PD group** (ages 70+ years).
  - Disease Duration: In previous research on PD, the average time from symptom onset to development of motor complications was 6 years[14, 15]. Based on previous research, the participants in this study were divided into the groups **Early Stage** versus **Advanced Stage PD, <6 years and 6+ years**, respectively, to define a valid partition between early and advanced disease states. To better illustrate the impact of disease duration on autonomic dysfunction, the **Advanced Stage PD group** was further divided into **Advanced Stage PD 6-10 years** and **Advanced Stage PD 11+ years**.

- Autonomic dysfunction gets worse with age and disease duration (see Tables 2 & 3).
  - After taking into account disease duration, autonomic dysfunction was reported in greater frequency and severity as age increases.
  - After taking into account age, autonomic dysfunction was reported in greater frequency and severity as disease duration increases.

- **Table 2** illustrates high percentages of autonomic symptoms reported in each domain of the SCOPA-AUT across age and disease duration. Notably, to highlight the significance of the prevalence of autonomic dysfunction, Table 2 includes the percentage of participants who reported two or more symptoms within a specific domain of autonomic function, with exception of pupillary dysfunction (light sensitivity), since this domain only had one question/item.
    - Urinary difficulties and gastrointestinal symptoms were the most frequently reported symptoms of autonomic dysfunction across age and disease duration cohorts (percentage of particiants reporting urinary symptoms ranged between 87% to 98%; percentage of participants reporting gastrointestinal symptoms ranged from 69% to 84%).
    - More than half of the participants reported swallowing disturbance, sexual dysfunction, thermodysregulation (sensitivity to temperature), and pupillary dysfunction (light sensitvity) across age and disease duration cohorts.
    - Cardiovascular, albeit highly prevalent across age and disease duration, was the domain least reported (ranging from 28% to 40%).
    - Swallowing difficulties appear to have the largest increase in frequency of being reported as individuals get older and as the disease progresses.

Table 2: Participants Reporting Two or More Autonomic Symptoms within a Domain: Across Age and Disease Duation Cohorts

	Early PD Group (< 6 years duration)		Advanced PD Group			
			6-10 years duration		11+ years duration	
Two or more symptoms reported within the respective domains on the SCOPA	**Younger (50-69) (*n* =235)**	**Older (70+) (*n* =308)**	**Younger (50-69) (*n* =157)**	**Older (70+) (*n* = 235)**	**Younger (50-69) (*n* =261)**	**Older (70+) (*n* =253)**
Urinary	89%	95%	87%	97%	94%	98%
Gastrointestinal	72%	69%	74%	77%	80%	84%
Swallowing	50%	45%	57%	59%	66%	66%
Cardiovascular	28%	33%	33%	38%	29%	40%
Sexual Function	56%	58%	63%	64%	64%	61%
Thermoregulatory	49%	41%	63%	41%	56%	53%
Pupillomotor (light sensitivity)	52%	49%	54%	54%	57%	58%

* Higher scores reflect greater number of participants reporting autonomic dysfunction.

** Notably, Pupillomotor (light sensitivity) is only comprised of one item in the domain, while all other domains have two or more items.

- **Table 3** provides the average scores for each SCOPA-AUT domain and the Total Score.
  - The increase in autonomic dysfunction between age cohorts was statistically significant (after taking into account disease duration); the **Older PD group** experienced more autonomic dysfunction than the **Younger PD group**.
  - The increase in autonomic dysfunction between disease duration cohorts was statistically significant (after taking into account age); the **Advanced PD Group** reported more autonomic dysfunction than the **Early PD Group**.
  - Note: Since the number of questions in each domain differs, one cannot compare one domain score to another domain score.

Table 3: Average Total Score and Domain Scores on the SCOPA-AUT Across Age and Disease Duration Cohorts

	Early PD Group (< 6 years duration)		Advanced PD Group			
			6-10 years duration		11+ years duration	
Domains on the SCOPA	**Younger (50-69) (*n* =235)**	**Older (70+) (*n* =308)**	**Younger (50-69) (*n* =157)**	**Older (70+) (*n* = 235)**	**Younger (50-69) (*n* =261)**	**Older (70+) (*n* =253)**
SCOPA Total Score (range: 0-69)	17.21	17.08	19.31	18.96	19.85	20.56
Urinary (range: 0-18)	6.29	6.47	6.74	7.21	6.76	7.63
Gastrointestinal (range: 0-12)	3.06	2.96	3.12	3.22	3.44	3.63
Swallowing (range: 0-9)	1.85	1.74	2.21	2.34	2.60	2.83
Cardiovascular (range: 0-9)	1.06	1.02	1.26	1.21	1.08	1.31
Sexual Function (range: 0-6)	2.29	2.34	2.51	2.75	2.72	2.66
Thermoregulatory (range: 0-12)	2.26	1.78	2.73	1.73	2.49	2.32
Pupillomotor (light sensitivity) (range: 0-3)	0.73	0.67	0.82	0.81	0.81	0.93

* Higher scores reflect greater report of autonomic dysfunction. Although there may appear to be modest to small changes in the average scores, the change in scores are significant across age and disease duration.

* Note: Since the number of questions in each domain differs, one cannot compare one domain score to another domain score.

THE RELATIONSHIP BETWEEN EMOTIONAL WELL-BEING AND AUTONOMIC DYSFUNCTION:

- There was a significant relationship between emotional status and autonomic dysfunction. Specifically, the greater the experience of autonomic dysfunction, the greater the report of depression and anxiety.
- Quality of life for the participants in this study was rated as (N=1,445):
  - Excellent: 15%
  - Good: 54%
  - Fair: 26%
  - Poor: 5%
  - The worst imaginable: <1%

AUTONOMIC DYSFUNCTION AND DBS AND NON-DBS SUBGROUPS (after controlling for age and disease duration):

- There was not a statistically significant difference between the **DBS** and **Non-DBS Group** on the SCOPA-AUT Total Score.
- When looking at the SCOPA-AUT domains, the majority of domains did not reveal a statistically significant difference between the **DBS Group** and the **Non-DBS Group**: Urinary, Gastrointestinal, Sexual Dysfunction, Thermoregulation, and Pupillary Dysfunction (light sensitivity) were comparable between groups.
  - There was a statistically significant difference between the **DBS Group** and the **Non-DBS Group** as it relates to the Cardiovascular domain. The participants in the **DBS group** reported less cardiovascular symptoms than the **Non-DBS group.**
  - There was a statistically significant difference between the **DBS Group** and the **Non-DBS Group** as it relates to the Swallowing domain. The participants in the **DBS group** reported more swallowing difficulties than the **Non-DBS group.**
    - There was also a statistically significant difference between the **STN-DBS** and **GPi-DBS** targets as it relates to swallowing, with the **STN-DBS group** reporting more swallowing difficulties than the **GPi-DBS group**. There were no other significant differences for GPi and STN targets, as it relates to the SCOPA-AUT findings.

SUMMARY AND DISCUSSION

There is a burgeoning interest in autonomic dysfunction in Parkinson's disease (PD), as such symptoms can substantially and adversely impact health-related quality of life[1,2]. The autonomic nervous system controls a number of functions in the body involving the cardiovascular system (i.e., impacting blood pressure, breathing, etc.), digestion, urination, sexual arousal, thermo-regulation (e.g., managing temperature sensitivity), pupillary functions (i.e., light sensitivity), and swallowing.

Despite the growing interest in autonomic dysfunction in PD, few studies have focused on the profile of autonomic dysfunction in PD, the "patient's perspective" about autonomic symptoms, and a differential profile between **DBS** and **Non-DBS** participants as it relates to autonomic disturbances. This survey's main objectives included: (1) To investigate the prevalence of autonomic dysfunction in a large sample of individuals with PD using the Scale for Outcomes in PD for Autonomic Symptoms (SCOPA-AUT), and (2) To investigate the similarities and differences of self-reported autonomic dysfunction in individuals who have PD **with DBS** and **without DBS**.

TAKE HOME POINTS FROM THIS SURVEY:

Objective 1: To identify the prevalence of and symptom manifestation of autonomic dysfunction in a large sample (1,489 individuals):

- Participants in this survey reported autonomic dysfunction at a very high frequency.
  - Autonomic dysfunction is highly prevalent in both Younger and Older Participants and in both Early Stages and Advanced Stages of PD.
  - Autonomic dysfunction becomes more frequently reported and presents with increased severity as one gets older and as PD progresses.

- The most frequently experienced symptoms, which were reported by the vast majority of the participants in this survey across age (Younger and Older) and Disease Duration (Early and Advanced Stages), included urinary and gastrointestinal issues.
- Sexual dysfunction, followed by swallowing difficulties, pupillomotor (light sensitivity), thermoregulation (managing temperature sensitivity), and cardiovascular, were also reported with high frequency.
- Emotional disturbance was prevalent and significantly related to autonomic dysfunction.

Objective 2: To investigate the similarities and differences of self-reported autonomic dysfunction in individuals who have PD **with DBS** and **without DBS**.

- There was not a statistically significant difference between the **DBS** and **Non-DBS Group** on the SCOPA-AUT Total Score.
- The SCOPA-AUT Total Score and the majority of domains did not reveal a statistically significant difference between the **DBS Group** and the **Non-DBS Group**.
    - There was a statistically significant difference between the **DBS Group** and the **Non-DBS Group** as it relates to the Cardiovascular domain, where the participants in the **DBS group** reported less cardiovascular symptoms than the **Non-DBS group.**
        - This finding is consistent with other research stating that DBS may have a beneficial effect on cardiovascular autonomic symptoms, possibly by decreasing dopaminergic medications.
    - There was a statistically significant difference between the **DBS Group** and the **Non-DBS Group** as it relates to the Swallowing domain, where the participants in the **DBS group** reported more swallowing difficulties than the **Non-DBS group.**
        - This finding is consistent with other research that has found that STN-DBS may have an adverse impact on swallowing[16, 17, 18].

Quality of Life:

- Despite the significant and challenging symptoms that are known to accompany PD, 95% of the participants in this survey rated their quality of life as either "Fair," "Good," or "Excellent."

General Implications and Recommendations:

- Keeping your doctor/treatment team informed about the experience of autonomic symptoms, including difficulties with urinary functions, gastrointestinal issues, cardiovascular problems, swallowing, sexual disturbance, thermoregulation (managing temperature sensitivity), and light sensitivity, is important in helping to facilitate appropriate intervention.
- Cardiovascular changes and orthostatic hypotension are common in PD and are significant risk factors for falls, morbidity and mortality. Early identification of risk factors, careful diagnosis, and treatment of vascular disease may help reduce adverse health outcomes related to the severity of autonomic-related disorders.
- If you are experiencing orthostatic hypotension, some recommendations regarding the management of orthostatic hypotension include (consult with your doctor first, however):
    - Address the use of medications or medication changes. Consultation with your doctor may help address some possible causes for blood pressure changes.
    - Sit up or stand up slowly.
    - Avoid crossing your legs while sitting.
    - Drink plenty of fluids (if swallowing difficulties are present, consult your doctor about fluid intake).
    - Drink little or no alcohol.
- Swallowing dysfunction is a significant health hazard for individuals with PD[19].
        - Should swallowing difficulties be experienced, consult with your doctor and discuss the possible need for assessment and treatment by a Speech Language Pathologist (specialists in swallowing disorders).
        - Target selection for DBS candidates may also be a relevant implication for individuals with swallowing difficulties prior to DBS surgery. Troche, et al.[17] commented that the GPi target for DBS is selected more often for individuals with impaired swallowing prior to surgery.

- Troche and colleagues[17] stated, "Future studies should help to elucidate the mechanisms underpinning the effects of DBS on swallowing function and potentially lead to modification of DBS procedures that will minimize adverse effects and improve long-term outcomes for these patients. ... Since the use of DBS as an effective treatment modality for PD continues to increase, this information is critical to the field." (pages 429-430).

- Treatment for urinary, gastrointestinal, and sexual functioning changes/difficulties can be challenging. Changes in medications or additional medications can assist in treating symptoms within these domains, and nutrition and behavioral intervention may also be of help[20]. Consulting with your doctor can help address some of these issues. Always ask if a new medication has the potential for a negative effect on memory and other intellectual or mental functions. For example, anticholinergic medications used to treat urinary symptoms, e.g., oxybutynin (Detrol), can contribute to memory problems, hallucinations, and confusion. In such cases, the relative risks and benefits of the treatment need to be considered carefully.

- Regular monitoring of emotional status is indicated for individuals with PD.
  - Psychiatric/psychological changes, such as depression and anxiety, may be related to reactions to a medical condition or psychosocial stressors, medication effects, or neurologic changes due to PD. A conversation with your doctor and/or an evaluation by a mental health professional can assist in identifying appropriate treatment for symptoms of psychological disturbance and/or difficulties adjusting to your medical condition.

- As it relates to autonomic dysfunction, better patient information, education and understanding about autonomic dysfunction are recommended to better manage these non-motor symptoms commonly experienced for individuals with PD.

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Margaret Tuchman,
Bilateral DBS-STN, 2000
President,
The Parkinson Alliance

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