THE IMPACT AND DETECTION OF NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE

Janis Miyasaki, MD, MEd, FRCPC, FAAN
University of Alberta
Edmonton, Alberta, CANADA

In the end of the twentieth century, neurology focused on motor symptoms as the primary source of disability in Parkinson's disease (PD). Studies were designed to reduce the frequency and severity of motor complications such as motor fluctuations and dyskinesias. Physicians became accustomed to strategies to delay the initiation of levodopa to this end. The twenty-first century may be thought of as a revolution in the philosophy of PD care. We acknowledge that PD is not just an illness of dopamine depletion, but a complex illness with impacts throughout and beyond the central nervous system. This dawn of non-motor discovery only reaffirms the first description by James Parkinson that did include the non-motor features that were discounted for their impact and significance to our patients' lives.

Despite this, let me first emphasize that no study has asked patients about values for eliminating disability from motor or non-motor symptoms. Would a patient tolerate all the non-motor symptoms in order to retain mobility? Or would they choose a wheelchair bound state to be rid of the non-motor complications that plague them? Therefore, caring for people with PD requires attention to motor symptoms, non-motor features and vigilance for the complications that our treatments may cause.

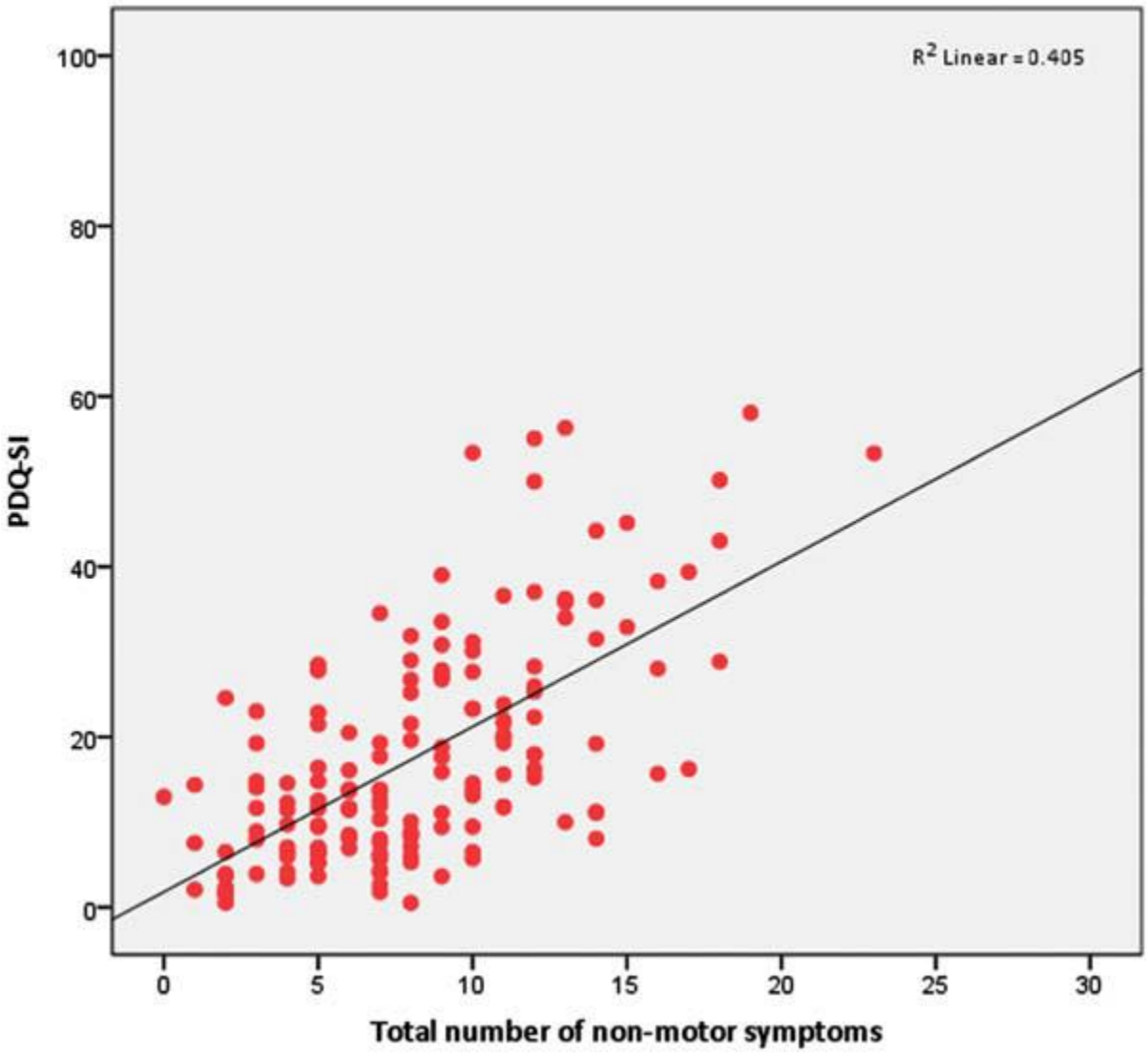
The Impact of Non-motor Symptoms on PD patients

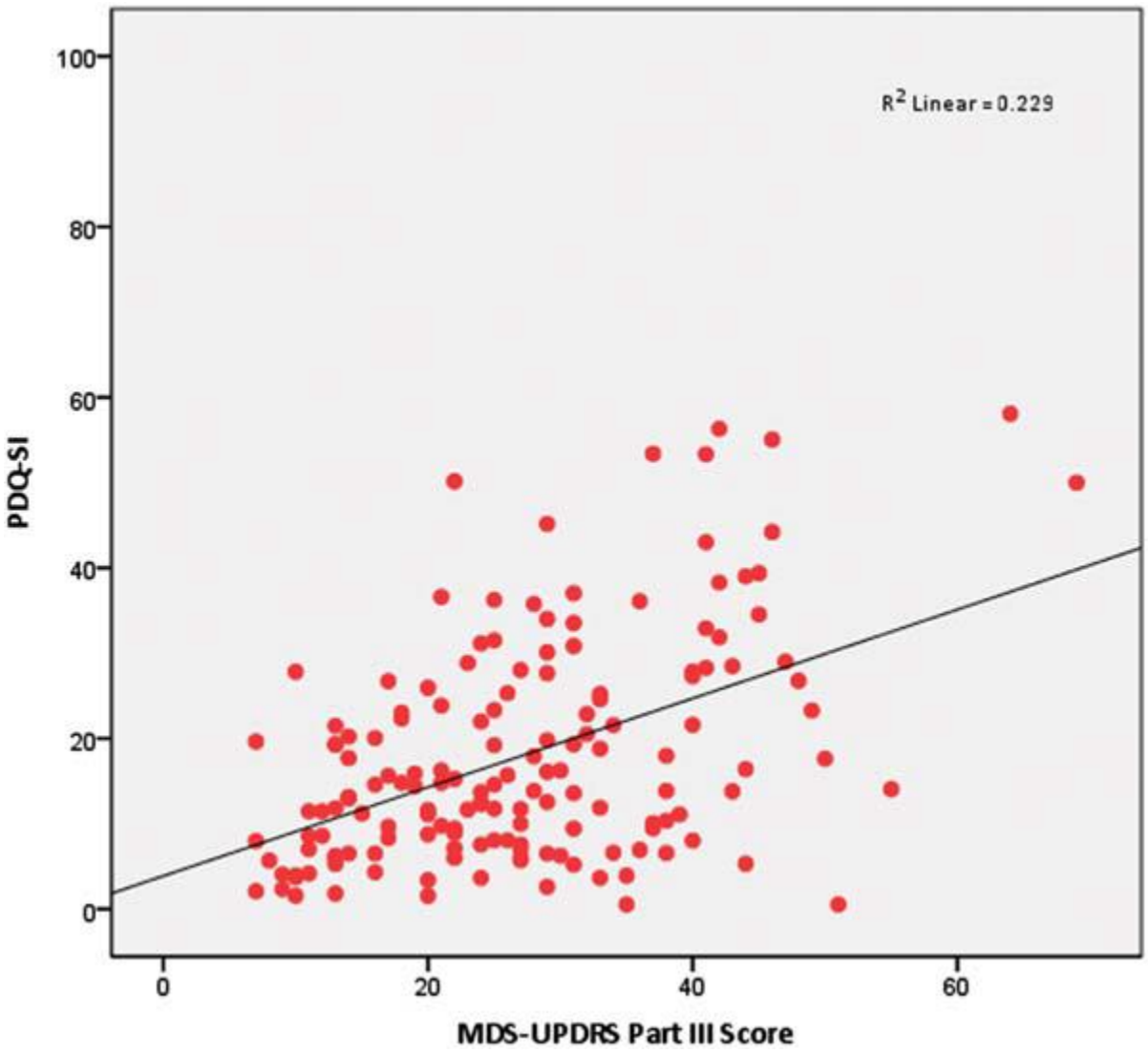
The first study to systematically assess non-motor studies was reported in 2002 by Shulman and colleagues (Shulman, Taback, Rabinstein, & Weiner, 2002). They found 44% had depression, 39% had anxiety, 42% reported fatigue and 43% reported sleep disturbance. More than half of these cases were undetected by their neurologist and sleep disturbance was undetected in 40% of patients. Since that time, awareness is increasing detection. Non-motor symptoms are the focus of clinical trials and physicians can incorporate surveys to detect non-motor symptoms.

The PRIAMO study found among 1072 patients that non-motor symptoms resulted in more disability as measured by the PDQ-39 (Barone et al., 2009). The features most strongly associated with worse quality of life were apathy, fatigue, problems with attention and memory and psychiatric symptoms. The average number of non-motor symptoms was 7.8.

Meanwhile, in those undergoing deep brain stimulation, pain was reduced and quality of life increased (Cury et al., 2014). Prior to DBS, pain was present in 70% of subjects and following surgery, only 21% of the 41 patients continued to have pain. Dystonia and musculoskeletal pain responded well to DBS while central pain and neuropathic type pain were not improved. One must consider that motor function also improved as does sleep in typical PD patients receiving DBS, hence this evidence is considered a case series report, Class IV.

Among those with newly diagnosed PD, non-motor symptoms are common with PD patients reporting 8.3 non-motor symptoms vs 2.8 for controls (Duncan et al., 2014; Duncan et al., 2014). Although a study of early PD, only 20 patients (12%) were drug naïve. Motor disability also correlated with reduced quality of life to a similar degree as the total number of non-motor symptoms. Of note, lower MOCA or MMSE did not correlate with lower quality of life, but patient self-report of impaired concentration and forgetfulness did impact negatively. Of note, age matched controls also reported these symptoms and the absolute difference was 13% higher among PD patients and not significantly different. The impact of impaired concentration and forgetfulness in the non-PD population on quality of life was not reported. However, this study points to the joint effects of mobility and non-motor symptoms on quality of life as well as the need to screen even newly diagnosed patients for these symptoms.





Above charts from (Duncan et al., 2014).

Detecting Non-Motor Symptoms in PD

The workhorse of PD assessments in clinical trials has been the Unified Parkinson Disease Rating Scale (Richards, Marder, Cote, & Mayeux, 1994). This scale includes some features of non-motor function (namely cognition, sleep disturbance, orthostatic hypotension, apathy, depression, pain, drooling, nausea and vomiting) but omits many other important symptoms. As a result, patient-completed surveys of cognition, autonomic dysfunction and sleep have been developed but are not comprehensive. A simple checklist of yes/no comprised the Non-motor Symptoms Scale (Chaudhuri, Yates, & Martinez-Martin, 2005). The benefits are: 2 pages, severity now estimated as well as frequency. Find the newest version here for your office: http://www.movementdisorders.org/MDS/Education/Rating-Scales.htm

The MDS-UPDRS is a newer version of the Unified Parkinson Disease Rating Scale and incorporates Experiences of Daily Living that is comprehensive and patient reported (Khoo et al., 2013). The benefit of this is some quantification of the severity of symptoms. A review of measures for subjects in a previous study of potential neuroprotective agents found that the MDS-UPDRS is more sensitive to change in early and mid-stage patients and less sensitive for those after 10 years of illness (Lang et al., 2013). Hence, other measures may be required for those with advanced illness. Find the scale here for your office use (caution, it is very long!!!): http://www.movementdisorders.org/MDS/Education/Rating-Scales.htm

Detecting and the subsequent efforts to address non-motor symptoms is indeed time-consuming. Patient-reported surveys can reduce the burden on physicians. Physicians must be aware that patient report may be not reflect all symptoms accurately, in particular, apathy, depression and impulsive behaviours. A separate scale is available for impulse control disorders, however, does require clinician guidance for accurate completion and optimally requires an "informed other" to accurately detect all behaviours. Get a copy for your office here: http://www.toolkit.parkinson.org/content/impulse-control-disorders

Although the MDS-UPDRS does assess sleep, whether it can predict sleepiness during activities that require wakefulness such as operating heavy machinery, flying a plane or driving a car is not known. Although the Multiple Sleep Latency Test is the standard for sleepiness during the day and other tests exist to assess wakefulness, the most commonly used tool to assess sleepiness in PD is the Epworth Sleepiness Scale before and after treatment is initiated. Get a copy for your office here: http://www.toolkit.parkinson.org/content/sleep-disturbances

For Caregiver Burden, I would suggest the Zarit Caregiver Burden Inventory – get the scale here http://scale-library.com/pdf/Zarit_Burden_Interview.pdf

A scale used in palliative care for Parkinson's disease was developed at the University of Toronto and reported in Parkinsonism and Related Disorders 2012. The full scale is appended.

With the adoption of the Electronic Health Record, hopefully some of these scales can be adopted in your charting routine and some patient completed forms directly uploaded to the records (wouldn't that be awesome?).

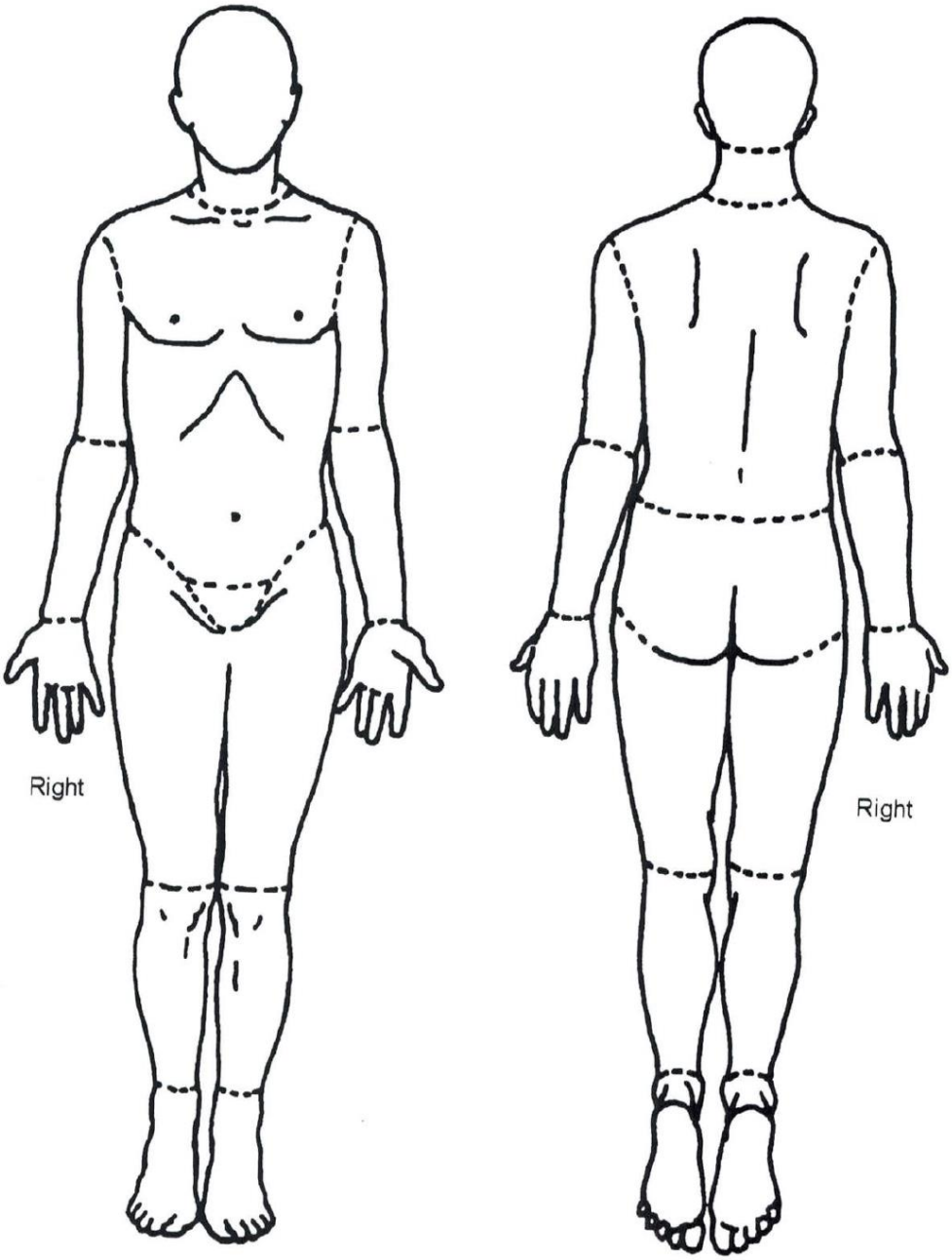
Please circle the number that best describes how you feel NOW:

No Pain	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Drowsiness
No Nausea	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Nausea
No Lack of Appetite	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Lack of Appetite
No Shortness of Breath	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Wellbeing
No _____ Other Problem	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst possible _____

Please circle the number that best describes how you feel NOW:

No Stiffness	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Stiffness
No Constipation	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Constipation
No Swallowing Difficulties	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Swallowing Difficulties
No Confusion	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Confusion

Please mark on these pictures where it is that you hurt:



	Experience Symptoms	Usually improves After my next dose
1. Tremor		
2. Difficulty in speech		
3. Anxiety		
4. Experience sweating		
5. Mood changes		
6. Weakness		
7. Problems with balance		
8. Slowness of movement		
9. Reduced dexterity		
10. Numbness		
11. General stiffness		
12. Experience panic attacks		
13. Cloudy mind/dullness thinking		
14. Abdominal discomfort		
15. Muscle cramping		
16. Difficulty getting out of the chair		
17. Experience hot and cold		
18. Pain		
19. Aching		

Wearing Off Questionaire, Mark Stacy
http://img.medscape.com/fullsize/701/816/58977_Questionnaire_WearingOff.pdf

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