REVIEW

The *Movement* Disorders Task Force Review of Dysautonomia Rating Scales in Parkinson's Disease with Regard to Symptoms of Orthostatic Hypotension

Anne Pavy-Le Traon, MD, PhD,[1]* Gerard Amarenco, MD,[2] Susanne Duerr, MD,[3] Horacio Kaufmann, MD,[4] Heinz Lahrmann, MD,[5] Stephanie R. Shaftman, MSc, MS,[6] François Tison, MD, PhD,[1,7] Gregor K. Wenning, MD, MSc, PhD,[3] Christopher G. Goetz, MD,[8] Werner Poewe, MD,[9] Cristina Sampaio, MD,[10] Anette Schrag, FRCP, PhD,[11] Glenn T. Stebbins, PhD,[8] and Olivier Rascol, MD[1,12]

[1]*Reference Centre for MSA, University Hospital, INSERM U1048 Eq8, Toulouse, France, and Explorations Fonctionnelles, University Hospital, Brest, France*
[2]*Service de Rééducation Neurologique et d'Explorations Périnéales, Rothschild Hospital, Paris, France*
[3]*Division of Clinical Neurobiology, Medical University, Innsbruck, Austria*
[4]*Department of Neurology, New York University, New York, New York, USA*
[5]*Department of Neurology, Kaiser Franz Josef Hospital, Vienna, Austria*
[6]*Biostatistics, Bioinformatics, and Epidemiology, Medical University of South Carolina, Charleston, South Carolina, USA*
[7]*Department of Neurology, University Hospital of Bordeaux, Pessac, France*
[8]*Department of Neurological Services, Rush University School of Medicine, Chicago, Illinois, USA*
[9]*Department of Neurology, Innsbruck Medical University, Innsbruck, Austria*
[10]*Laboratory of Clinical Pharmacology and Therapeutics, Lisbon School of Medicine, Lisbon, Portugal*
[11]*Department of Clinical Neurosciences, Royal Free Hospital, University College London, London, United Kingdom*
[12]*Department of Clinical Pharmacology and Clinical Investigation Center, University Hospital and University of Toulouse III, Toulouse, France*

ABSTRACT: Orthostatic hypotension is defined as a blood pressure fall of > 20 mm Hg systolic and/or 10 mm Hg diastolic within 3 minutes of an upright position. The *Movement* Disorders Society commissioned a task force to assess existing clinical rating scales addressing symptoms of orthostatic hypotension in Parkinson's disease. Seven neurologists and a clinimetrician assessed each scale's previous use and critiqued its clinimetric properties. A scale was "recommended" if it had been applied to populations of patients with Parkinson's disease, with data on its use in studies beyond the group that developed the scale, and was found to be clinimetrically valid. A scale was considered "suggested" if it had been applied to Parkinson's disease, but only 1 of the other criteria was applied. A scale was "listed" if it met only 1 criterion. Symptoms of orthostatic hypotension are generally assessed in scales on wider autonomic or nonmotor symptoms. Some scales designed to detect orthostatic hypotension–related symptoms provide information on their severity: the AUTonomic SCale for Outcomes in PArkinson's Disease and the COMPosite Autonomic Symptom Scale met criteria for recommended with some limitations; the Novel Non-Motor Symptoms Scale and the Orthostatic Grading Scale were classified as suggested. The Self-completed Non-Motor Symptoms Questionnaire for Parkinson's Disease was classified as suggested as a tool for screening orthostatic symptoms. However, these and the listed scales need further validation and application before they can be recommended for clinical use in patients with Parkinson's disease.

Key Words: orthostatic hypotension; Parkinson's disease; autonomic failure; rating scales; clinimetrics; orthostatic symptoms

Additional Supporting Information may be found in the online version of this article.

***Correspondence to:** Anne Pavy-Le Traon, Reference Centre for MSA, Department of Neurology, Hôpital Purpan, Pavillon Riser, 31059 Toulouse cedex 9, France; pavy-letraon.a@chu-toulouse.fr

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The prevalence of orthostatic hypertension (OH) increases with age[1–3] and is associated with increased morbidity and mortality.[4,5] OH affects 20%–50% of patients with Parkinson's disease (PD).[6–10] Different definitions and assessments of OH have contributed to discrepancies in reported prevalence estimates.[3] In PD, OH mainly results from lesions of sympathetic efferent pathways and dopaminergic therapies.[7,10–14] There is

a poor correlation between orthostatic BP drops and symptoms. Some patients with OH are asymptomatic.[15] Whereas the gold standard of orthostatic BP monitoring involves tilt tables and other equipment, the *Movement* Disorders Society Task Force assignment involved the evaluation of rating scales that can be applied in a general clinical setting.

Materials and Methods

Administrative Organization and Critique Process

The *Movement* Disorders Society commissioned a task force to assess existing clinical rating scales addressing symptoms of OH in PD. The objectives were to assess the scales' previous use and to critique clinimetric properties. The committee included 7 neurologists who specialize in movement disorders and/or autonomic disorders and a statistician with clinimetric expertise.

Literature Search Strategy

A systematic search was conducted using PubMed (up to February 2010) entering the combined search terms "orthostatic hypotension" (and "autonomic disorders," "autonomic failure") and "Parkinson" in the English-language literature. Articles were retrieved and examined, and references were searched for rating scales or questionnaires on OH. For each scale, a search was conducted for "Parkinson" and the name of the respective scale. Only published or in-press peer-reviewed articles were considered for analysis.

Selection of Scales or Questionnaires

Scales previously used in PD patients were searched for further evaluation. If no appropriate scales were identified, scales used in other populations could be selected for evaluation. General scales that included symptoms related to OH were also considered for analysis.

Evaluation of Clinimetric Properties

Criteria were detailed in a previous report on digestive dysautonomia[16] (see Supporting Material 1.1). The clinimetric properties of each analyzed scale are detailed in Supporting Material 1.2.

Each scale was classified as follows:

- "Recommended" if it had been applied to PD populations, there were data on its use in studies beyond the group that developed the scale, and it had been found to be valid, reliable, and sensitive to change. The clinimetric criteria could be met by documentation of the scale's sound properties in conditions other than PD, but scales validated in PD itself were considered at a higher level.
- "Suggested" if it had been applied to PD populations, but only 1 of the other criteria applied.
- "Listed" if it met only 1 of the 3 criteria defined for recommended scales.

Results

Definition and Assessment of Orthostatic Hypotension

OH is defined as a decrease in systolic BP $\geq$ 20 mm Hg and/or in diastolic BP $\geq$ 10 mm Hg from supine to upright position by consensus.[1,2] The period in supine position before the measurement should last 5 minutes or longer until BP and heart rate (HR) stabilization. Three to 5 minutes in an upright position is recommended.[17] BP also can be decreased by fluid depletion, medication intake, food ingestion, increased room temperature, and physical deconditioning.[18] BP measurements have to be repeated if symptoms are likely related to OH. Passive head-up tilt is recommended if the active standing test is negative or in patients with severe motor impairment. If available, automatic HR and BP measurements are recommended.[17] Changes in HR induced by the orthostatic maneuver have to be evaluated, and symptoms should be recorded. An autonomic neuropathy would be suspected if there is a limited or inappropriate rise in HR. Other disorders known to induce OH such as diabetes mellitus[19] should be taken into account.

A list of symptoms possibly related to OH and their inclusion in the evaluated scales is given in Table 1.

Analysis of Scales and Questionnaires

Twelve scales/questionnaires were screened for full review. Most were part of larger scales/questionnaires designed to assess nonmotor or autonomic symptoms:

- SCOPA-AUT.[20]
- Composite Autonomic Symptom Scale, orthostatic subsection (COMPASS).[21]
- Self-completed Non-Motor Symptoms Questionnaire for Parkinson's Disease (NMS Quest).[22,23]
- Non-Motor Symptoms Scale for Parkinson's Disease.[24]
- MDS-UPDRS part I[25] and the original UPDRS part IV.
- Freiburg questionnaire.[26]
- Autonomic Dysfunction in PD Questionnaire.[27]
- Hobson et al Scale.[28]

One questionnaire focused only on OH:

- Orthostatic Grading Scale.[29]

TABLE 1. Symptoms of orthostatic hypotension targeted by the questionnaires

	Symptoms on standing						
Scale	Faintness or syncope	Dizziness	Light-headedness	Blurred vision	Difficulty thinking	Weakness[a]	Decreased hearing
SCOPA-AUT[20]	X		X	X	X		
COMPASS[21]	X	X			X		
NMSQuest[22,23]	Falling	X	X			X	
NMSScale[24]	Falling because of fainting	X	X			X	
UPDRS			X				
MDS-UPDRS[25]			X			Fatigue	
Freiburg Questionnaire[26]		X					
Autonomic dysfunction in PD[27]	X	X					
Hobson scale[28]		X					
Orthostatic Grading Scale[29b]	Maximal standing time[c]						
Senard et al[6]	X, standing test, abortion	X + vertigo, postural instability	X	X		X	X
Matthias et al (L_Threo DOPS)[30,31]	X, maximal standing time[c]	X	X	X		X + fatigue, tiredness, maximal unassisted walking distance	

[a]X, weakness; "fatigue" is also used for some scales (UPDRS); both are used in the L-Threo DOPS Scale.
[b]In the OGS, symptoms are not listed (see text). This group used the COMPASS[21] as a scale to assess autonomic symptoms.
[c]Maximal standing time is s a global criterion used in quantitative scales such as the OGS and scales designed to assess drug efficiency.

Other symptom checklists or scales have been used to assess OH symptoms in specific studies[6] or in clinical trials of drugs against OH[30–33]:

- Symptoms list used by Senard et al.[6]
- Scale used to assess L-Threo DOPS effects.[31]

Some scales provide information on the severity and/or frequency of OH-related symptoms, whereas others only look for the presence of OH symptoms. However, symptoms per se may also provide information on severity level, for example, syncope is generally induced by severe OH.

Two scales, the UMSARS (Unified Multiple System Atrophy Rating Scale)[34] and the CASS (Composite Autonomic Scoring Scale),[35,36] were reviewed but not evaluated (see Supporting Material 2):

- The UMSARS has never been used in PD.
- The CASS is a rating tool for test results but not a scale for OH-related symptoms.

Detailed Analysis of Selected Scales and Questionnaires

SCOPA-AUT

Clinical use. The AUTonomic SCale for Outcomes in PArkinson's Disease (SCOPA-AUT) is a self-administered questionnaire.[20] Its development was prompted by the need for a clinically applicable instrument to assess dysautonomia in PD. The SCOPA-AUT consists of 25 items including 3 CV (orthostatic symptoms), 7 gastrointestinal (GI), 6 urinary, 4 thermoregulatory, 1 pupillomotor, and 2 sexual items, with a frequency score from 0 = "never" to 3 = "often." Verbaan et al[37] used the SCOPA-AUT to evaluate the occurrence of autonomic symptoms in 420 PD patients compared with 150 control subjects. Only 12.9% of the patients had symptoms in the CV domain. This scale was also used in smaller studies.[38,39] The items are added for a summary score. The estimated time to complete is 10 minutes. In a recent validation study on 387 PD patients, the SCOPA-AUT was found to be an acceptable, consistent, valid, and precise scale.[40]

Advantages. It is a brief questionnaire and easy to implement.

Limitations. In a preliminary study comparing the use of SCOPA-AUT in MSA versus PD, sensitivity for screening orthostatic symptoms turned out to be low. The number of questions on orthostatic symptoms is limited, and some symptoms related to OH were not detected by this scale (unpublished data, F. Tison).

Conclusion. The SCOPA-AUT is a reliable, validated, and easily self-administered questionnaire for assessing the frequency and burden of autonomic dysfunction in PD patients. It has been used in PD studies by groups other than the developers. It can be classified as recommended for assessing the presence and severity

of OH-related symptoms with the limitations previously mentioned (see Supporting Material 3.1).

Composite Autonomic Symptom Scale, Orthostatic Subsection

Clinical use. The Composite Autonomic Symptom Scale (COMPASS)[21] comprises 73 questions assessing 9 domains of autonomic dysfunction, including 9 items for orthostatic symptoms. The orthostatic section has been used to study the efficacy of antihypotensive treatments in 17 PD patients.[41] It has been used in other disorders[42,43] but not in PD, possibly because of its complexity and length. The questionnaire is administered in approximately 20–30 minutes.

Advantages. It has high accuracy in the definition of autonomic symptoms. It has good correlation with CASS, which is an objective-based measure of adrenergic and CV regulation (a scoring system for autonomic test results developed and validated by the same center).

Limitations. It is a complex questionnaire, and the 73 items are time-consuming.

Conclusion. This questionnaire explores a wide range of autonomic dysfunctions and includes 9 items for orthostatic symptoms. The COMPASS has shown good correlation with autonomic test results (CASS). It meets the designation of recommended for assessing the presence and severity of OH-related symptoms. This questionnaire has not been specifically validated in PD patients and has to be evaluated more thoroughly in this population (see Supporting Material 3.2).

Non-Motor Symptoms Questionnaire

Clinical use. The Non-Motor Symptoms Questionnaire (NMS Quest)[22,23,44,45] is a 30-item self-completed questionnaire comprising autonomic domains: CV (2 questions: ''Feeling light-headed, dizzy or weak on standing from sitting or lying''; ''Falling''), GI (8), urinary (2), sexual (2), sleep/fatigue (5), sudomotor (1), and miscellaneous (10), with scoring as ''yes'' or ''no.'' The checklist is easily completed in 5–7 minutes; there is no total score to assess severity or burden.

Advantages. It is easy to score.

Limitations. It is not a rating scale.

Conclusion. It is the first validated tool to screen for the presence of NMS in PD. It comprises autonomic domains including 2 questions possibly related to OH. This is not a rating scale but may be a good tool for screening orthostatic symptoms. The validation studies included patients and controls recruited worldwide; however, its use beyond the validation studies is limited. Few key validation statistics have been performed on this instrument. The NMS meets the designation of suggested as a screening tool (see Supporting Material 3.3).

Non-Motor Symptoms Scale

Clinical use. The Non-Motor Symptoms Scale (NMSS),[24,44,45] completed by physicians, was developed to provide a method to quantify NMS as evaluated in the NMS Quest. The NMS Scale is divided into 9 domains containing 30 questions, including 2 CV items (''Does the patient experience light-headedness, dizziness, weakness on standing from sitting or lying position?'' ''Does the patient fall because of fainting or blacking out?''). The NMSS reflects the questions flagged in the NMS Quest and is aimed to be a practical tool for health professionals. Item scoring is obtained by multiplying the severity score (ranging from 0 = ''none'' to 3 = ''severe'') and the frequency score (from 1 = ''rarely'' to 4 = ''very frequent''). It takes 10–15 minutes to administer.

Advantages. It is a questionnaire to quantify NMS that may be used for the evaluation of therapeutic effects, and it is relatively easy to score. The scale can capture symptoms that are severe but relatively infrequent and those less severe but persistent.

Limitations. The NMSS has not yet been used by groups other than the developers.

Conclusion. The NMSS (physician complete) has been developed to quantify NMS as evaluated in the previous NMS Quest. It comprises 2 questions related to OH. Its use has not yet been reported outside the validation study. The NMSS fits criteria 1 and 3 and meets the designation of suggested for the assessment of the presence and severity of OH-related symptoms. It has to be studied further in PD patients (see Supporting Material 3.4).

UPDRS and MDS-UPDRS Part I

Clinical use. Light-headedness is assessed as present or absent in item 42 of the original UPDRS part IV (related to treatment complications). In a few studies, results regarding OH are reported; for example, Zibetti et al,[46] who used the UPDRS to evaluate motor and nonmotor symptoms in PD patients undergoing bilateral deep brain stimulation, mentioned no effect on symptomatic OH. The UPDRS is a multidimensional, reliable, and valid scale, translated into several languages. However, item 42 has not been clinimetrically analyzed as a single item.

In the new MDS-UPDRS, light-headedness on standing is assessed in 1 item (0- to 4-point rating system) of part I (nonmotor experiences of daily living).[25]

Advantages. There is large use of the whole scale.

Limitations. Only 1 item is directly related to OH.

Conclusion. The original UPDRS meets the designation of suggested for screening. It meets criteria 1 and 2, but not 3 (the single item [Y/N] related to orthostatic dizziness has not been tested clinimetrically as an isolated item). This item does not address severity.

The MDS-UPDRS meets the designation of listed for screening and severity. It meets criteria 1 but has not been used by other groups yet; the single question related to orthostatic dizziness has not been tested clinimetrically as an isolated item.

Freiburg Questionnaire

Clinical use. The Freiburg Questionnaire[26] considers symptoms of autonomic failure in PD and their impact on daily life. In 5 short questions with 3–6 subitems each, the main domains of autonomic failure are represented: orthostatic symptoms, bladder function, GI symptoms, male erectile dysfunction, and sudomotor dysfunction. One question with 3 subitems deals with OH.

Conclusion. This short questionnaire, easy to implement, was developed for PD patients. As it was not used in other studies and not validated, it is classified as listed. Further studies and validation are needed (see Supporting Material 3.5).

Autonomic Dysfunction in Parkinson's Disease Questionnaire

Clinical use. The purpose of this study was to examine autonomic dysfunction in a comprehensive manner by performing a global survey of autonomic symptoms in PD patients and in a control group without extrapyramidal dysfunction. The Autonomic Dysfunction in Parkinson's Disease Questionnaire[27] includes 2 CV items (orthostatic dizziness, syncope), 6 GI items, 7 urinary items, 3 sexual dysfunction items, and 11 sudomotor function items; the severity of symptoms is graded on a 0–4 scale.

Conclusion. This questionnaire has been developed for assessing autonomic symptoms specifically in PD, including 2 questions on the presence and severity of OH. This questionnaire has not yet been used in other studies. Further studies and validation are needed. This scale only meets criterion 1 and is therefore listed (see Supporting Material 3.6).

Orthostatic Grading Scale

Clinical use. The Orthostatic Grading Scale (OGS)[29] is a short self-report questionnaire comprising 5 items, each rated on a scale from 1 to 4. The questions address frequency and severity of orthostatic symptoms, relationship of symptoms to orthostatic stressors, and the impact of the symptoms on activities of daily living and standing time. Adding the scores for all items gives the total score for the instrument. Time to administer is not specifically discussed, but the questionnaire is brief.

Advantages. It is short and may be self-completed by the patient; it correlates with CASS (developed and validated by the same center).

Limitations. This questionnaire has not yet been used specifically in PD patients.

Conclusion. This is a reliable tool designed for assessing the presence and severity of orthostatic symptoms. This questionnaire needs further validation in PD patients. The OGS fits criteria 1 and 3 and meets the designation of suggested (see Supporting Material 3.7).

Additional Questionnaires

The following questionnaires have not been validated or used beyond the original study:

- Hobson et al[28]
  This scale has been used in a study designed to estimate the prevalence of bladder and autonomic symptoms in a community-based sample of PD patients. Only 1 item is related to OH (''Feel dizzy on standing?''). This scale only meets criterion 1 for the presence and severity of OH and therefore is listed (see Supporting Material 3-8).
- Senard et al[6]
  This questionnaire comprises 8 subjective items on orthostatic symptoms. It has been used to investigate the prevalence of OH and the nature of postural events related to a fall in BP in PD patients. It does not include a score for frequency and/or severity. This scale only meets criterion 1 for the presence of OH and therefore is listed (see Supporting Material 3-9).
- L-Threo DOPS Scale–Matthias et al[30,31]
  Multicenter studies have been conducted to assess effects of L-Threo DOPS in MSA, PAF, and PD. In these studies, patients completed a clinical symptoms checklist at different times. Each symptom was rated on a 10-point scale: light-headedness, dizziness, feeling of weakness, fatigue, tiredness, blurred vision, maximal standing time, and maximal unassisted walking distance. This scale has not yet been used by other groups. This

TABLE 2. Overview of the scales (with scoring of severity and/or frequency) according to the criteria

	Use in PD	Use in PD beyond original developers	Successful clinimetric testing in PD	Classification
SCOPA-AUT[20]	X	X	X	Recommended (with some limitations)
COMPASS[21]	X	X	X	Recommended (with some limitations)
	Few patients with parkinsonism	One study	Strong but needs more validation	
NMSS (physician complete)[24]	X		X	Suggested
MDS – UPDRS item on OH	X		Not clinimetrically analyzed as a s ingle item	Listed
Freiburg Questionnaire[26]	X			Listed
Autonomic Dysfunction in PD[27]	X			Listed
Orthostatic Grading Scale[29]	X (not only patients with PD)		X Needs more validation	Suggested
Hobson Scale[28]	X			Listed
Mathias et al (LThreoDOPS)[30,31]	X			Listed

scale only meets criterion 1 for the presence and severity of OH and therefore is listed.

General Comments

The comparability of these scales is limited with regard to sensitivity, validity, and clinimetric properties related to OH, as most include questions on autonomic function as part of a larger scale on autonomic dysfunction (see Table 1). Symptoms that may predict OH on standing are elicited in most of the scales (see Table 1). Other symptoms of OH such as postural headache, coat-hanger ache, and backache are underrecognized. Some scales (such as the OGS and those used in clinical trials) use maximal standing time and emphasize the impact that OH has on patients' activities of daily living. In addition, some PD patients may have neurological symptoms such as postural instability that confound assessment of OH symptoms. Provoking and aggravating factors may help to relate such symptoms to OH, for example, worse symptoms in the morning, aggravation by prolonged recumbency, heat, or a heavy meal, and improvement by sitting or being in the supine position. Only the scales focusing on OH, such as the COMPASS orthostatic subsection and the OGS clearly take these factors into account.

Conclusions and Recommendations

Based on clinimetric studies, there are few well-validated questionnaires on symptoms of OH that can be administered to PD patients (Tables 1 and 2).

Some scales are used to screen for OH-related symptoms and provide information on their severity and/or frequency (Table 2). SCOPA-AUT and COMPASS are "recommended" with limitations. The strongest clinimetric testing has been performed on the SCOPA-AUT. The NMMS and the OGS are "suggested."

Other scales can be considered screening tools because they screen for OH symptoms but without scoring their severity and/or frequency (Table 3). The NMS Quest and the only item related to OH in section IV of the UPDRS may serve as screening tools for the presence of orthostatic symptoms, with some limitations. The strongest clinimetric testing has been performed on the NMS Quest. However the NMSS is suggested because its use has not yet been reported outside the validation study. As a single item, the item related to OH of the original UPDRS is weakly suggested because it is probably not sensitive enough to detect OH.

TABLE 3. Overview of the scales (screening tools) according to the criteria

	Use in PD	Use in PD beyond original developers	Successful clinimetric testing in PD	Classification
NMS Quest[22,23]	X		X	Suggested
UPDRS item on OH	X	X Limited use for OH screening	Not clinimetrically analyzed as a single item (Y/N)	Suggested (with limitations)
Senard et al (6)	X			Listed

All above-mentioned questionnaires need to be tested further in both longitudinal and cross-sectional studies in PD patients, even the ones classified as recommended or suggested.

The view of the task force members is that it is not feasible to develop a single ideal scale for both epidemiologic and interventional studies. They recommend that different scales be applied for different purposes. In addition to a global scale designed to assess autonomic symptoms, there is a need to validate a simple scale specifically designed to screen for or to assess the severity of symptoms related to OH in PD. The OGS, the COMPASS orthostatic subsection, and some scales used in clinical trials designed to assess the effects of antihypotensive drugs may serve as a basis for such a severity scale. Complex and extensive scales such as COMPASS may be more useful in clinical research studies. At this point, the task force does not recommend developing a new scale but rather validating further the existing ones in PD. ■

References

1. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. Neurology 1996;46:1470.
2. Kaufmann H. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. Clin Auton Res 1996;6:125–126.
3. Low PA. Prevalence of orthostatic hypotension. Clin Auton Res 2008;18(Suppl 1):8–13.
4. Rose KM, Eigenbrodt ML, Biga RL, et al. Orthostatic hypotension predicts mortality in middle-aged adults: the Atherosclerosis Risk In Communities (ARIC) Study. Circulation 2006;114:630–636.
5. Verwoert GC, Mattace-Raso FU, Hofman A, et al. Orthostatic hypotension and risk of cardiovascular disease in elderly people: the Rotterdam study. J Am Geriatr Soc 2008;56:1816–1820.
6. Senard JM, Raï S, Lapeyre-Mestre M, Brefel C, Rascol O, Rascol A, Montastruc JL. Prevalence of orthostatic hypotension in Parkinson's disease. J Neurol Neurosurg Psychiatry 1997;63:584–589.
7. Goldstein DS. Dysautonomia in Parkinson's disease: neurocardiological abnormalities. Lancet Neurol 2003;2:669–676. Review. Erratum in: *Lancet Neurol*. 2004;3:68.
8. Allcock LM, Ullyart K, Kenny RA, Burn DJ. Frequency of orthostatic hypotension in a community based cohort of patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 2004;75:1470–1471.
9. Pathak A, Senard JM. Pharmacology of orthostatic hypotension in Parkinson's disease: from pathophysiology to management. Expert Rev Cardiovasc Ther 2004;2:393–403.
10. Pathak A, Senard JM. Blood pressure disorders during Parkinson's disease: epidemiology, pathophysiology and management. Expert Rev Neurother 2006;6:1173–1180.
11. Kujawa K, Leurgans S, Raman R, Blasucci L, Goetz CG. Acute orthostatic hypotension when starting dopamine agonists in Parkinson's disease. Arch Neurol 2000;57:1461–1463.
12. Senard JM, Brefel-Courbon C, Rascol O, Montastruc JL, Orthostatic hypotension in patients with Parkinson's disease: pathophysiology and management. Drugs Aging 2001;18:495–505.
13. Goldstein DS, Eldadah BA, Holmes C, et al. Neurocirculatory abnormalities in Parkinson disease with orthostatic hypotension: independence from levodopa treatment. Hypertension 2005;46:1333–1339.
14. Fujishiro H, Frigerio R, Burnett M, et al. Cardiac sympathetic denervation correlates with clinical and pathologic stages of Parkinson's disease. Mov Disord 2008;23:1085–1092.
15. Novak V, Novak P, Spies JM, Low PA. Autoregulation of cerebral blood flow in orthostatic hypotension. Stroke 1998;29:104–111.
16. Evatt ML, Chaudhuri KR, Chou KL, et al. Dysautonomia Rating Scales in Parkinson's Disease: Sialorrhea, Dysphagia, and Constipation. Critique and recommendations to Movement Disorders Task Force on Rating Scales for Parkinson's disease. Mov Disord 2009;24:635–646.
17. Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W, Tassinari M. EFNS guidelines on the diagnosis and management of orthostatic hypotension. Eur J Neurol 2006;13:930–936.
18. Gilman S, Wenning GK, Low PA, et al. Second consensus statement on the diagnosis of multiple system atrophy. Neurology 2008;71:670–676.
19. Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. Circulation 2007;115:387–397.
20. Visser M, Marinus J, Stiggelbout AM, Van Hilten JJ. Assessment of autonomic dysfunction in Parkinson's disease: the SCOPA-AUT. Mov Disord 2004;19:1306–1312.
21. Suarez GA, Opfer-Gehrking TL, Offord KP, Atkinson EJ, O'Brien PC, Low PA. The Autonomic Symptom Profile: a new instrument to assess autonomic symptoms. Neurology 1999;52:523–528.
22. Chaudhuri KR, Martinez-Martin P, Schapira AH, et al. International multicenter pilot study of the first comprehensive self-completed nonmotor symptoms questionnaire for Parkinson's disease: the NMSQuest study. Mov Disord 2006;21:916–923.
23. Martinez-Martin P, Schapira AH, Stocchi F, et al. Prevalence of nonmotor symptoms in Parkinson's disease in an international setting; study using nonmotor symptoms questionnaire in 545 patients. Mov Disord 2007;22:1623–1629.
24. Chaudhuri KR, Martinez-Martin P, Brown RG, et al. Results from an international pilot study. Mov Disord 2007;22:1901–1911.
25. Goetz CG, Tilley BC, Shaftman SR, et al,for the Movement Disorder Society UPDRS Revision Task Force.Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. Mov Disord 2008;23:2129–2170.
26. Magerkurth C, Schnitzer R, Braune S. Symptoms of autonomic failure in Parkinson's disease: prevalence and impact on daily life. Clin Auton Res 2005;15:76–82.
27. Siddiqui MF, Rast S, Lynn MJ, Auchus AP, Pfeiffer RF. Autonomic dysfunction in Parkinson's disease: a comprehensive symptom survey. Parkinsonism Relat Disord 2002;8:277–284.
28. Hobson P, Islam W, Roberts S, Adhiyman V, Meara J. The risk of bladder and autonomic dysfunction in a community cohort of Parkinson's disease patients and normal controls. Parkinsonism Relat Disord 2003;10:67–71.
29. Schrezenmaier C, Gehrking JA, Hines SM, Low PA, Benrud-Larson LM, Sandroni P. Evaluation of orthostatic hypotension: relationship of a new self-report instrument to laboratory-based measures. Mayo Clin Proc 2005;80:330–334.
30. Mathias CJ, Senard JM, Braune S, et al. L-threo-dihydroxyphenylserine (L-threo-DOPS; droxidopa) in the management of neurogenic orthostatic hypotension: a multi-national, multi-center, dose-ranging study in multiple system atrophy and pure autonomic failure. Clin Auton Res 2001;11:235–242.
31. Mathias CJ. L-dihydroxyphenylserine (Droxidopa) in the treatment of orthostatic hypotension: the European experience. Clin Auton Res 2008;18(Suppl 1):25–29.
32. Low PA, Gilden JL, Freeman R, Sheng KN, McElligott MA, Efficacy of midodrine vs placebo in neurogenic orthostatic hypotension. A randomized, double-blind multicenter study. Midodrine Study Group. JAMA 1997;277:1046–1051.
33. Wright RA, Kaufmann HC, Perera R, et al. A double-blind, dose-response study of midodrine in neurogenic orthostatic hypotension. Neurology 1998;51:120–124.
34. Wenning GK, Tison F, Seppi K, et al. Multiple System Atrophy Study Group.Development and validation of the Unified Multiple System Atrophy Rating Scale (UMSARS). Mov Disord 2004;19:1391–1402.
35. Low PA. Composite autonomic scoring scale for laboratory quantification of generalized autonomic failure. Mayo Clin Proc 1993;68:748–752.

36. Low PA, Opfer-Gehrking TL, McPhee BR, et al. Prospective evaluation of clinical characteristics of orthostatic hypotension. Mayo Clin Proc 1995;70:617–622.

37. Verbaan D, Marinus J, Visser M, van Rooden SM, Stiggelbout AM, van Hilten JJ. Patient-reported autonomic symptoms in Parkinson disease. Neurology 2007;69:333–341.

38. Papapetropoulos S, Argyriou AA, Chroni E. No correlation between the clinical severity of autonomic symptoms (SCOPA-AUT) and electrophysiological test abnormalities in advanced Parkinson's disease. Mov Disord 2006;21:430–431.

39. Idiaquez J, Benarroch EE, Rosales H, Milla P, Ríos L. Autonomic and cognitive dysfunction in Parkinson's disease. Clin Auton Res 2007;17:93–98.

40. Rodriguez-Blazquez C, Forjaz MJ, Frades-Payo B, de Pedro-Cuesta J, Martinez-Martin P; Longitudinal Parkinson's Disease Patient Study, Estudio Longitudinal de Pacients con Enfermedad da Parkinson Group.Independent validation of the scales for outcomes in Parkinson's disease-autonomic (SCOPA-AUT). Eur J Neurol 2010; 17:194–201.

41. Schoffer KL, Henderson RD, O'Maley K, O'sullivan JD. Nonpharmacological treatment, fludrocortisone, and domperidone for orthostatic hypotension in Parkinson's disease. Mov Disord 2007; 22:1543–1549.

42. Newton JL, Okonkwo O, Sutcliffe K, Seth A, Shin J, Jones DE. Symptoms of autonomic dysfunction in chronic fatigue syndrome. QJM 2007;100:519–526.

43. Cai FZ, Lester S, Lu T, et al. Mild autonomic dysfunction in primary Sjögren's syndrome: a controlled study. Arthritis Res Ther 2008;10:31.

44. Chaudhuri KR, Martinez-Martin P. Quantitation of non-motor symptoms in Parkinson's disease. Eur J Neurol 2008;15(Suppl 2): 2–7.

45. Chaudhuri KR, Naidu Y. Early Parkinson's disease and non-motor issues. J Neurol 2008;255(Suppl 5):33–38.

46. Zibetti M, Torre E, Cinquepalmi A, et al. Motor and nonmotor symptom follow-up in parkinsonian patients after deep brain stimulation of the subthalamic nucleus. Eur Neurol 2007;58:218–223.