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Brief Communication

Autonomic complaints in patients with restless legs syndrome

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ABSTRACT

Background: Data regarding autonomic function in restless legs syndrome (RLS) are limited to heart rate and blood pressure changes in cases with periodic limb movements (PLMS).
Methods: We compared autonomic symptoms of 49 subjects with RLS vs 291 control subjects using the Scales for Outcome in Parkinson disease-Autonomic (SCOPA-AUT) questionnaire, consisting of 23 items in six domains scored from 0 to 3. The total score and domain scores were transformed to 0–100 points. Subjects with neurodegenerative disorders (i.e., dementia, Parkinsonism) were excluded.
Results: The RLS group was younger (mean ± standard deviation, 77.9 ± 8.0 vs 80.5 ± 7.9 years; $P = .03$) and included more women (84% vs 69%; $P = .04$). The mean SCOPA-AUT total score was higher in the RLS group compared with the control group (20 ± 11 vs 16 ± 9; $P = .005$). Additionally the RLS group had abnormalities in gastrointestinal, cardiovascular, and pupillomotor domains. When comparing the percentage of subjects with any complaint on individual questions (score of $\geqslant 1$), the RLS group had a greater number of subjects with sialorrhea, constipation, early abdominal fullness, lightheadedness when standing, and heat intolerance.
Conclusions: Autonomic complaints, especially gastrointestinal, cardiovascular, and oversensitivity to light, were significantly increased in subjects with RLS. Causes for autonomic dysfunction in RLS require further investigation.

1. Introduction

Restless legs syndrome (RLS) is a relatively common neurologic disorder with an estimated prevalence in the Western adult population of approximately 5–11%; it also is more common in women and increases with age [1,2]. RLS is a clinical diagnosis with subjective criteria which include uncomfortable feelings in the legs that appear or worsen during periods of inactivity, occurrence at night, and relief by moving the legs [3]. Periodic limb movements during sleep (PLMS) and wakefulness (PLMW) are involuntary flexions of the legs that are present in approximately 90% of patients with RLS [4,5].

Although RLS is associated with sleep difficulties, there is little data regarding autonomic function in RLS. One study reviewed the evidence suggesting a relationship between RLS and PLMS with hypertension [6], cardiovascular disease, and cerebrovascular disease [7]. Another study found a higher frequency of erectile dysfunction in men with RLS vs the control group [8].

The objective of our study was to compare autonomic complaints in patients with RLS vs control subjects using an autonomic questionnaire.

2. Methods

As part of the longitudinal study conducted by the Arizona Parkinson's Disease Consortium and the Banner Sun Health Research Institute Brain and Body Donation Program, RLS and control subjects undergo annual examinations, including a comprehensive movement examination, a full cognitive examination, and an assessment for autonomic function using the Scales for Outcome in Parkinson disease-Autonomic (SCOPA-AUT) questionnaire [9]. The SCOPA-AUT questionnaire is divided into subscores for the following domains: gastrointestinal, urinary, cardiovascular, thermoregulatory, pupillomotor, and sexual. An additional item assessed the use of medications. Each autonomic domain was scored by the frequency of occurrence with response options ranging from 0 (never) to 3 (often). All questions included symptoms within the past month, except for syncope (past 6 months) [9]. PLMS only were assessed by the questioning examiner and not with a sleep study.

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Our retrospective analysis included subjects with RLS compared to a non-RLS control population. Subjects with neurodegenerative disorders including Parkinsonism or dementia were excluded. We selected each subject's most recent autonomic examination with a valid SCOPA-Aut total score. The SCOPA-Aut total score and domain scores were considered to be valid if responses were provided for at least 75% of the items. The total score and domain scores were transformed to a scale from 0 to 100 points. Comparisons were made using the two-sample t test. Adjusted means were compared using a general linear model analysis. The proportion of subjects with a score greater than zero was compared using the Pearson χ^2 test.

3. Results

There were 49 subjects with RLS and 291 without RLS included in our analysis. The RLS group was younger and included more women (Table 1). The RLS rating scale score (0–40) at the time of autonomic testing was available for 48 of the RLS subjects. The mean RLS rating scale score was 8.8 (standard deviation, ±8.0; range, 0–29). Scores were severe ($n = 5$), moderate ($n = 15$), mild ($n = 14$), and none ($n = 14$). Mean body mass index did not substantially differ between the RLS and control groups. Smoking, use of cholinesterase inhibitors, and use of antipsychotic agents also did not substantially differ between groups. Use of antidepressant, anxiolytic, and dopaminergic agents was more common in the RLS group than in the control group. PLMS also was more common in the RLS group than in the control group.

The mean SCOPA-Aut total score was higher in the RLS group than the control group (Table 2). There were significant differences in gastrointestinal, cardiovascular, and pupillomotor domains (Table 2). Urinary, thermoregulatory, and sexual function did not significantly differ. When comparing the percentage of subjects with any complaint on the individual questions (score of $\geqslant 1$), RLS had a significantly greater number of subjects with sialorrhea (39% in RLS vs 25% in control group; $P = .046$), constipation (47% vs 31%; $P = .03$), early abdominal fullness (44% vs 22%; $P = .002$), lightheadedness when standing (27% vs 14%; $P = .03$), and heat intolerance (51% vs 33%; $P = .02$) (Fig. 1). Adjustment for age and sex and adjustment for PLMS did not substantially alter the mean difference in SCOPA-Aut scores between the RLS and control groups (Table 3). Adjustment for medication use reduced the difference between groups. Adjusting for antidepressant agents reduced the mean difference in SCOPA-Aut total score from 4.1 to 3.0 (a 27% reduction) and reduced the mean difference in the gastrointestinal score by 24%; increased the mean difference in urinary score by 5%; reduced the mean difference in cardiovascular score by 74%; reduced the mean difference in thermoregulatory score by 37%; and reduced the mean difference in pupillomotor score by 41%. However, the scores still differed by over seven points. With adjustment for antidepressant agents, the groups differed by at least 2.6 points for all subscales except on the cardiovascular score.

Table 1
Demographics and medications of the study sample.

	RLS	Control	Δ	P
Age, y; mean (SD), n	77.9 (8.0), 49	80.5 (7.9), 291	−2.6	.03
Women	41/49 (85%)	201/291 (69%)	0.15	.04
BMI, kg/m^2; mean (SD), n	25.5 (5.4), 40	25.8 (4.6), 242	−0.3	.71
Ever smoked	6/15 (40%)	55/109 (50%)	−0.10	.45
Current smoker	0/15 (0%)	2/109 (2%)	−0.02	>.99
Cholinesterase inhibitor	2/36 (6%)	8/186 (4%)	0.01	.67
Antidepressant	14/35 (40%)	29/186 (16%)	0.24	.001
Antipsychotic	0/35 (0%)	1/185 (1%)	−0.01	>.99
Anxiolytic/sedative	11/36 (31%)	24/185 (13%)	0.18	.008
Dopaminergic agent	6/36 (17%)	4/186 (2%)	0.15	.002
PLMS	5/49 (10%)	2/291 (1%)	0.10	.001

Abbreviations: RLS, restless legs syndrome; y, years; SD, standard deviation; n, number of patients; BMI, body mass index; PLMS, periodic limb movements during sleep.

Table 2
Results of the scales for outcome in Parkinson disease-Autonomic questionnaire.

	RLS mean (SD), n	Control mean (SD), n	P value
Total (0–100)	20 (11), 49	16.0 (9.1), 291	.005
Gastrointestinal (0–100)	14 (11), 49	10.1 (9.2), 283	.005
Swallowing/choking	0.36 (0.60), 49	0.24 (0.50), 290	.19
Sialorrhea	0.55 (0.84), 49	0.28 (0.51), 287	.002
Dysphagia	0.31 (0.58), 49	0.21 (0.47), 289	.23
Early abdominal fullness	0.46 (0.54), 48	0.25 (0.49), 284	.007
Constipation	0.55 (0.65), 49	0.40 (0.66), 286	.13
Straining for defecation	0.63 (0.64), 49	0.61 (0.65), 284	.79
Fecal incontinence	0.16 (0.37), 49	0.18 (0.45), 285	.86
Urinary (0–100)	31 (19), 49	28 (16), 289	.12
Urinary urgency	0.84 (0.87), 49	0.64 (0.71), 288	.08
Urinary incontinence	0.67 (0.81), 48	0.58 (0.68), 288	.44
Incomplete emptying	0.62 (0.67), 48	0.51 (0.70), 290	.29
Weak stream of urine	0.71 (0.76), 49	0.59 (0.73), 291	.29
Frequency	1.04 (0.76), 49	1.00 (0.78), 289	.76
Nocturia	1.78 (0.82), 49	1.64 (0.75), 290	.25
Cardiovascular (0–100)	9 (14), 48	4.6 (9.8), 286	.02
Lightheaded standing up	0.38 (0.64), 48	0.23 (0.53), 287	.10
Lightheaded standing for some time	0.33 (0.62), 49	0.17 (0.45), 290	.03
Syncope	0.06 (0.24), 49	0.02 (0.13), 290	.06
Thermoregulatory (0–100)	16 (14), 49	12 (14), 289	.06
Hyperhidrosis during the day	0.29 (0.58), 49	0.27 (0.60), 287	.87
Hyperhidrosis during the night	0.33 (0.69), 49	0.27 (0.56), 291	.54
Cold intolerance	0.65 (0.90), 49	0.41 (0.65), 287	.02
Heat intolerance	0.61 (0.70), 49	0.44 (0.71), 285	.12
Pupillomotor (0–100)	33 (34), 48	21 (26), 289	.003
Oversensitive to bright light	1.0 (1.0), 48	0.62 (0.79), 289	.003
Sexual (men) (0–100)	50 (17), 3	49 (33), 58	.95
Erection problem	1.67 (0.58), 3	1.6 (1.0), 70	.97
Ejaculation problem	1.33 (0.58), 3	1.4 (1.1), 58	.86
Sexual (women) (0–100)	40 (32), 12	25 (27), 39	.10
Vaginal lubrication	1.2 (1.3), 12	0.84 (0.95), 45	.23
Problem with orgasm	1.1 (1.1), 15	0.62 (0.81), 40	.11

Abbreviations: RLS, restless legs syndrome; SD, standard deviation; n, number of patients.

4. Discussion

Given that data regarding autonomic dysfunction in patients with RLS is limited, our study established that subjects with RLS

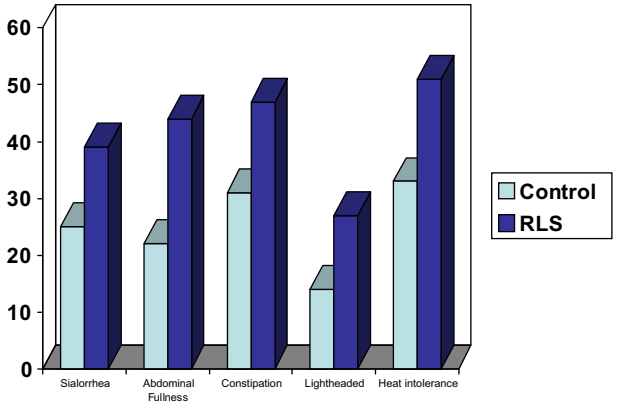

Fig. 1. Percentage of subjects with a Scales for Outcome in Parkinson disease-Autonomic item score greater than zero.