



Change in the Parkinson Anxiety Scale correlates with change in other clinical measures of anxiety over time

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ABSTRACT

The Parkinson's disease (PD)-specific Parkinson Anxiety Scale (PAS) is an anxiety rating scale that has been validated in cross-sectional studies. In a study of buspirone for anxiety in PD, it appears that the PAS may be sensitive to change in anxiety demonstrating moderate-to-high correlation with participant-reported and clinician-administered scales.

Anxiety is common in Parkinson's disease (PD) and negatively impacts health-related quality of life [1]. Validated anxiety rating scales are needed to help improve recognition and treatment of PD anxiety. The Parkinson Anxiety Scale (PAS) is a PD-specific anxiety scale that was developed in response to the recognition that existing rating scales, such as the Beck Anxiety Inventory, Hamilton Anxiety Rating Scale (HAM-A), and Hospital and Anxiety Depression Scale (HADS-Anxiety) lack sufficient clinimetric properties (e.g. convergent validity and construct validity) for use in PD [2]. The 12-item PAS self-rated and observer-rated versions include subscales that assess persistent anxiety, episodic anxiety, and avoidance behavior over a four-week time period [3]. The reliability and validity of this scale as a measure of anxiety has been established in a large cross-sectional study [3]. The self-rated version has excellent test-retest reliability, high convergent validity with other anxiety measures, high divergent validity with a depression measure, and the identified optimal cut-off has high sensitivity and specificity [3]. However, the sensitivity to change of this measure has not been previously examined.

Here, we report pilot data on sensitivity to change of the self-rated PAS as assessed in a single-center, randomized, double-blind clinical trial of the tolerability of buspirone for anxiety in PD. The study was approved by the University of Rochester Institutional Review Board (RSRB00061141) and was registered with clinicaltrials.gov (NCT02803749). All participants provided written informed consent. The study methods and primary results have been previously published [4].

In brief, twenty-one participants with PD, clinically significant anxiety (defined as a score ≥ 14 on the self-rated PAS), and on stable dosages of anxiolytics, antidepressants, and PD medications enrolled in the 12-week study. Participants were randomized to either flexible-dosage buspirone or placebo with a 4:1 allocation ratio. Investigators increased the dosage based on response and tolerability up to a maximum of 30 mg twice daily. The primary outcome measure was tolerability, defined as the proportion of participants who failed to complete the study on study drug, and secondary anxiety outcome measures included the HAM-A, HADS-Anxiety, Clinical Global Impression-Improvement (CGI-I), and Patient Global Impression-Improvement (PGI-I). As an exploratory analysis, we assessed the

relationship between the mean 12-week change in PAS with the mean 12-week change in the CGI-I, PGI-I, HAM-D, and HADS-Anxiety scores using Spearman correlation coefficients.

The buspirone group ($n = 17$) (mean (SD) age of 65.5 (9.8) with 76.5% of participants male, 94.1% white, 11.8% Hispanic/Latino) had a mean disease duration 5.8 years (4.6), 100% were on PD medication, and 88.2% were on a concomitant antidepressant or anxiolytic. The placebo group ($n = 4$) (mean (SD) age of 70.3 (10.6) with 25% of participants male, 100% white, 0% Hispanic/Latino) had a mean disease duration 6.5 years (6.2), 75% were on PD medication, and 50% were on a concomitant antidepressant or anxiolytic. At baseline, the buspirone group had a mean (SD) PAS of 19.1 (3.9), HADS-A of 8.2 (3.1), and HAM-A of 11.4 (4.0). Among those in the active treatment arm who completed the study ($n = 12$), mean (SD) change from baseline to week 12 was PAS -7.1 (6.4), HADS-A -2.0 (2.5), and HAM-A -3.9 (3.8). At baseline, the placebo group ($n = 4$) had mean (SD) PAS of 19.3 (5.1), HADS-A of 6.8 (3.1), and HAM-A of 12.3 (2.9). Among those in the placebo arm who completed the study ($n = 4$), mean (SD) change from baseline to week 12 was PAS -7.0 (10.4) HADS-A -0.5 (6.4), and HAM-A -4.3 (6.7). Among the participants who completed the study across both groups ($n = 16$), changes in the PAS from baseline to week 12 were moderately correlated with changes in the HAM-A ($r = 0.50$) and PGI-I ($r = 0.51$) and highly correlated with changes in the HADS-Anxiety ($r = 0.77$) and CGI-I ($r = 0.73$) (Table 1). Five participants, all in the buspirone group, did not complete the study; three withdrew due to an intolerability, one due to non-compliance, and one due to study burden.

We examined correlations between change in the PAS, anxiety-specific measures, and global measures over time. We found that change in self-rated PAS score from baseline to week 12 correlated moderately-to-highly with change in clinician-rated measures (HAM-A, CGI-I) and participant-rated measures (PGI-I, HADS-Anxiety). While a small and relatively short study, the correlation with other clinical measures suggests that the PAS may be sensitive to changes in anxiety symptoms over time in the context of a clinical trial. In addition to the small sample size, investigators were not blinded to performance on participant-rated measures. Therefore, performance on the PAS may have informed investigator assessment of the participant on the CGI-I, which could explain the high correlation between change in PAS and

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Table 1

Spearman Correlations between Changes in Rating Scales and Global Impression – Improvement at Week 12 for 16 Subjects who Completed Study.

	PAS	HAM-A	HADS-Anxiety	CGI-I	PGI-I
PAS	1				
HAM-A	0.50	1			
HADS-Anxiety	0.77	0.38	1		
CGI-I	0.73	0.70	0.52	1	
PGI-I	0.51	0.33	0.34	0.82	1

PAS = Parkinson Anxiety Scale; HAM-A = Hamilton Anxiety Rating Scale; HADS-Anxiety = Hospital Anxiety and Depression Scale - Anxiety; CGI-I = Clinical Global Impression-Improvement; PGI-I = Patient Global Impression-Improvement.

CGI-I. Furthermore, this study was limited to individuals with clinically significant anxiety and we cannot draw any conclusions about the sensitivity to change of the PAS among those without clinically significant anxiety. This study supports moving forward with longer, larger studies to validate the sensitivity to change of the PAS for use as a longitudinal outcome measure in clinical trials.

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Declarations of interest

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CRedit authorship contribution statement

R.B. Schneider: . P. Auinger: . C.G. Tarolli: . J. Iourinets: . M.C.

Gil Díaz: . H. Richard: Funding acquisition, investigation, writing - review and edits.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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