The Parkinson Anxiety Scale (PAS): development and validation of a new anxiety scale.

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#### Abstract

Background: Existing anxiety rating scales have limited construct validity in patients with Parkinson's disease (PD).

Aim: To develop and validate a new anxiety rating scale, the Parkinson Anxiety Scale (PAS), that would overcome the limitations of existing scales.

Design and methods: The general structure of the PAS was based on the outcome of a Delphi procedure. Item selection was based on a canonical correlation analysis and a Rasch analysis of items of Hamilton Anxiety Rating Scale (HARS) and Beck Anxiety Inventory (BAI) from a previously published study.

Validation was done in a cross-sectional international multicenter study involving 362 patients with idiopathic PD. Patients underwent a single screening session in which the PAS was administered, along with the Hamilton Depression Rating Scale, the HARS and BAI. The Mini International Neuropsychiatric Interview was administered to establish DSM diagnoses of anxiety and depressive disorders.

Results: The PAS is a 12-item observer or patient-rated scale with three subscales, for persistent, episodic anxiety, and avoidance behavior.

Properties for acceptability and reliability met predetermined criteria. The convergent and known groups validity was good. The scale has a satisfactory factorial structure. The AUC and Youden index of the PAS is higher than that of existing anxiety rating scales.

Conclusion: The PAS is a reliable and valid anxiety measure for use in PD patients. It is easy and brief to administer, and has better clinimetric properties than existing anxiety rating scales. The 'sensitivity to change' of the PAS remains yet to be assessed.

#### Introduction

Anxiety disorders are common in patients with Parkinson's disease (PD). Twenty-five to 43% of PD patients have a circumscribed anxiety disorder using DSM IV criteria <sup>1-4</sup>, making anxiety disorders more prevalent than depressive disorders, which have an average prevalence of 17% <sup>5</sup>. Four to 8% of patients suffers from panic disorder, 2 to 16% from agoraphobia without panic, 3 to 21% from generalized anxiety disorder (GAD), and 8% to 13% from social phobia (or social anxiety disorder) <sup>1, 2, 4</sup>. Anxiety disorders with persisting symptomatology, such as GAD, are thus more common than episodic anxiety disorders, such as panic disorders. Anxiety in PD is associated with increased subjective motor symptoms, more severe gait problems and dyskinesias, freezing and on/off fluctuations <sup>6-8</sup>. Anxiety symptoms in PD patients also have a negative impact on health related quality of life <sup>6-8</sup>. Reliable assessment and measurement of symptoms may help to establish a diagnosis, guide the decision to start treatment for anxiety, and monitor this treatment. A recent review of anxiety rating scales commissioned by the Movement Disorder Society (MDS) revealed that none of the available anxiety rating scales had been validated in patients with Parkinson's disease (PD) <sup>9</sup>. A subsequent validation study of the Hamilton Anxiety Rating Scale (HARS), the Beck Anxiety Inventory (BAI) and the Hospital Anxiety and Depression Scale (HADS) raised questions about the construct validity of these scales. It was shown that the BAI, with its focus on symptoms of panic, identifies a different group of patients than the HARS, with its focus on generalized anxiety. Moreover, the positive predictive value of all scales was poor, and the negative predictive value was only moderate. In addition, it was not possible to identify a satisfactory factorial structure for the BAI and HADS <sup>10</sup>.

The aim of this study was to develop and validate an anxiety scale that would overcome the limitations of existing scales and have adequate construct validity and clinimetric properties

in patients with PD. The scale should be brief and easy to administer, and have both an observer-rated version, to be scored by the clinician or researcher and a self-rated version, to be scored by the patient. The authors furthermore state that this scale should be in the public domain and can be used free of charge for research and clinical purposes.

#### Patients and Methods

#### Development of the PAS

The authors of this paper held a consensus meeting to reach agreement on the general format and structure of the scale. A first exploratory Delphi round focused on the general format of the scale, including the time frame used for symptom reporting, potential subscales, number of items, as well as scoring issues, such as the range of scoring options and the formulation of Likert scores. Initial item selection was based both on a canonical correlation analysis (CCA) of items of the HARS and BAI to ensure a broad enough scope of symptoms, as well as on a Rasch analysis of these scales to ensure selection of items that would represent the whole spectrum of severity<sup>11, 12</sup>. Decisions were guided by exploratory analysis on data of the previously published study of the validation of the HARS and BAI {Leentjens, 2011 #1618}. In a first step, items influenced by age, sex and severity of motor symptoms were eliminated, as were items that were shown not to be reliable in the Rasch analysis. Items with too little item difficulty (less than minus 2 logits) in the Rasch analysis were also eliminated, as were items that did not cluster with recognizable anxiety symptoms in the CCA analysis. A second Delphi round was held focusing on item selection from the remaining pool of items and item formulation. A more detailed description of the development process is reported in the supplementary material (Appendix 1).

#### Validation of the PAS

#### Design and setting

The newly developed scale was validated in a one-year cross-sectional international multicentre study that included 362 patients from six tertiary referral centers: two in the United States (Johns Hopkins University School of Medicine, Baltimore, Maryland and the University of Pennsylvania, Philadelphia, Pennsylvania), three in Europe (Lille University Medical Center, Lille, France, the Carlos III Institute of Health, Madrid, Spain, and Maastricht University Medical Center, Maastricht, the Netherlands) and one in Australia (Fremantle Hospital, Fremantle). Patients were recruited from Movement Disorders clinics, as well as from Neurology and Psychiatry outpatient clinics of the participating centers. Enrollment occurred between March 2012 and April 2013.

#### Inclusion - and exclusion criteria

Patients diagnosed with idiopathic PD according to the Queen Square Brain Bank criteria, and who gave informed consent met inclusion criteria <sup>13</sup>. Patients with neurodegenerative disorders other than PD, and those with severe cognitive impairment, operationalised as a score on the Mini Mental State Examination (MMSE) < 23 were excluded <sup>14</sup>.

#### Assessment

Demographic and disease related variables were recorded. Motor function, activities of daily living (ADL) function, complications of therapy, and disease stage were assessed with the Unified Parkinson's Disease Rating Scale (UPDRS) sections 2,3 and 4, and the Hoehn & Yahr staging system (H&Y) <sup>15</sup>; assessment of cognitive abilities and instrumental ADL were done with the MMSE, the Clinical Dementia Rating Scale (CDR) and Lawton Instrumental

ADL (IADL) scale <sup>14, 16, 17</sup>. Quality of life was assessed with the eight item Parkinson's Disease Questionnaire (PDQ-8) <sup>18</sup>. The presence of DSM-defined depressive and anxiety disorders was determined with the Mini International Neuropsychiatric Inventory (MINI, a structured interview for DSM disorders) sections for depression (A, B) and anxiety (D, E, F, H) <sup>19</sup>. The severity of depressive symptoms was quantified with the 17-item Hamilton Depression Rating Scale (HAMD) <sup>20</sup>.

The anxiety measures included the observer-rated and patient-rated versions of the PAS (for a description: see below). Other measures included the observer-rated Clinical Global Impression (CGI) and patient-rated Patient Global Impression (PGI) of the severity of anxiety symptoms <sup>21</sup>, the observer-rated Hamilton Anxiety Rating Scale (HARS) <sup>22</sup>, and the self-rated Beck Anxiety Inventory (BAI) <sup>23</sup>. Patients suffering from 'on/off' fluctuations were only assessed during 'on' states, following the advice of the MDS task force <sup>9</sup>.

Inter-rater reliability of the observer-rated PAS was assessed by administering this scale twice in the same session to a minimum of 10 patients in every institution, by two different raters (total sample size = 60). For feasibility reasons, test-retest reliability was only assessed for the self-rated version of the PAS. This was accomplished by asking patients to complete a second set of these scales spaced one week apart from the in-person assessment and return them by post-mail.

#### Power calculation

The aforementioned validation study of anxiety rating scales showed a prevalence of anxiety disorders of 34% in 342 PD patients. As this study followed the same design and involved the same analyses<sup>10</sup>, we expected that a sample size of 360 would be more than adequate to perform all planned analyses. The most demanding sample size is usually related to the factor analysis. Allowing for a minimum of 20 subjects per scale item, and a total of 13 items we

surpass this requirement (minimum 260 subjects) widely. To assess inter-rater reliability and test-retest reliability, the proposed sample size of 60 exceeds the minimum sample size of 50 subjects following the generally accepted algorithm of Cicchetti <sup>24</sup>.

#### Statistical analyses

All analyses were performed using SPSS version 21.0 for Windows (SPSS Inc. Chicago, 2007). Demographic and disease related variables are presented in a descriptive way. The Kolmogorow-Smirnow (K-S) Z test statistic was used to check whether the distribution was gaussian. In order to identify between-institute differences in enrolled patients, demographic and disease related variables were compared with chi-square or Kruskal-Wallis test. If p < 0.05, the differences were considered significant. The prevalence of DSM- defined anxiety disorders in this population is reported.

Acceptability was assessed in the form of percentage of missing responses, with less then 5% considered acceptable  $^{25}$ . Observed versus possible score range for items and total scores were analyzed with distribution of scores assessed with mean, SD, median, floor and ceiling effects, and skewness. Observed mean versus median scores can be considered a measure of distribution and a difference < 10% of the maximum possible scale score was considered acceptable. For floor and ceiling effects, 15% was taken as maximum acceptable  $^{26}$ . For skewness the accepted limits were -1.0 to +1.0  $^{27}$ .

As a measure of internal consistency, Cronbach's alpha, mean inter-item correlation (or 'item homogeneity coefficient') and range, as well as corrected item-total correlation are reported. A Cronbach's alpha  $\geq$ 0.70 was considered acceptable <sup>28</sup>, as was item-total correlation  $\geq$ 0.40 <sup>29</sup>, and an inter item coefficient of >0.30 <sup>30</sup>.

Inter-rater reliability will only be reported for the observer-rated version of the PAS using weighted kappa (quadratic weights) to assess reproducibility for individual item scores and

the intraclass correlation coefficient (ICC, two-way random effect) for the total score. Test-retest reliability was assessed for the self-rated version of the PAS only, by intraclass correlation coefficient (ICC, one-way random effect). A kappa or ICC  $\geq$  0.70 was considered satisfactory <sup>31</sup>. Precision (standard error of measurement, SEM) is reported.

Convergent validity of the PAS with the BAI and HARS was assessed with Spearman rank correlation coefficients. Correlation coefficients  $\geq$ 0.60 were demonstrative of a high association  $^{32}$ .

Known-groups validity was assessed by comparing scores on anxiety scales with scores on the CGI and PGI using the Kruskal-Wallis test.

Dimensionality was assessed by means of exploratory factor analysis with principal component method and promax rotation (since it was expected that the different factors would be correlated with each other). A scree plot and Kaiser's criterion (Eigenvalue ≥ 1) were used to determine the number of factors, if these factors were clinically interpretable.

In order to assess the properties of the scales as diagnostic tests, criterion validity was tested against DSM diagnoses using Receiver Operating Characteristics (ROC) curves. This was done for the full scale (any anxiety disorder versus no anxiety disorder) and for each subscale. For subscales the diagnostic properties were assessed in relation to specific anxiety disorders: the persistent subscale with GAD, the episodic subscale with panic disorder and the avoidance scale with social phobia and agoraphobia combined. Sensitivity, specificity, area under the ROC curve (AUC) and Youden index (highest sum of sensitivity and specificity) are reported.

#### Approval and consent

This study received ethical approval from the Institutional Review Boards of each participating center. Patients received written information about the study and gave their written informed consent before participating. They received a small financial compensation

for participating. This study was sponsored by the Michael J. Fox Foundation for Parkinson Research (MJFF).

#### Results

#### Development of the PAS

In the consensus meeting it was agreed that the main aim of the scale was to provide a reliable measurement of the severity of anxiety symptoms, rather than designing an instrument specifically intended for screening or diagnosis. Although the scale would be developed specifically for patients with PD, the study group agreed that item selection and formulation should be such that the scale could be administered to patients with other neurological and physical diseases as well.

Participants reached consensus that the scale should consist of three subscales: one pertaining to persisting anxiety (five items), one to episodic anxiety (four items), and one to avoidance behavior (three items). These first two subscales were supported by evidence from a CC analysis <sup>11</sup>, while 'avoidance' was considered a third characteristic of anxiety disorders, not captured by the other two scales. The total scale thus consists of 12 items. Items were scored on a 5 point Likert scale, with '0' meaning 'not or never' and '4' meaning 'severe or almost always'. It was decided to formulate items as questions, as this way the patient-rated and clinician rated versions would be identical. The self-rated version can be completed in less than two minutes, while the observer-rated version may take up to five minutes if answering options for every item are read out to the patient.

The scale was first written in English. Translations into Spanish, French and Dutch were made for the sake of the study, following the procedure of translation and back translation to check for inconsistencies in formulation. The English, Spanish, French and Dutch scales are

published in the Supplementary material as Appendix 2. The scale, including existing translations is in the public domain and can be used free of charge for clinical and investigational purposes.

#### Demographic and disease related data

Demographic and disease related variables for the included patients are displayed in Table 1. We included 362 patients, 62.7% male, with a mean age of 65.3 years, and a median H&Y stage of 2. Age, disease duration, as well as scores on the MMSE and IADL, differed significantly between the centers (Supplementary material, Appendix 3) but these differences were small and not considered clinically relevant. Scores on the UPDRS section III, H&Y stage and PD treatment variables also differed between institutions, which was most likely due to the different spectrum of disease severity and complexity across institutions, thought to reflect different areas of interest or expertise.

#### Prevalence of anxiety disorders

Table 1 also shows the prevalence of the different anxiety disorders. Twenty-seven percent of patients were suffering from a current DSM anxiety disorder. Among those, generalized anxiety disorder was the most prevalent diagnosis (15.2%), followed by agoraphobia (10.5%) and social phobia (9.1%). Panic disorder was less frequent (3.4%).

#### Acceptability and distribution

With less than 0.01% missing data on any of the subscales, in both the observer-rated and patient-rated version of the instrument, the scale demonstrated good acceptability. Mean, standard deviation, and skewness are reported in Table 2. For the total scale, no floor effects were seen, but a floor effect could be observed for the episodic and avoidant subscales, likely

due to the lower prevalence of episodic anxiety and avoidance behavior. None of the subscales has significant ceiling effects. The observed range of scores was close to the theoretical range. For all scales, the difference between observed mean and median scores were < 10% of the maximum possible scale score. Overall, the score distributions were acceptable. None of the scales had normally distributed scores (p< 0.01 for the K-S Z). Individual item performance is shown in the supplementary material (Supplementary material; Appendix 4).

#### Reliability and stability

Cronbach's alpha was good for both the patient-rated and the observer-rated total scale scores. For the subscales Cronbach's alpha was good for the persistent subscale, and acceptable for the episodic subscale and acceptable for the avoidance subscale (Table 3). Item-total correlations were high for all subscales; for the total scale the item-total correlation was slightly less than that for the subscales, which is to be expected given the scale was designed to represent the discrete dimensions of anxiety. Both Cronbach's alpha and item total correlations were slightly better for the self-rated version of the PAS. For all subscales, interitem correlation met the predetermined criterion. Inter-rater reliability for the observer-rated scale and test-retest reliability for the self-rated version were both excellent (Table 4).

#### Convergent validity and known-groups validity

Convergent validity of PAS total scale with the CGI and PGI for anxiety, HARS and the BAI was high (Table 5). For the subscales, this correlation was moderate to high. Divergent validity with the HAMD was also high, although there was a moderately strong correlation between the persistent anxiety subscale and the HAMD score, indicating that generalized anxiety and depression are overlapping concepts.

Known groups validity was good: total PAS scores, as well as scores in subscales of the PAS, were significantly higher in patients with higher scores on the CGI and PGI for both the observer-rated as the self-rated scale (Supplementary material; Appendix 5). Scores on PGI and CGI were strongly correlated: 0.814 (p<0.001).

#### **Dimensionality**

A scree plot, as well as Eigenvalues  $\geq 1$  were co-incident in identifying three factors (Supplementary material; Appendix 6). Each PAS item loaded onto a factor with the other items from its PAS subscale, in line with the design of the scale. For the observer-rated version, two items (B1, 'panic or intense fear' and B4, 'fear of losing control') had a moderately strong loading on both the persistent and the episodic factor. For the self-rated version, all items loaded as expected and in line with the design of the scale. The three factors explained 63% of variance for the observer-rated PAS, and 65% of variance for the self-rated version of the PAS.

All subscales correlated strongly with the PAS total score for both the observer-rated version and the self-rated version. For both versions correlations amongst subscales was moderate, indicating that these subscales measure different dimensions of anxiety (Supplementary material Appendix 7).

#### Properties of the scales as diagnostic tests

The diagnostic properties of the PAS were assessed with ROC curves and Youden indeces (highest sum of specificity and sensitivity) was calculated. For both, the observer-rated and self-rated scales, the AUC and sensitivity and specificity for any anxiety disorder was high. The performance of subscales was assessed in relation to specific anxiety disorders: the persistent subscale with GAD, the episodic subscale with panic disorder and the avoidance

scale with social phobia and agoraphobia combined. For each subscale a high AUC was found, as well as a high sensitivity and specificity at the optimal cut-off (Table 6). The observer-rated version had a better specificity than the self-rated scale, whereas the self-rated scale had a better sensitivity than the observer-rated scale.

#### Discussion

The aim of this study was the development and validation of a new anxiety scale for PD that would be brief, easy to administer and overcome most of the limitations of existing anxiety scales. The general design and format was decided upon by consensus during a Delphi procedure. Division into subscales and item selection was evidence based and guided by analyses on the database of a published validation study of the HARS, BAI and HADS {Leentjens, 2011 #1618}. This evidence-based approach is reflected in the satisfactory clinimetric properties that the new scale shows. Face validity is better than existing scales, given the division into the clinically evident and relevant symptom domains of persistent anxiety, episodic anxiety and avoidance behavior. The scale is not biased towards persistent symptoms, such as is the case with the HARS, or to episodic symptoms, such as is the case with the BAI. Avoidance behavior is not assessed by existing scales. Properties for acceptance, distribution, reliability and stability met defined criteria. The concurrent and known groups validity is good. The scale has a plausible and satisfactory factorial structure, which is not the case with the BAI and HADS. The AUC and Youden index of the PAS is higher than that of the HARS, BAI and HADS. In addition, the scale is brief and easy to administer.

This study also has limitations. Although decisions were based on evidence, judgements were made. For instance, a decision was made about anchoring the item responses to frequency or severity of symptoms, or both. For persistent anxiety symptoms, severity is more relevant,

and for episodic anxiety frequency. For avoidance behavior, both may be relevant. The investigators ultimately opted for a dual formulation, incorporating both frequency and severity because this makes the answering options for all scale items uniform. The authors believed that patients would know what is relevant for each item. The results of the study indicate that this way of formulating items does not lead to problems in the clinical use of the scale and probably did not affect the clinimetric properties. Another potential limitation is the fact that study samples differed per institution. This reflects a diversity of cultures, environments, raters, and patients, which may also be regarded as an advantage for a scale to be used internationally. For practical reasons, researchers administering the MINI to the patients are the same as those administering the PAS and other anxiety scales, so that the researcher administering the scales was not blinded for potential clinical diagnoses.

While not a limitation of the present study, not all clinimetric properties of the PAS were assessed. For instance, the sensitivity to change was not assessed, since this can only be done longitudinally in an observational or treatment study. This was outside the scope of the present study.

#### Conclusion

The PAS has some clear clinimetric advantages over existing anxiety rating scales, but still requires additional validation, especially in the area of 'sensitivity to change'. The authors hope that additional validation will take place and will also involve other research groups and diverse populations of PD patients. Since the scale does not incorporate specific PD related questions, validation could also be done in other neurological populations. The authors hope that this scale will be used routinely in clinical care and research.

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#### **Author roles**

1. Research project: A. Conception, B. Organization, C. Execution;

2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;

3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique

Leentjens AFG: 1 A, B, C; 2 A, B; 3 A

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Table 1: Demographic and disease related data of the study population (continuous and categorical variables) (n=360)

Variable	Percentage	Mean	SD	range
Age		65.3	8.9	41.0-88.0
Sex (female)	37.3			
Years of education		13.6	4.0	3.0-22.0
Marital status				
- never married	5.0			
- married	81.8			
- widowed	3.3			
- divorced	9.9			
Handedness (right)	92.6			
MMSE		28.5	2.1	21.0-30.0
CDR scores		median 0.5		0.0-1.0
0	46			
0.5	54			
1.0	0.3			
higher				
PDQ8 (standardized)		26	5.4	0.0-84.0
IADL		10.1	4.0	4.0-28.0
HAMD		7.5	5.5	0.0-35.0
HARS		10.0	6.9	0.0-47.0
BAI		11.8	8.6	0.0-46.0
PGI		median 2.0	IQR 1.0-3.0	1.0-6.0

17 3 23 4 16 5 4 6 2 7 0  CGI median 2.0 IQR 1.0-3.0 1.0-7.0  1 39 2 16 3 24 4 14 5 4 6 2	1	38			
3					
4       16         5       4         6       2         7       0         CGI       median 2.0       IQR 1.0-3.0       1.0-7.0         1       39         2       16       3         3       24       4         4       14       5	2	17			
5 4 6 2 7 0	3	23			
6 2 0	4	16			
7     0       CGI     median 2.0       1     39       2     16       3     24       4     14       5     4	5	4			
CGI median 2.0 IQR 1.0-3.0 1.0-7.0  1 39 2 16 3 24 4 14 5 4	6	2			
1     39       2     16       3     24       4     14       5     4	7	0			
2     16       3     24       4     14       5     4	CGI		median 2.0	IQR 1.0-3.0	1.0-7.0
3     24       4     14       5     4	1	39			
4     14       5     4	2	16			
5 4	3	24			
	4	14			
6 2	5	4			
	6	2			
7 0.6	7	0.6			
Major depressive dis 7.2	Major depressive dis	7.2			
Dysthymia 8.0	Dysthymia	8.0			
GAD 15.2	GAD	15.2			
Social phobia 9.1	Social phobia	9.1			
Agoraphobia without 10.5	Agoraphobia without	10.5			
panic	panic				
Panic disorder (total) 3.4	Panic disorder (total)	3.4			
Panic without 1.7	Panic without	1.7			
agoraphobia	agoraphobia				
Panic with 1.7	Panic with	1.7			

agoraphobia				
no. of anxiety disord				
0	73			
1	17			
2	7			
3	3			
4 or more	0			
History depression	37.3			
FH depression	24.0			
History anxiety	32.3			
FH anxiety	14.3			
History other	12.7			
psychiat				
FH other psychiatry	11.3			
FH parkinson	25.4			
Antidepressant	31.8			
Beta-blocker	11.0			
Benzodiazepine	21.3			
antipsychotic	3.9			
PD disease duration		10.4	6.1	1.0-52.0
UPDRS 2		12.7	6.6	1.0-35.0
UPDRS 3		24.7	12.1	3.0-73.0
UPDRS 4		3.6	3.1	0.0-17.0
H&Y				
1	17.9			

2	51.4			
3	22.9			
3.5	6.1			
4	1.1			
Anticholinergic	6.6			
Dopa-agonist	63.5			
Levodopa	90.9			
NMDA antagonist	21.3			
COMT inhibitor	27.3			
Apomorphine	2.2			
Other PD medication	4.1			
LEDD		811	581	0-3724
DBS				
- GPI	0.8			
- STN	11.6			
pallidotomy	1.1			

Table 2. Description of PAS scores

Range, floor and ceiling effects, distribution and acceptability of the observer and selfrated PAS.

variable	Theoret	Observ	% floor	%	Mean	SD	median	skewness	kurtosis	Acceptability
	ical	ed	score	ceilin						(% missing
	range	range		g						scores)
				score						
Observer-rated	l PAS									
PAS obs total	0-48	0-43	6.9	0	9.4	7.9	7	1.2	1.3	0.003
PAS obs	0-29	0-20	13.3	0	5.5	4.9	4	0.8	-0.2	0
persistent										
PAS obs	0-16	0-11	44.2	0	1.7	2.3	1	1.7	2.8	0.003
episodic										
PAS obs	0-12	0-10	34.0	0	2.3	2.5	2	1.2	1.1	0
avoidance										
PAS selfrated										
PAS self total	0-52	0-42	8	0	12.2	8,9	11	0.8	0.1	0
PAS self	0-24	0-20	14.9	0	6.7	4.9	6	0.5	-0.5	0
persistent										
PAS self	0-16	0-12	35.1	0	2.6	2.9	2	1.0	0.3	0
episodic										
PAS self	0-12	0-12	29.0	1.1	2.3	2.5	2	0.8	0.1	0
avoidance										

Table 3. Reliability parameters of the full scale and subscales of the observer and self-rated PAS.

parameter →	Cronbach's alpha	mean inter-item	mean item-total
scale ↓		correlation (range)	correlation (range)
PAS observer-rated	1		
PAS obs total	0.87	0.33 (0.06-0.78)	0.63 (0.35-0.83)
PAS obs persistent	0.91	0.60 (0.54-0.80)	0.85 (0.80-0.90)
PAS obs episodic	0.69	0.48 (0.25-0.52)	0.72 (0.69-0.78)
PAS obs avoidance	0.57	0.39 (0.15-0.47)	0.73 (0.58-0.83)
PAS self-rated			
PAS self total	0.89	0.41 (0.18-0.76)	0.663 (0.53-0.82)
PAS self persistent	0.88	0.60 (0.44-0.74)	0.825 (0.76-0.87)
PAS self episodic	0.78	0.47 (0.35-0.59)	0.777 (0.76-0.81)
PAS self avoidance	0.67	0.39 (0.25-0.58)	0.769 (0.65-0.81)

Table 4. Inter rater reliability of the PAS, test-retest reliability, standard error of measurement (SEM) the full scale as well as subscales of the observer-rated and self-rated PAS.

parameter →	inter-rater	test-retest reliability	SEM
scale ↓	reliability	(ICC)	
	(ICC)		
PAS observer-rated	1		
PAS obs total	0.92		0.46
PAS obs persistent	0.92		0.30
PAS obs episodic	0.85		0.12
PAS obs avoidance	0.84		0.13
PAS selfrated	1		I
PAS self total		0.89	0.51
PAS self persistent		0.85	0.30
PAS self episodic		0.79	0.15
PAS self avoidance		0.75	0.15

Table 5. Convergent validity of PAS total scales and subscales with the CGI and PGI for anxiety, HARS and BAI, and divergent validity with the HAMD (Spearman rank correlation coefficients . All correlation coefficients are significant (p<0.001).

	CGI	PGI	HARS	BAI	HAMD			
PAS observer								
PAS obs total	0.79	0.71	0.68	0.71	0.61			
PAS obs persistent	0.79	0.72	0.62	0.67	0.60			
PAS obs episodic	0.52	0.51	0.46	0.56	0.39			
PAS obs avoidance	0.47	0.38	0.50	0.41	0.37			
PAS self-rated	<b>-</b>	<b>-</b>		1	1			
PAS self total	0.77	0.76	0.58	0.71	0.55			
PAS self persistent	0.77	0.77	0.57	0.69	0.58			
PAS self episodic	0.57	0.55	0.36	0.54	0.33			
PAS self avoidance	0.52	0.49	0.45	0.47	0.36			

Table 6: 'ROC curves' values for observer-rated and self-rated total scales and subscales. Anxiety disorders characterized by avoidance are: agoraphobia and social phobia (here taken together as avoidant anxiety disorders). The Youden index is the highest sum of sensitivity and specificity. The cut-off score at which the Youden index is reached is the optimal cut-off score for dichotomisation of patients with and without anxiety disorder. For screening or diagnosis, higher or lower cut-offs can be selected.

scale	grouping variable	AUC	optimal	sensitivity	specificity	Youden index
		(%)	cut-off	at opt cut-	at opt cut-	
				off	off	
PAS obs total	any anxiety disorder	85.9	13/14	0.71	0.91	1.61
PAS obs persistent	generalized anx dis	88.9	9/10	0.76	0.89	1.65
PAS obs epis	panic disorder	96.5	3/4	1.00	0.84	1.84
PAS obs avoidance	avoidant anx disorders	88.2	3/4	0.81	0.88	1.69
PAS self total	any anxiety disorder	85.1	13/14	0.81	0.74	1.54
PAS self persistent	generalized anx dis	89.6	10/11	0.89	0.77	1.66
PAS self epis	panic disorder	95.6	5/6	1.00	0.86	1.86
PAS self avoidance	avoidant anx disorders	85.0	4/5	0.70	0.84	1.54

Appendix 1. Development of the Parkinson Anxiety Scale (PAS): Minutes of the Delphi procedure

On October 14, 2011, an investigator meeting was held in Madrid in which 7 investigators participated: 5 principal investigators (AL, KD, PMM, GP, and DW) and two affiliated investigators (Forjaz MJ and Rojo-Abuin JM). During this meeting a modified Delphi procedure was used to construct the Parkinson Anxiety Scale. In this process use was made of the personal opinion and expertise of the participants, as well as of previously published and unpublished data of a prior validation study of anxiety rating scales in Parkinson's disease (PD) [1]. A first exploratory Delphi round focused on the general format of the scale, including potential subscales, item number, as well as scoring issues, including who scores (patient or researcher/clinician), the range of scoring options and the formulation of Likert scores. After consensus had been reached, a second Delphi round was held focusing on item selection and item formulation.

It was agreed that the principal aim of the scale was reliable measurement of the severity of anxiety symptoms, rather than designing an instrument specifically intended for screening or diagnosis. It was thought that prediction of 'caseness', in case of screening or diagnosis, would be best served by this approach. Although the scale would be developed specifically for patients with Parkinson's disease, the study group agreed that item selection and formulation would be such that the scale can be administered in patients with other neurological and physical diseases as well.

Participants reached consensus that the scale should consist of three subscales: one pertaining to persisting anxiety, one pertaining to episodic anxiety, and one pertaining to avoidance behavior. These first two subscales are supported by evidence from a canonical correlation (CC) [2]. This analysis revealed that CC of items of the BAI and HARS resulted in two main components that were interpreted as persistent and episodic anxiety. Persistent anxiety is present in disorders such as 'generalized anxiety disorder', while episodic anxiety is present in 'panic disorder', 'social phobia', and 'specific phobia'. Avoidance behavior was considered a specific feature of anxiety, since it is listed in the DSM criteria of social phobia, specific phobia and agoraphobia. However, this feature is not represented in the BAI or HARS, and was considered as third factor. For research purposes a clinician rated scale was preferred, but it was agreed that routine clinical practice was probably better served with a self-rated scale. For this reason the study group decided to validate two versions of the new scale: one patientrated and one clinician rated. Since anxiety is characterized by highly personal feelings of distress that may not be evident to close companions, the study group did not consider a caregiver rated version. It was agreed that the scale should be concise, but still have a wide enough representation of symptoms. For this reason it was considered desirable that the total number of items would be between 10 and 20.

Items will be scored on a five point Likert scale with severity and/or frequency anchors: not at all/never, very mild/very rarely, mild/sometimes, moderate/frequently and severe/most of the time. The 'very mild/very rarely' anchor was introduced to make the scale more sensitive to anxiety symptoms in the lower severity range, since Rasch analysis revealed that items/answers reflecting a lower severity of anxiety were underrepresented in the BAI and HARS [3].

Item selection was partially based on results of CC and Rasch analysis of the BAI and HARS items [2,3]. Items influenced by age, sex and motor symptoms (such as urogenital symptoms on the HARS, and tremor) were eliminated, as were items were shown to be not reliable in the Rasch analysis (such as gastro-intestinal symptoms and insomnia). Items with too little item difficulty (less than minus 2 logits) in the Rasch analysis were also eliminated (such as concentration difficulties), as were items that in the CFA did not cluster with recognizable anxiety symptoms (gastro-intestinal symptoms and insomnia). A second Delphi round was held to select items for the new scale from the remaining items. Items had to be characteristic for persistent or episodic anxiety presentations, and located across the item difficulty spectrum in the Rasch analysis. Five items were chosen for the 'persistent anxiety' subscale. Because 'depressed mood' was one of the symptoms most predictive of anxiety severity, it was decided to keep this item in as well. It was agreed that depressed mood is not a symptom of anxiety disorders and the item should eventually be deleted. However, allowing the item to be included during the study phase would enable the study group to assess the influence of this item on scale performance. Four items were chosen for the 'episodic anxiety' subscale. For the third subscale 'avoidance behavior', three types of avoidance behavior were chosen as items: avoiding public activities, avoiding specific triggers (heights, spiders, etc.), and avoiding wide or narrowed spaces, reflecting core features of social phobia, specific phobia and agoraphobia. These were chosen on the basis of consensus and, since they are not included in the BAI or HARS, not based on evidence.

After item selection is was decided to formulate items as questions, because in this way the patient-rated and clinician rated version could be most similar textually. The scale will be formulated in English. Translations in Dutch, French and Spanish will be made for the sake of the study, which will be backtranslated for inconsistencies in formulation.

After construction of the scale, an initial exploratory validation analysis was performed on BAI and HARS items most closely resembling the items of the new scale, making use of the database of a prior validation study[1]. This analysis revealed good internal consistency of the subscales, good representation of scored on subscales across the range of severity of anxiety, good correlation of the 'persistent anxiety' subscale with the diagnosis of 'generalized anxiety disorder', and of the 'episodic anxiety subscale' with 'panic disorder'. These results were considered satisfying and were celebrated with roast lamb and a superb 2004 Rioja at the Posada de la Ville in old Madrid.

#### References

- 1. Leentjens AFG, Dujardin K, Marsh L, Richard IH, Starkstein SE, Martinez-Martin P. Anxiety rating scales in Parkinson's disease: a validation study of the Hamilton Anxiety Rating Scale, The Beck Anxiety Inventory and the Hospital Anxiety and Depression Scale. Movement Disorders 2011;26(3):407-415.
- 2. Martinez-Martin P, Rojo-Abuin JM, Dujardin K, et al. Designing a new scale to measure anxiety symptoms in Parkinson's disease: item selection based on canonical correlation analysis. European Journal of Neurology 2013;20:1198-1203.
- 3. Forjaz MJ, Martinez-Martin P, Dujardin K, et al. Rasch analysis of anxiety scales in Parkinson's disease. Journal of Psychosomatic Research 2013;74:414-419.

#### Appendix 2. English, Spanish, French and Dutch versions of the PAS

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## The Parkinson Anxiety Scale (PAS); English version

## A. Persistent anxiety

#### Please mark one circle for each item below

In the past four weeks, to what extent did you experience the following symptoms?

#### A.1. Feeling anxious or nervous

- Not at all, or never
- o Very mild, or rarely
- o Mild, or sometimes
- o Moderate, or often
- o Severe, or (nearly) always

#### A.2. Feeling tense or stressed

- Not at all, or never
- o Very mild, or rarely
- Mild, or sometimes
- o Moderate, or often
- Severe, or (nearly) always

#### A.3. Being unable to relax

- o Not at all, or never
- o Very mild, or rarely
- o Mild, or sometimes

- o Moderate, or often
- o Severe, or (nearly) always

## A.4. Excessive worrying about everyday matters

- o Not at all, or never
- o Very mild, or rarely
- o Mild, or sometimes
- o Moderate, or often
- o Severe, or (nearly) always

### A.5. Fear of something bad, or even the worst, happening

- o Not at all, or never
- o Very mild, or rarely
- o Mild, or sometimes
- o Moderate, or often
- o Severe, or (nearly) always

## B. Episodic anxiety

## Please mark one circle for each item below

In the past four weeks, did you experience episodes of the following symptoms?

#### **B.1.** Panic or intense fear

- Never
- o Rarely
- Sometimes
- o Often
- o Nearly always

#### **B.2. Shortness of breath**

- o Never
- o Rarely
- Sometimes
- o Often
- o Nearly always

## **B.3.** Heart palpitations or heart beating fast (not related to physical effort or activity)

- Never
- o Rarely
- Sometimes
- o Often
- Nearly always

## **B.4.** Fear of losing control

- Never
- o Rarely
- o Sometimes
- o Often
- Nearly always

## C. Avoidance behavior

#### Please mark one circle for each item below

In the past four weeks, to what extent did you fear or avoid the following situations?

- C.1. Social situations (where one may be observed, or evaluated by others, such as speaking in public, or talking to unknown people)
  - o Never
  - o Rarely
  - Sometimes
  - o Often
  - Nearly always
- C.2. Public settings (situations from which it may be difficult or embarrassing to escape, such as queues or lines, crowds, bridges, or public transportation)
  - o Never
  - o Rarely
  - Sometimes
  - o Often
  - Nearly always

# C.3. Specific objects or situations (such as flying, heights, spiders or other animals, needles, or blood)

- o Never
- o Rarely
- o Sometimes
- o Often
- o Nearly always

# The Parkinson Anxiety Scale (PAS); Spanish version

### Escala de Ansiedad en Parkinson

### A. Ansiedad rasgo

En las últimas cuatro semanas, ¿en qué grado ha padecido los siguientes síntomas?

### A.1. Sentirse ansioso o nervioso

- o Para nada, ninguna vez
- o Algo, pero casi nada
- o A veces
- o Con frecuencia
- o Muchas veces, casi siempre

### A.2. Sentirse tenso o estresado

- o Para nada, ninguna vez
- o Algo, pero casi nada
- A veces
- o Con frecuencia
- Muchas veces, casi siempre

# A.3. Ser incapaz de relajarse

- o Para nada, ninguna vez
- o Algo, pero casi nada
- o A veces
- o Con frecuencia
- Muchas veces, casi siempre

# A.4. Excesivamente preocupado por problemas cotidianos

- o Para nada, ninguna vez
- o Algo, pero casi nada
- o A veces
- o Con frecuencia
- Muchas veces, casi siempre

# A.5. Tener miedo de que pase algo malo, o muy malo

- o Para nada, ninguna vez
- o Algo, pero casi nada
- A veces
- o Con frecuencia
- o Muchas veces, casi siempre

### B. Ansiedad estado

En las pasadas cuatro semanas, ¿ha experimentado episodios con estos síntomas?

## B.1. Pánico o miedo intenso

- o Nunca
- o Rara vez
- o Alguna vez
- o Con frecuencia
- o Casi siempre

# **B.2.** Quedarse sin aliento

- o Nunca
- o Rara vez
- o Alguna vez
- o Con frecuencia
- o Casi siempre

# B.3. Taquicardias, (no relacionadas con actividad física)

- o Nunca
- o Rara vez
- o Alguna vez
- o Con frecuencia
- o Casi siempre

## **B.4.** Miedo a perder el control

- Nunca
- o Rara vez
- o Alguna vez
- o Con frecuencia
- o Casi siempre

### C. Conductas de evitación

En las últimas cuatro semanas, ¿en qué medida ha temido o ha evitado estas situaciones?

- C.1. Situaciones sociales( donde uno puede ser observado y/o evaluado por los otros, tales como hablar en público, o charlar con un desconocido)
  - Nunca
  - o Rara vez
  - o A veces
  - o A menudo
  - Casi siempre
- C.2. Sitios públicos con gran afluencia de gente, donde puede ser complicado escapar; tales como el metro en hora punta, una manifestación, etc.
  - o Nunca
  - o Rara vez
  - o A veces
  - o A menudo
  - Casi siempre
- C.3. Determinados objetos o situaciones (tales como volar en avión, las arañas, las alturas, etc.)
  - o Nunca
  - o Rara vez
  - o A veces
  - o A menudo
  - o Casi siempre

### The Parkinson Anxiety Scale (PAS) (Version française)

### A. Anxiété persistante

Au cours des quatre dernières semaines, dans quelle mesure avez-vous ressenti les symptômes suivants? Merci de cocher une réponse pour chacune des manifestations ci-dessous.

### A.1. Vous sentir anxieux ou nerveux

- o Pas du tout ou jamais
- Très peu ou rarement
- Légèrement ou parfois
- Modérément ou souvent
- o Fortement ou (presque) toujours

### A.2. Vous sentir tendu ou stressé

- o Pas du tout ou jamais
- o Très peu ou rarement
- Légèrement ou parfois
- Modérément ou souvent
- o Fortement ou (presque) toujours

# A.3. Etre incapable de vous détendre

- Pas du tout ou jamais
- Très peu ou rarement
- o Légèrement ou parfois
- Modérément ou souvent
- o Fortement ou (presque) toujours

# A.4. Vous faire trop de soucis pour des petits problèmes de la vie de tous les jours

- Pas du tout ou jamais
- o Très peu ou rarement
- Légèrement ou parfois
- Modérément ou souvent
- o Fortement ou (presque) toujours

# A.5. Craindre qu'un malheur, ou même le pire, va se produire

- Pas du tout ou jamais
- o Très peu ou rarement
- Légèrement ou parfois
- Modérément ou souvent
- o Fortement ou (presque) toujours

# B. Anxiété épisodique

Au cours des quatre dernières semaines, avez-vous ressenti par moment les symptômes suivants ? Merci de cocher une réponse pour chacune des manifestations ci-dessous.

### B.1. Etre pris de panique ou d'une peur intense

- o Jamais
- o Rarement
- o Parfois
- o Souvent
- Presque toujours

# B.2. Avoir de la difficulté à respirer

- o Jamais
- o Rarement
- o Parfois
- o Souvent
- Presque toujours

# B.3. Avoir des palpitations ou le cœur qui s'emballe (sans lien avec un effort ou une activité physique)

- o Jamais
- o Rarement
- o Parfois
- o Souvent
- Presque toujours

### B.4. Avoir peur de perdre le contrôle

- o Jamais
- o Rarement
- o Parfois
- o Souvent
- Presque toujours

### C. Comportements d'évitement

Au cours des quatre dernières semaines, dans quelle mesure avez-vous redouté ou évité les situations suivantes ? Merci de cocher une réponse pour chacune des manifestations ci-dessous.

C.1. Les situations sociales (où on pourrait être observé ou jugé par	
d'autres, comme prendre la parole en public ou discuter avec des incon	nus)

- o Jamais
- o Rarement
- o Parfois
- Souvent
- o Presque toujours

# C.2. Les lieux publics (situations dont il peut être difficile ou gênant de s'échapper, telles que les files d'attente, la foule, les ponts ou les transports en commun)

- o Jamais
- o Rarement
- o Parfois
- o Souvent
- o Presque toujours

# C.3. Des objets ou des situations spécifiques (comme prendre l'avion, être en hauteur, les araignées ou d'autres animaux, les piqûres ou la vue du sang)

- o Jamais
- o Rarement
- o Parfois
- o Souvent
- o Presque toujours

# The Parkinson Anxiety Scale (PAS); Dutch version

# De Parkinson Angst Scaal (PAS)

# A. Persisterende Angst

# Kruis één antwoord aan voor elk van de volgende items:

In welke mate heeft u <u>in de afgelopen vier weken</u> de volgende klachten gehad?

### A.1. Angst of nervositeit

- o helemaal niet of nooit
- o in heel geringe mate of zelden
- o in geringe mate of soms
- o matig ernstig of vaak
- o in ernstig mate of (bijna) altijd

### A.2. Spanning of stress

- o helemaal niet of nooit
- o in heel geringe mate of zelden
- o in geringe mate of soms
- o matig ernstig of vaak
- o in ernstig mate of (bijna) altijd

#### A.3. Zich niet kunnen ontspannen

- o helemaal niet of nooit
- o in heel geringe mate of zelden
- o in geringe mate of soms
- o matig ernstig of vaak
- o in ernstig mate of (bijna) altijd

### A.4. Overmatig piekeren over alledaagse dingen

- o helemaal niet of nooit
- o in heel geringe mate of zelden
- o in geringe mate of soms
- o matig ernstig of vaak
- o in ernstig mate of (bijna) altijd

### A.5. Angst dat er iets heel ergs zal gaan gebeuren

- o helemaal niet of nooit
- o in heel geringe mate of zelden
- o in geringe mate of soms
- o matig ernstig of vaak
- o in ernstig mate of (bijna) altijd

# B. Episodische Angst

# Kruis één antwoord aan voor elk van de volgende items:

In welke mate heeft u <u>in de afgelopen vier weken</u> de volgende symptomen ervaren?

## **B.1.** Paniek of intense angst

- o Nooit
- o Zelden
- o Soms
- o Vaak
- o Meestal

### **B.2.** Kortademigheid

- o Nooit
- o Zelden
- o Soms
- o Vaak
- o Meestal

### B.3. Hartkloppingen of versnelde hartslag (niet gerelateerd aan lichamelijke inspanning)

- o Nooit
- o Zelden
- o Soms
- o Vaak
- o Meestal

### **B.4.** Angst voor controleverlies

- o Nooit
- o Zelden
- o Soms
- o Vaak
- o Meestal

# C. Vermijdingsgedrag

# Kruis één antwoord aan voor elk van de volgende items:

Hoe vaak heeft u <u>in de afgelopen vier weken</u> angst gehad voor de volgende situaties of deze situaties vermeden?

- C.1. Sociale situaties (waarin men door anderen geobserveerd of beoordeeld zou kunnen worden, zoals spreken in het openbaar of spreken met onbekenden)
  - o Nooit
  - o Zelden
  - o Soms
  - o Vaak
  - o Meestal
- C.2. Openbare gelegenheden (situaties waarin het moeilijk of gênant kan zijn om te ontsnappen, zoals 'in een wachtrij staan', zich in een mensenmassa bevinden, op bruggen lopen, of reizen met het openbaar vervoer)
  - o Nooit
  - o Zelden
  - o Soms
  - o Vaak
  - o Meestal
- C.3. Specifieke objecten of situaties (zoals reizen met het vliegtuig, hoogtes, spinnen of andere dieren, naalden of bloed)
  - o Nooit
  - o Zelden
  - o Soms
  - o Vaak
  - o Meestal

Vertaling: Moonen AJH, Leentjens AFG, 2011

Appendix 3: Number of included patients, demographic and disease related data *by institute*, as well as the significance of differences of proportions or means across institutes by chi-square or ANOVA.

	Baltimore	Perth	Lille	Maastricht	Madrid	Philadelphia	p
n	60	60	61	61	60	60	
Age (years)	65.0	68.0	59.7	66.8	67.2	63.1	0.00
% female	60	57	66	62	73	63	0.45
MMSE (/30)	28.8	28.5	27.4	29.0	28.5	28.5	0.02
IADL	10.4	11.4	8.2	10.7	9.3	10.1	< 0.001
Disease duration	12.1	11.4	10.4	10.9	8.6	8.9	0.01
UPDRS 3	24.3	33.8	18.2	30.1	21.0	21.0	0.00
H&Y (median)	2	3	2	2.5	2	2	0.00
Major depression (%)	5	3	2	7	15	12	0.04
Dysthymia	0	0	5	2	33	13	0.00
GAD	5	8	28	2	17	32	<0.001
Social Phobia	8	2	13	2	15	15	0.02
agoraphobia	0	7	20	3	15	18	0.00
Panic (total)	2	0	10	5	2	2	0.29
HAMD	6.9	7.3	5.5	5.6	9.7	9.7	0.00
HARS	13.1	8.7	9.3	5.9	13.0	10.1	0.00
BAI	11.4	11.4	15.5	8.5	12.3	11.5	0.00
PAS obs full	8.9	8.2	15.2	8.5	11.4	11.1	0.00
PAS self full	11.0	12.8	19.1	11.7	11.4	14.5	0.00
Anticholinergic	10	5	3	10	2	10	0.22
Dopa-agonist	53	75	57	63	73	60	0.06
Levo-dopa	93	93	90	92	88	88	0.86
NMDA antagonist	18	0	18	33	33	25	0.00

MAO-B inhibitor	35	2	31	11	50	35	0.00
apomorphine	0	2	5	0	3	3	0.35
LEDD	996	530	1044	888	486	811	< 0.001
Antidepressant	47	35	20	20	32	38	0.01
Beta blocker	15	10	8	8	3	22	0.03
benzodiazepine	20	3	20	11	42	32	0.00
antipsychotics	7	2	2	0	10	3	0.04

# Appendix 4. Scores on individual PAS items

Mean (SD), median (IQR) and range of scores on individual items of the observer-rated and self-rated PAS items.

# Observer-rated PAS

item	mean	SD	median	range	inter-rater
item	Incun	SD	meatun	runge	inter-rater
					reliability
					(ICC)
Persistent subscale					
1	1.34	1.20	1	0 - 4	0.94
2	1.36	1.14	1	0 - 4	0.95
3	1.05	1.15	1	0 - 4	0.88
4	1.00	1.18	1	0 - 4	0.93
5	0.76	1.06	0	0 - 4	0.92
Episodic subscale	1	I	l		
1	0.30	0.70	0	0 - 3	0.87
2	0.53	0.94	0	0 - 4	0.87
3	0.35	0.73	0	0 - 3	0.90
4	0.52	0.82	0	0 - 3	0.90
Avoidance subscale	1	I	I	I	
1	0.94	1.16	0	0 - 4	0.91
2	0.91	1.25	0	0 - 4	0.93
3	0.45	0.95	0	0 - 4	0.76
	1	1			

# Selfrated PAS

item	mean	SD	median	range	Test-retest
					reliability
					(ICC)
Persistent subscale	•				
1	1.48	1.18	1	0-4	0.89
2	1.60	1.14	2	0-4	0.88
3	1.28	1.19	1	0-4	0.81
4	1.38	1.25	1	0-4	0.85
5	0.96	1.23	1	0-4	0.81
Episodic subscale		1	<u>I</u>	<u>I</u>	
1	0.52	0.85	0	0-4	0.80
2	0.79	1.03	0	0-4	0.86
3	0.54	0.85	0	0 – 3	0.79
4	0.80	0.98	0	0-4	0.73
Avoidance subscale	L	1	1	<u>I</u>	1
1	1.10	1.23	1	0 - 4	0.85
2	1.14	1.30	1	0-4	0.84
3	0.66	1.06	1	0-4	0.79

Appendix 5: Known groups validity: mean scores and standard deviations across severity groups defined by CGI or PGI scores for observer and self-rated scales. For CGI = 7, the number of included patients in this category is only n=2. For PGI = 7, no patients rated this severity.

CGI score	n	PAS total obs	PAS pers obs	PAS epis	PAS avoid
↓/scale →				obs	obs
1	141	3.9	1.9	0.7	1.3
2	59	6.7	4.1	1.1	1.6
3	85	10.9	6.8	1.7	2.6
4	50	18.0	10.9	3.2	3.9
5	15	23.3	13.4	5.4	4.5
6	8	28.3	15.4	6.5	6.4
7	2	32	16.5	5.0	10.5
p (Kruskal-		<0.001	<0.001	<0.001	<0.001
Wallis)					

CGI score	n	PAS total self	PAS pers self	PAS epis	PAS avoid
↓/scale →				self	self
1	141	5.6	2.9	1.1	1.5
2	59	10.4	5.9	2.2	2.3
3	85	14.6	8.3	3.0	3.2
4	50	21.3	11.7	4.6	5.1

5	15	26.2	13.7	6.8	5.7
6	8	31.8	16.3	8.0	7.5
7	2	27.0	11.5	5.0	10.5
p (Kruskal-		<0.001	<0.001	< 0.001	<0.001
Wallis)					

PGI score		PAS total obs	PAS pers obs	PAS epis obs	PAS avoid
↓/scale →					obs
1	138	4.0	1.9	0.6	1.5
2	60	8.1	4.9	1.5	1.7
3	81	10.5	6.5	1.6	2.6
4	58	16.0	9.9	2.8	3.3
5	16	26.7	14.6	6.3	5.8
6	6	26.2	14.3	6.5	5.3
7	0				
p (Kruskal-		<0.001	<0.001	<0.001	<0.001
Wallis)					

PGI score	n	PAS total self	PAS pers self	PAS epis	PAS avoid
↓/scale →				self	self
1	138	5.4	2.8	1.1	1.6
2	60	10.3	6.1	2.2	2.0

81	15.2	8.5	3.2	3.5
58	19.3	10.7	4.1	4.5
16	31.3	15.7	8.3	7.3
6	28.0	15.2	7.0	5.8
0				
	<0.001	<0.001	<0.001	<0.001
	58 16 6	58 19.3 16 31.3 6 28.0	58       19.3       10.7         16       31.3       15.7         6       28.0       15.2         0       15.2	58       19.3       10.7       4.1         16       31.3       15.7       8.3         6       28.0       15.2       7.0         0       0       0       0

Appendix 6: Principal Component Analysis of the observer and self-rated PAS versions.

# Observer-rated PAS

KMO measure of sampling adequacy: 0.884; total variance explained: 62.6 %

item/loading	persistent	episodic	avoidance
A1	0.86	0.2	0.14
A2	0.83	0.18	0.13
A3	0.76	0.14	0.20
A4	0.83	0.13	0.19
A5	0.77	0.19	0.13
B1	0.45	0.5	0.1
B2	0.12	0.83	0.08
В3	0.16	0.81	0.04
B4	0.46	0.35	0.3
C1	0.40	0.01	0.59
C2	0.33	0.07	0.69
C3	-0.42	0.1	0.74
% variance	33	16	13
explained			

Self-rated PAS

KMO measure of sampling adequacy: 0.897; total variance explained : 64.9 %

item/loading	persistent	episodic	avoidance
A1	0.8	0.28	0.20
A2	0.8	0.22	0.28
A3	0.79	0.12	0.06
A4	0.75	0.22	0.31
A5	0.63	0.36	0.27
B1	0.26	0.62	0.36
B2	0.20	0.78	-0.01
В3	0.19	0.78	0.14
B4	0.30	0.60	0.44
C1	0.27	0.14	0.75
C2	0.23	0.02	0.83
C3	0.10	0.28	0.54
% variance	27	20	18
explained			

Appendix 7. Divergent validity of PAS subscales (Spearman correlation coefficients; all coefficients are significant for P<0.01)

# Observer-rated PAS

	Total PAS	Persistent	Episodic	Avoidance
		subscale	subscale	subscale
Total PAS	1	0.93	0.74	0.72
Persistent subscale		1	0.55	0.51
Episodic subscale			1	0.35
Avoidance subscale				1

# Self-rated PAS

	Total PAS	Persistent	Episodic	Avoidance
		subscale	subscale	subscale
Total PAS	1	0.91	0.81	0.77
Persistent subscale		1	0.61	0.55
Episodic subscale			1	0.50
Avoidance subscale				1