ORIGINAL ARTICLE

Psychometric properties of the apathy evaluation scale in patients with Parkinson's disease

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Abstract

Parkinson's disease (PD) frequently entails non-motor symptoms, worsening the course of the disease. Apathy is one of the core neuropsychiatric symptoms that has been investigated in recent years; research is however hampered by the limited availability of well-evaluated apathy scales for these patients. We evaluated the psychometric properties of the Apathy Evaluation Scale (AES) in a sample of PD patients. Psychometric properties, convergent and discriminant validity and sensitivity/specificity were evaluated in patients with ($n = 582$) or without dementia/depression ($n = 339$). Internal consistency was high in the entire sample as well as in patients without dementia/depression. Correlations were moderate for convergent validity (UPDRS I item 4: motivation). While apathy could be differentiated from cognitive decline, it was related to depression (Geriatric Depression Scale, GDS-15). The overall classification accuracy based on the UPDRS I item 4 was comparable for AES and GDS scores. The AES exhibits good psychometric properties in PD patients with and without dementia and/or depression. Commonly used screenings on the presence of apathy had low detection rates compared to the AES and reflected both apathetic and depressive symptoms. Psychometric evaluation of available instruments will support further research on the clinical relevance of apathy for disease progression and treatment approaches in PD patients.

KEYWORDS

apathy, depression, Parkinson's disease, psychometrics, validity

1 | INTRODUCTION

Parkinson's disease (PD) is a severe and progressive neurodegenerative disorder that frequently entails neuropsychiatric symptoms such as apathy and depression (Aarsland & Kramberger, 2015; Aarsland, Marsh, & Schrag, 2009). These non-motor symptoms are associated with a worse disease progression, the development of dementia, and care-dependency (Fitts et al., 2015; Riedel et al., 2012).

The core symptom of apathy is a lack of motivation characterized by diminished goal-oriented behavior. However, as it is of a multi-dimensional nature, further domains are affected, including a reduced emotional expression and reduced cognition (Marin, Biedrzycki, & Firinciogullari, 1991; Starkstein & Leentjens, 2008).

Due to different methods used, previously reported prevalences of apathy in PD have been varying considerably between 16.5% (Aarsland et al., 1999) and up to 62.4% (Tanaka, Wada-Isoe, Nakashita, Yamamoto, & Nakashima, 2013). In a recently published meta-analysis (den Brok et al., 2015), which was based on 23 studies that have been published between 1992 and 2013, the authors calculated a pooled prevalence of 39.8%. Concomitant depression was present in 57.2% of patients with apathy. The same meta-analysis also revealed that apathy was associated with higher age, increased motor symptoms and more severe disability, and cognitive decline: compared to patients without apathy, patients with apathy are older by an average of 3.3 years, have a higher motor score by an average of 6.5 points according to the Unified Parkinson's Disease Rating Scale (Goetz et al., 2003), and have a lower score on the established Mini-Mental State Exam by an average of 1.4 points (Folstein, Folstein, & McHugh, 1975).

In order to investigate neuropsychiatric symptoms in PD, reliable and valid instruments are required, evaluated for this specific patient group (Schrag, 2011). The need of studies reporting psychometric data on existing instruments for PD has been emphasized (Leentjens et al., 2008), including the Apathy Evaluation Scale (AES) (Marin et al., 1991). The AES allows for testing apathy as an independent syndrome in different patient groups and addresses the areas of motivation, self-initiative behavior, endurance, interest, emotional responsiveness, and awareness of problems. Good psychometric properties have been reported for the original (Marin et al., 1991) as well as for its German version (Lueken et al., 2006) which are available in different versions (self, clinician, informant). A previous study recently published by Santangelo et al. (2014) has already generated evidence on the psychometric properties of the self-rated version of the AES in PD patients. The results were based on 60 non-demented, non-depressed, untreated, drug-naïve, *de novo* PD patients. However, dementia and depression are in fact frequent complications during the course of PD. Previously published meta-analyses have estimated a mean prevalence of 35% for depression (range 2.7–89%) and 24.5% for dementia (range

8.3–41.3%), respectively (Aarsland, Zaccai, & Brayne, 2005; Reijnders, Ehrt, Weber, Aarsland, & Leentjens, 2008). This clearly limits the generalizability of their results to the majority of PD patients in daily routine care.

We thus aimed to provide a psychometric characterization of the AES based on data of a large, more heterogeneous and thus clinically representative sample of PD patients. In particular, we intended to test the quality of psychometric properties in relation to the co-occurrence of depression or dementia. Thus, the sample was split into two sub-samples with or without the presence of these comorbidities using data from a longitudinal, prospective study on dementia in PD (Dementia in Parkinson's disease [DEMPARK/LANDSCAPE] study).

2 | METHODS

2.1 | Sample characteristics

The methods of DEM PARK have been previously described in greater detail (Balzer-Geldsetzer, Braga da Costa, et al., 2011). The patients were recruited in eight movement disorder units (university hospitals) distributed across Germany. At baseline, the study sample consisted of 665 PD patients. Inclusion criteria were: age between 45 and 80 years, idiopathic PD according to UK Brain Bank criteria (Hughes, Daniel, Kilford, & Lees, 1992). Based on the neuropsychological assessment as described in the next section, patients were categorized as without cognitive impairment, mild cognitive impairment (MCI) or dementia. As suggested by Petersen (2004), the diagnosis of MCI required (1) cognitive dysfunction as reported by the patient, (2) no significant impairment in activities of daily living, (3) cognitive dysfunctions, defined as ≤ 1.5 standard deviations below normal mean values in at least one neuropsychological test. According to Emre et al. (2007) and Dubois et al. (2007), the diagnosis of dementia was made in case of (1) insidious onset and slow progression of cognitive deficits, (2) impairment of activities of daily living that cannot solely be attributed to the motor symptoms of PD, (3) impairments in at least two cognitive domains as demonstrated by the neuropsychological assessment, which also represent (4) a decline from the premorbid level.

Exclusion criteria encompassed atypical PD syndromes, other forms of dementia, pregnancy, and the incapability of consenting to the study. Eighty-three incomplete AES data sets were excluded, resulting in a sample size of $n = 582$ patients (sample 1, Supporting Information Figure S1, please see also section 2.3 for further details). In order to assess the psychometric properties of the AES independent from dementia/depression, analyses were repeated for a sub-sample of patients (sample 2 with $n = 339$ patients) who were neither demented according to consensus criteria for dementia in PD (Emre

et al., 2007) nor depressed. Depression was screened with the Geriatric Depression Scale-15 (GDS-15; Sheikh et al., 1991), and an established cutoff for PD-Patients of ≥ 5 was used according to Schrag (2011). The study protocol was reviewed by the Ethics Committee of the Philipps-University Marburg (approval no. 178/07) in March 2009. Patients gave written informed consent prior to participation.

2.2 | Procedure and material

Patients participated in a screening, a baseline and two follow-up assessments at six and 12 months after the baseline. The assessment comprised a comprehensive neuropsychological examination carried out by trained neuropsychologists. Global cognitive functions were assessed with the Mini-Mental State Examination (MMSE; Folstein et al., 1975) and the Parkinson Neuropsychometric Dementia Assessment (PANDA; Kalbe et al., 2008). Specific cognitive functions were measured with the CERAD-Plus (Consortium to Establish a Registry for Alzheimer's Disease) test (Aebi, 2002), which comprises subtypes for the assessment of single cognitive domains including verbal memory (subtests word-list learning, delayed recall and recognition of the word list), non-verbal figural memory (delayed recall of copied figures), executive functions (phonemic and semantic verbal fluency subtests, Trail Making Test), visuospatial abilities (constructional praxis subtest, which requires the copying of figures), and language (Boston Naming Test). In addition to that, five further neuropsychological tests were applied, including the Stroop interference test, the Brief Test of Attention, the Modified Card Sorting Test, as well as the subtests "mental rotation" and "spatial imagination" from the German test battery "Leistungsprüfsystem 50+" (for a full description of the neuropsychological assessment including references please refer to Balzer-Geldsetzer et al. [2011]).

Apathy was assessed with the self-rated version of the AES, the answers were recorded by trained clinical psychologists. The AES consists of 18 items on a 4-point Likert scale. Items are scored from 1 to 4 with three inverted items that are recoded accordingly (items 6, 10, and 11). A higher score indicates greater apathy (range: 18–72). The Unified Parkinson's Disease Rating Scale I (UPDRS I; Goetz et al., 2003) item 4 has been recommended for screening purposes in PD patients by the Movement Disorder Task Force on apathy (Leentjens et al., 2008). Convergent validity of the AES was therefore tested with this item assessing lack of motivation in PD patients on a 4-point Likert scale. In accordance with (Pedersen, Larsen, & Aarsland, 2008), a cutoff >2 was used to indicate the presence of apathy. The UPDRS III score on motor symptoms was used to differentiate apathy from motor disabilities and levodopa equivalent daily doses (LEDDs) were calculated according to (Tomlinson et al., 2010) in order to investigate the relationship between apathy and dopaminergic medication. The UPDRS I item 4 was used to determine sensitivity and specificity of the AES for classification accuracy. Performance was compared to the GDS-15 in order to test whether the UPDRS I "motivation" item was sufficiently capable to distinguish between symptoms of apathy versus depression.

2.3 | Analyses of missing items of the AES

Among patients with incomplete AES data sets ($n = 83$), one item was missing for $n = 39$ patients (45.8%), while all items of the AES were missing for $n = 29$ patients (34.9%). The median number of missing items was 2. Patients who were excluded because of incomplete AES data sets were older (70.3 versus 67.4 years, $p < 0.001$), at higher stages of PD (median Hoehn and Yahr Scale stage III versus stage II, $p < 0.01$) and scored lower on the MMSE (27.4 versus 27.9, $p < 0.05$) than patients with complete AES data sets. No differences between both groups were found for sex ($p = 0.609$), duration of PD ($p = 0.073$), motor impairment according to the UPDRS III score ($p = 0.689$), levodopa equivalent dose ($p = 0.743$), depression according to the GDS score ($p = 0.339$) or cognitive impairment according to the PANDA score ($p = 0.052$).

Among the AES items, the frequency of missing items ranged between $n = 31$ (item 5: "S/he is interested in learning new things.") and $n = 41$ (item 11: "S/he is less concerned about problems than s/he should be.").

2.4 | Statistical analysis

Descriptive data were calculated for sample 1 (all patients included) and sample 2 (patients without dementia or depression). Differences between patients from sample 2 and excluded patients from sample 1 were tested using chi squared (χ^2) tests and t-tests for independent samples. Internal consistency of the AES was determined using Cronbach's alpha and item-total correlations (part-whole corrected).

We tested the data for normal distribution with the Shapiro-Wilks test which is feasible for variables with less than 2000 observations. The assumption of normal distribution could not be confirmed for the UPDRS I score, the total scores of the GDS-15, MMSE, PANDA, and the AES. However, parametric methods were applied anyway because: (1) the sample size ($n > 300$) gives theoretical power enough for similar results using parametric or non-parametric tests, and (2) results of both tests were previously checked and, in fact, were quite similar. As a consequence, parametric methods were used to keep consistency in the report. Thus, Pearson's correlations were computed between the AES total score, UPDRS I item 4, GDS-15, MMSE, PANDA, UPDRS III total score, and LEDD. Partial correlations were computed between the AES, MMSE, and PANDA scores, controlling for the influence of depressive symptoms (GDS-15 total score). The factor structure of the AES was analyzed using a principal components factor analysis, Varimax (orthogonal) rotation, and an Eigenwert criterion of ≥ 1 for factor extraction. Receiver operating characteristic (ROC) curve analyses and the area under the curve (AUC) were computed to test the sensitivity and specificity of the AES. This analysis was repeated for the GDS-15 score to compare the relative contribution of apathetic versus depressive symptoms to the classification of apathy based on the UPDRS I item 4 and the expert rating. All analyses were carried out using IBM SPSS Statistics 23 (IBM, Armonk, NY, USA). An α -level of $p < 0.05$ indicated statistical significance. Due to the large sample size and high statistical power, we additionally report the magnitude of correlations as small ($r < 0.30$), moderate ($r = 0.30$ – 0.50), or large ($r > 0.50$).

3 | RESULTS

3.1 | Sample characteristics

Sample characteristics for samples 1 and 2 are given in Table 1. According to the UPDRS item 4 cutoff, 3.20% of sample 1 and 0.90% of sample 2 were classified as apathetic. Applying an AES cutoff >38 with a minimum specificity >80%, rates increased to 19.60% (sample 1) and 8.30% (sample 2). Sample 2 was significantly younger than the excluded patients ($t(580) = 3.095, p = 0.002$), had a lower Hoehn and Yahr Scale stage ($\chi^2(4) = 30.631, p < 0.001$), milder motor symptoms (UPDRS III: $t(414) = 5.231, p < 0.001$), lower LEDD ($t(569) = 2.997, p < 0.01$), less apathetic and depressive symptoms (AES: $t(438) = 9.709, p < 0.001$; GDS-15: $t(198) = 20.093, p < 0.001$), and less cognitive impairment (MMSE: $t(356) = -6.401, p < 0.001$; PANDA: $t(434) = -5.585, p < 0.001$).

3.2 | Internal consistency

A Cronbach's alpha of $r = 0.917$ indicated a high internal consistency of the AES in sample 1. Items 6, 10, and 11 yielded low correlations with the corrected total scores and Cronbach's alpha improved when omitting these items. For sample 2, similar results were obtained (Cronbach's alpha $r = 0.897$; see Table 2 and

Supporting Information Table S1 for item characteristics for samples 1 and 2).

3.3 | Validity

In sample 1, the AES correlated moderately with UPDRS I item 4 ($r = 0.410, p < 0.001$). Stronger correlations were observed for the GDS-15 score ($r = 0.512, p < 0.001$). The AES exhibited small correlations with cognitive impairment (MMSE: $r = -0.270, p < 0.001$, small effect; PANDA: $r = -0.270, p < 0.001$). Controlling for the impact of depressive symptomatology on cognitive performance, partial correlations with the AES were even reduced (MMSE: $r = -0.198, p < 0.001$, small effect; PANDA: $r = -0.192, p < 0.001$, small effect). Similarly, low correlations were observed with motor dysfunction (UPDRS III: $r = -0.210, p < 0.001$, small effect) and dopaminergic medication (LEDD: $r = 0.078, p = 0.063$, small effect). In sample 2, this correlation profile was replicated, albeit on a lower correlational level due to the restricted range of symptoms in patients without depression and/or dementia (UPDRS I item 4: $r = 0.220, p < 0.001$; GDS-15: $r = 0.274, p < 0.001$; MMSE: $r = -0.162, p = 0.003$; PANDA: $r = -0.182, p = 0.001$; UPDRS III: $r = 0.091, p = 0.102$; LEDD: $r = 0.082, p = 0.135$; partial correlations: MMSE: $r = -0.145, p = 0.007$; PANDA: $r = -0.172, p = 0.002$; all small effects). All correlations remained stable after controlling for years of schooling.

TABLE 1 Sample characteristics

	Sample 1 (n = 582)		Sample 2 (n = 339)	
Socio-demographic characteristics				
Male gender (%)	395	(67.90)	238	(70.20)
Age in years	67.37	(7.90)	66.52	(7.96)
Years of schooling	10.40	(1.68)	10.57	(1.70)
Clinical characteristics				
Disease duration in years	6.71	(5.30)	6.34	(5.05)
H&Y status (%)				
Stage 1 (%)	89	(15.40)	63	(18.64)
Stage 2 (%)	293	(50.69)	188	(55.62)
Stage 3 (%)	152	(26.30)	74	(21.89)
Stage 4 (%)	37	(6.40)	11	(3.25)
Stage 5 (%)	7	(1.21)	2	(0.69)
UPDRS III	23.34	(12.88)	21.03	(10.73)
LEDD in mg	767.08	(537.40)	710.29	(526.41)
Neuropsychiatric characteristics				
MMSE	27.94	(2.23)	28.47	(1.58)
PANDA	21.64	(6.03)	22.89	(5.18)
AES	30.63	(9.49)	27.96	(7.59)
GDS-15	3.34	(3.01)	1.81	(1.33)
Number of subjects (%) classified as apathetic				
UPDRS I item 4: cutoff 2/3	18	(3.20)	3	(0.90)
AES cutoff: 38/39	114	(19.60)	28	(8.30)

Note: Means (standard deviation) except where noted. H&Y status, Hoehn and Yahr status; AES, Apathy Evaluation Scale; GDS-15, Geriatric Depression Scale – short version; MMSE, Mini-Mental State Examination; PANDA, Parkinson Neuropsychometric Dementia Assessment; UPDRS, Unified Parkinson's Disease Rating Scale; LEDD, levodopa equivalent daily dose; UPDRS I item 4, UPDRS item on motivation. Disease duration available for 574 (sample 1)/335 (sample 2) patients; H&Y status available for 578/338 patients; UPDRS III available for 550/324 patients; LEDD available for 571/332 patients; PANDA available for 581/339 patients; GDS-15 available for 505/339 patients; UPDRS item 4 available for 569/332 patients.

TABLE 2 Item characteristics for sample 1 ($n = 582$); Cronbach's alpha = 0.917

Item	Mean	Standard deviation	Corrected item-total correlation	Squared multiple correlation	Cronbach's alpha without item
1 S/he is interested in things	1.61	0.703	0.677	0.523	0.910
2 S/he gets things done during the day	1.66	0.729	0.715	0.566	0.909
3 Getting things started on his/her own is important to her/him	1.68	0.807	0.669	0.518	0.910
4 S/he is interested in having new experiences	1.86	0.888	0.737	0.671	0.907
5 S/he is interested in learning new things	1.97	0.909	0.683	0.597	0.909
6 ^a S/he puts little effort into anything	1.44	0.769	0.236	0.115	0.920
7 S/he approaches life with intensity	2.05	0.829	0.660	0.485	0.910
8 Seeing a job through to the end is important to her/him	1.62	0.755	0.625	0.424	0.911
9 S/he spends time doing things that interest her/him	1.63	0.718	0.610	0.453	0.911
10 ^a Someone has to tell her/him what to do each day	1.46	0.798	0.290	0.131	0.919
11 ^a S/he is less concerned about problems than she/he should be	1.80	0.864	0.212	0.109	0.922
12 S/he has friends	1.74	0.847	0.543	0.600	0.913
13 Getting together with friends is important to her/him	1.69	0.840	0.560	0.605	0.912
14 When something good happens, she/he gets excited	1.60	0.773	0.606	0.474	0.911
15 S/he has an accurate understanding of her/his problems	1.86	0.825	0.540	0.374	0.913
16 Getting this done during the day is important for her/him	1.65	0.742	0.709	0.603	0.909
17 S/he has initiative	1.81	0.810	0.795	0.749	0.906
18 S/he has motivation	1.87	0.811	0.794	0.747	0.906

^aInverted items.

3.4 | Factorial structure

In sample 1, a three-factorial solution was identified, accounting for 58.00% of the total variance (see Table 3 for rotated component matrix). Factor 1 accounted for 38.27% of the variance and encompassed constitutive elements of the construct of apathy; factor 2 accounted for 10.86% and included items that dealt with friendship (items 12 and 13). Factor 3 accounted for 8.88% and included items

that exhibited the lowest corrected item-total correlation (inverted items 6, 10, and 11). In sample 2 (59.54% explained variance), results on the factorial structure differed for the third factor where item 10 loaded separately (see Supporting Information Table S2). For both analyses, factor post-estimation tests indicated the appropriateness of the analyses (sample 1: Kayser–Meyer–Olkin value: 0.933, Bartlett test on sphericity: < 0.0001 ; sample 2: Kayser–Meyer–Olkin value: 0.912, Bartlett test on sphericity: < 0.0001).

TABLE 3 Rotated component matrix of the apathy evaluation scale (AES) for sample 1 ($n = 582$)

Item		Factor		
		1	2	3
1	S/he is interested in things	0.680	0.141	0.259
2	S/he gets things done during the day	0.709	0.140	0.289
3	Getting things started on his/her own is important to her/him	0.764	0.001	0.139
4	S/he is interested in having new experiences	0.774	0.171	0.120
5	S/he is interested in learning new things	0.706	0.153	0.172
6 ^a	S/he puts little effort into anything	0.100	0.012	0.699
7	S/he approaches life with intensity	0.672	0.215	0.137
8	Seeing a job through to the end is important to her/him	0.659	0.173	0.090
9	S/he spends time doing things that interest her/him	0.592	0.226	0.214
10 ^a	Someone has to tell her/him what to do each day	0.256	−0.094	0.530
11 ^a	S/he is less concerned about problems than she/he should be	0.003	0.227	0.664
12	S/he has friends	0.299	0.871	0.100
13	Getting together with friends is important to her/him	0.346	0.842	0.050
14	When something good happens, she/he gets excited	0.692	0.255	−0.180
15	S/he has an accurate understanding of her/his problems	0.593	0.195	−0.034
16	Getting this done during the day is important for her/him	0.765	0.134	0.086
17	S/he has initiative	0.811	0.192	0.162
18	S/he has motivation	0.803	0.222	0.145

^aInverted items.

3.5 | ROC curve analyses

Due to the exclusion of depressive symptoms in sample 2, ROC curves were calculated only for sample 1. Sensitivity and specificity of the AES and the GDS-15 to both criteria are given in the Supporting Information Table S3. Assuming a sufficient specificity ($\geq 80\%$), a cutoff of 38/39 was obtained for the AES from the UPDRS I item 4. ROC curves of the AES and GDS-15 (Figure 1) were visually compared to the diagonal "line of no information" on which prediction is no better than chance ($AUC = 0.50$). For the UPDRS I item 4, the AUC for the AES was 0.763 and 0.801 for the GDS-15.

4 | DISCUSSION

Apathy is one of the most prevalent neuropsychiatric symptoms in PD that is associated with cognitive decline, depression, and care dependency (den Brok et al., 2015; Fitts et al., 2015). Research is hampered by the limited availability of psychometrically well-evaluated apathy scales for this patient group (Leentjens et al., 2008). Supplementing a previous report (Santangelo et al., 2014) on the psychometric characterization of the AES in PD, we here present results from a comprehensive sample of 582 PD patients, 339 of them without dementia and/or depression. Main findings were: (a) a high internal consistency of the AES for patients with or without dementia and depression; (b) moderate convergent validity for the UPDRS motivation item; (c) delineation of apathy from motor dysfunction, dopaminergic medication, and cognitive decline, but high overlap with depressive symptoms; (d) commonly used screenings on the presence of apathy (UPDRS I item 4; expert judgment) had low detection rates for apathy and were likely to reflect both apathetic and depressive symptoms.

Meta-analytic evidence suggests a pooled prevalence rate of 39.80% of apathy in PD with 22.60% in patients without depression and/or dementia (den Brok et al., 2015). Owing to the prospective-longitudinal DEMPARK/LANDSCAPE study, patients in early disease stages (Hoehn and Yahr Scale stage 1 + 2) prevailed in the present sample. This was reflected by discrete cognitive dysfunction and low

prevalence rates of apathy of 19.60% in patients with and 8.30% in patients without depression and/or dementia using an AES cutoff >38 (Butterfield, Cimino, Oelke, Hauser, & Sanchez-Ramos, 2010; Santangelo et al., 2014). Two studies on untreated, early stage or *de novo* PD patients with a lower mean age and disease duration than the present sample did report higher prevalence rates of 18.90% using the Lille Apathy Rating Scale (LARS) (Dujardin et al., 2014) or 33.30% using proposed diagnostic criteria as a gold standard (Santangelo et al., 2014). In contrast, employing a comparable sample in terms of mean age and disease duration, Butterfield et al. (2010) reported lower rates of 14.70% using the AES with a mean AES score of 30.29 (being comparable to a prevalence rate of 19.60% and a mean AES score of 30.60 in sample 1) and a cutoff >38 . These findings limit assumptions about a general increase of apathy with disease progression to a certain extent. Sample characteristics should be taken into account when interpreting the interrelationship between apathy, depression, and cognitive decline and when applying present findings to other PD populations.

We observed a good internal consistency of the AES that was comparable to previous reports (Santangelo et al., 2014). Internal consistency was high in patients with and without dementia and/or depression, showing that the AES can be applied also to PD patients exhibiting other neuropsychiatric symptoms such as dementia or depression. Although the AES represents a homogenous apathy construct, three items (items 6, 10, and 11) did not fit into the scale. Previous evidence (Santangelo et al., 2014) also suggested a low item-total correlation of item 6, while items 10 and 11 worked well. These items contain a double negation probably inducing comprehension errors in the self-rating version. Previous analyses on the clinician-rated version showed homogenous corrected item-total correlations for all items, including the inverted ones (Lueken et al., 2006). These items also addressed aspects of apathy with a certain social stigma (item 6: "Puts little effort into anything"; item 10: "Someone has to tell what to do each day"; item 11: "Less concerned about problems than should be"), enhancing the probability of socially desired answers in the presence of the staff that was coding them. Rephrasing these items could improve the AES and its use in future studies.

FIGURE 1 Receiver operating characteristic (ROC) curves for the apathy evaluation scale (AES) and geriatric depression scale-15 (GDS-15) in relation to the unified Parkinson's disease rating scale (UPDRS) I item 4 (cutoff >2) and an expert judgment (apathy: yes/no)

Convergent validity of the AES to the UPDRS I item 4 was moderate with medium effect size correlations. Using the Neuropsychiatric Inventory (NPI) apathy subscale in an earlier study, we observed slightly higher correlations with the AES ranging from $r = 0.59$ to $r = 0.62$ in different patient groups such as stroke, PD, and dementia (Lueken et al., 2006; Lueken et al., 2007). Although the UPDRS I item 4 has been recommended for screening purposes in PD patients (Leentjens et al., 2008), it is based upon a single item and does not reflect the full range of apathetic symptoms. Associations between apathy and depression pointed toward substantial overlap between these constructs. Den Brok et al. (2015) reported that approximately 57.2% of patients with apathy also show depression. These findings imply that these two syndromes may be discriminable in PD, but also share related behavioral dimensions which may be reflected by correlational results between the GDS-15, UPDRS I item 4 and the AES score in the present study. Apathy could be well discriminated from cognitive dysfunction, particularly after controlling for the influence of depression. High and low apathetic patients were reported to show differences particularly in executive functioning (Butterfield et al., 2010; Santangelo et al., 2014; Varanese, Perfetti, Ghilardi, & Di Rocco, 2011) and recent evidence suggests that apathy predicts cognitive decline and dementia (Dujardin, Sockeel, Delliaux, Destee, & Defebvre, 2009; Fitts et al., 2015). Present findings do not indicate a substantial relation between apathy and cognitive dysfunction in this sample of predominantly mild PD patients, but a closer relationship could be assumed with disease progression.

In accordance with Santangelo et al. (2014), a three-factorial solution was detected. While the first (constitutive aspects of apathy) and second factor (social apathy dimension) highly overlapped, items on effort (item 6), drive (item 10), and insight (item 11) represented the third factor in the present analysis (those items also showed the lowest item-total correlation). Excluding patients with depression and/or dementia yielded a slightly different solution where item 10 loaded on a separate, fourth factor. The existence of a general apathy factor is in line with findings from Marin et al. (1991) for the original version of the AES, and was replicated for the German version (Lueken et al., 2006). Of note, those items that dealt with friendship did not load on this main factor in these analyses as well, indicating that friendship – particularly in aged patients – could be influenced by other factors such as the availability of friends or impairment due to the primary disorder (Lueken et al., 2007).

Sensitivity and specificity of the AES were characterized using a cutoff > 2 for the UPDRS I item 4 (Pedersen et al., 2008). This item has been suggested as “recommended” for screening purposes (Leentjens et al., 2008), but this cutoff exhibits poor sensitivity (Kirsch-Darrow et al., 2009). The low frequencies (3.2% versus 19.6% using the AES cutoff) in the present sample likely reflect an underestimation of affected patients. Obviously, this criterion appears to be at the costs of sensitivity. An AES cutoff of 38/39 seemed suitable with acceptable specificity $\geq 80\%$. This cutoff is also comparable to Santangelo et al. (2014) favoring specificity and similar to a cutoff of 37/38 proposed by Rabkin et al. (2000). Based on the present data we can confirm this AES cutoff based on clinimetric evidence. Highly comparable AUC values were obtained for the AES and GDS-15 score, evidencing a substantial overlap in the UPDRS I item 4. We conclude

that a mere expert rating is not sufficient for detecting apathy. The absence of a diagnostic “gold standard” has hampered the development and validation of appropriate apathy scales, but recently proposed consensus diagnostic criteria will improve research on apathy in PD (Drijgers, Dujardin, Reijnders, Defebvre, & Leentjens, 2010; Mulin et al., 2011; Pagonabarraga, Kulisevsky, Strafella, & Krack, 2015).

The main strength of our study is the sufficiently large sample size which allowed comprehensive analyses, stratified to patients with and without neuropsychiatric comorbidities which frequently occur in PD. However, one has to keep in mind the lack of a real “gold standard” in our study as a major limitation when interpreting our results. Specific and validated diagnostic criteria for apathy in PD as mentioned earlier were not yet available when the DEMPARK study was designed, and the data collection was started, respectively. Also, the detection and description of apathy was not a major outcome of the DEMPARK study, which primarily aimed at the detection and characterization of conversions between unimpaired intellectual abilities, mild cognitive impairment and full-blown dementia. The validation criterion UPDRS I item 4 on motivation has a limited capacity to adequately reflect the range of apathetic symptoms and may be suboptimal for measuring convergent validity of the AES. However, we had to refrain from including further established apathy scales as gold standard in order to minimize the strain of both patients and examiners and to keep the study feasible for the routine care. In further studies on apathy in PD, it is necessary to include other validated measures as well as proposed diagnostic criteria. Regarding our findings on the internal consistency of the AES, it should be noted Cronbach's alpha of the AES (18 items) may be spuriously high considering that alpha inflates with the number of items.

It should also be kept in mind that more than 12% of our initial study sample had to be excluded from further analyses due to missing or incomplete AES data. It remains unclear, however, whether these drop-outs on patient level can be regarded a selection bias. On the one hand, excluded patients were older, advanced in PD and scored marginally but significantly lower on the MMSE than patients with incomplete AES data. On the other hand, there were no differences regarding sex, clinical and treatment characteristics of the motor status and, most importantly, depression between included and excluded patients. Likewise, we found no hints for systematic omissions of certain AES items, i.e. no items were more likely to be missing than others. This is also important when considering biases that might have occurred due to using the self-rated version of the AES. While for the patient- and informant-based related version of the AES a good convergent validity has been stated (Leentjens et al., 2008), our results could not be controlled for lack of awareness, which also frequently occurs in depression or early stages of dementia. However, given that our analyses in patients with dementia and depression and in patients without these complications show similar results, we expect this bias to be negligible.

Despite these limitations, the present findings contribute to a better psychometric characterization of the AES as a frequently used apathy scale in neuropsychiatric disorders, including a cutoff based on clinimetric evidence for PD. Results indicate good psychometric properties in a sample of predominantly mild PD patients. Findings will

help to foster the use of the AES in future studies on apathy and to further characterize its role for disease progression and treatment approaches in PD.

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FULL FINANCIAL DISCLOSURE FOR THE PREVIOUS 12 MONTHS

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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