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Visuospatial memory profile of patients with Parkinson's disease

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ABSTRACT

Background: In Parkinson's Disease (PD) cognitive impairment may become evident at an early stage of the disease. Performance in the visuospatial domain has been pointed out as a possible predictor of cognitive decline for dementia.

Objectives: The goal was to characterize the visuospatial memory profile, explore the predictive value of a set of visuospatial measures that better distinguish patients from controls, and investigate the relevance of the 10/36 SPART, providing cutoff scores.

Methods: A total of 43 PD patients and 45 healthy controls (HC) were recruited from the Centro Hospitalar Universitário de São João and the community, respectively. The protocol included a set of tests assessing global cognitive functioning, visuoperceptive abilities, and visuospatial memory.

Results: PD patients performed significantly worse than HC, showing difficulties in global cognition, visuospatial learning, and visuoconstructive and perceptive abilities. Through a discriminant analysis, the Clock Drawing Test and ACE-R's visuospatial domain were revealed as good tools to be included in the evaluation protocol. Regarding the 10/36 SPART's performance, four predictors were found (age, sex, education, and emotional distress) and cutoff scores were determined.

Conclusions: The visuospatial memory profile found was congruent with that described in the literature. The results were discussed according to their relevance for clinical practice and future research.

KEYWORDS

Parkinson's disease; isuospatial memory; 10/36 sPAcRT; ut-off scores

Introduction

Parkinson's Disease (PD) is the most frequently diagnosed movement disorder, and the second most common neurodegenerative disease of the central nervous system (Tysnes & Storstein, 2017), only surpassed by Alzheimer's Disease (Hayes, 2019).

Considering the progressive nature of PD, a wide spectrum of behavioral and cognitive changes will invariably arise. It is known that cognitive impairment may become evident at an early stage of the disease, even before motor symptoms are reported (Aarsland et al., 2017; Simon et al., 2020). The cumulative risk of dementia is supported by several longitudinal studies indicating that most patients will develop dementia if they survive more than 10 years after the initial diagnosis (Aarsland et al., 2017), with not only executive, attentional, memory, and visuospatial impairment, but also a wide range of psychiatric symptomatology such as hallucinations and depression (Kehagia et al., 2013).

The impairment of visuospatial abilities has been reported in the literature as being present in PD, notably by Levin et al. (1991) who stated that dementia and duration of disease are closely related to the decline in visuospatial abilities, sharing a complex relationship. The impairment of visuospatial abilities results in difficulties in the extraction of central information for face recognition and visuospatial memory storage (Lazaruk, 1994), as well as an inaccurate perception of orientation in relation to space. The latter is essential for maintaining balance, for object orientation in a gravitational field, and for creating an accurate internal model of the body's orientation in space (Luvizutto et al., 2020). These difficulties are prevalent in PD and, consequently, these patients have a higher risk of falling, bumping into elements of space, getting lost, and/or having car accidents. There is also evidence that these patients have spatial learning, orientation, and navigation difficulties (Fernandez-Baizan et al., 2020), with a great impact on their quality of life and interaction with their surroundings.

The neuropsychological assessment of visuospatial function is, therefore, crucial in these patients and there is currently a set of tests allowing its assessment, such as intersecting pentagons copy item within the MMSE, and Clock Drawing Test, BVMT-R, Benton's Judgment of Line Orientation, and Royall's CLOX, recommended by the Movement Disorders Society Task Force Guidelines (Goldman et al., 2015; Litvan et al., 2012). Recently, the

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10/36 Spatial Recall Test (SPART), which integrates the Brief Repeatable Battery of Neuropsychological Tests (BRBN-T; Rao et al., 1991) widely used in clinical practice with Multiple Sclerosis (MS) patients, has been studied to be administered to other conditions. Galtier et al. (2014, 2021) used the 8/30 SPART, a modified version of the 10/36 SPART, with PD patients. In France, Dujardin et al. (2016) selected the 10/36 SPART to be part of the evaluation protocol lately achieved by expert consensus to evaluate PD patients. They suggested the use of this test as it does not require fine motor abilities or specific devices. However, in Portugal, it has not yet been used in PD and, therefore, no normative data for this specific population is available.

This study has three main goals: (1) to characterize the visuospatial memory profile of PD patients; (2) to explore the predictive value of a set of visuospatial measures that better distinguish between groups (clinical vs. controls); and (3) to investigate the potential of the 10/36 SPART and make available Portuguese cutoff scores to use in clinical practice.

Material and methods

Participants

Eighty-eight participants were included in the study: 43 PD patients and 45 healthy controls (HC). The Ethical approval for the prospective analysis was obtained from the Ethics Committee of the Centro Hospitalar Universitário de São João (CHUSJ, n.° 14/2022). The study was conducted in agreement with the Helsinki Declaration. All participants agreed to participate voluntarily and written informed consent was obtained prior to the protocol administration.

The clinical group had 43 participants with a confirmed diagnosis of PD performed by a neurologist, 27 males (62.8%) and 16 females (37.2%), with a mean age of around 65 years old ($M = 64.93$, $SD = 7.59$) and approximately eight years of formal education ($M = 8.09$, $SD = 4.42$). Motor symptoms and stage of the disease were assessed with the motor section (part III) of the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn & Elton, 1987) and with the Hoehn and Yahr Scale (Hoehn & Yahr, 1967), respectively. PD patients were classified as Tremor-Dominant (TD; $n = 21$, 48.8%) and Akinetic-Rigid (AR; $n = 22$, 51.2%) according to the motor symptoms. Pharmacological treatment included Levodopa/Carbidopa, non-ergot dopamine agonists, Monoamine oxidase B inhibitors, and Catechol-O-Methyltransferase inhibitors, among others. The criteria for eligibility were as follows: (1) a positive diagnosis of PD established by a neurologist and according to the UK Parkinson's Disease Brain Bank Criteria (Hughes et al., 1992); (2) European Portuguese native speakers; (3) 18 years old or more; (4) at least four years of education; (5) normal or corrected vision and audition; (6) absence of dementia, major psychiatric illness (e.g., major depression), or other autoimmune diseases that could interfere with cognitive performance and/or explain the presence of cognitive impairment confirmed by the neurologist's clinical data. Exclusion criteria were: (1) previously submitted to *Deep Brain Stimulation*; and (2) the presence of neurological, musculoskeletal, cardiovascular disorders or physical disability of the upper limbs (e.g., hemiparesis/paresis). According to the MoCA test scores, 27 patients had intact global cognition, and the remaining 16 obtained results either below 22 points (cutoff score for MCI, $n = 12$) or below 17 points (cutoff score for AD, $n = 4$). PD patients were matched for age, sex, and years of education to their healthy peers (see Table 1).

Forty-five participants were considered healthy controls with a mean age of 64 years old ($M = 64.43$, $SD = 8.36$) and eight years of education ($M = 8.44$, $SD = 4.56$), with no mild cognitive deficits. All of them were European Portuguese native speakers recruited into the community by means of personal contact and social media. They were autonomous, had normal or corrected vision/audition, and had no known history of alcohol or drug abuse, serious head trauma, and/or neurological, musculoskeletal, cardiovascular, or psychological diseases that could affect cognitive functioning.

As shown in Table 1, there were no statistically significant sociodemographic (i.e., age, sex, and education) differences between PD patients and HC. Emotional distress was pondered, but its presence was not considered an exclusion criterion as it is often associated with PD (Cabreira & Massano, 2019; Hayes, 2019).

Neuropsychological test procedures

All subjects were evaluated with the same neuropsychological protocol measuring: (1) Global Cognition (*Montreal Cognitive Assessment,* MoCA; Freitas et al., 2013); (2) Visuospatial Memory (10/36 Spatial Recall Test (SPART), Sousa et al., 2021; Wechsler Memory Scale-III's Visual Reproduction (immediate and delayed tasks) and Spatial Span (forward and backward) subtests (Wechsler, 2008); and (3) Visuospatial and Visuoperceptual Functioning (Visuospatial Cognitive Domain of the Addenbrooke Cognitive Evaluation Revised, ACE-R, Firmino et al., 2008). Additionally, the 18-point clock drawing scoring system by Babins et al. (2008) was used to obtain a more detailed visuospatial characterization of the Clock Drawing task compared to the one provided by MoCA and ACE-R: assessment of circle integrity (2 points), number placement and sequencing (6 points), placement and size of the hands (6 points), and two additional points for representation of the clock's center and two points for general gestalt.

The 10/36 SPART is one of five subtests that integrates the Brief Repeatable Battery of Neuropsychological Tests (BRBN-T; Rao et al., 1991; Portuguese version by Sousa et al., 2021). It consists of a 6×6 checkerboard with 10 pieces placed at random. The board is presented to the subject for 10 seconds. After that time, the subject's task is to try to reproduce the original pattern on a blank board. This process is repeated two more times. After 15 minutes, in a delayed recall trial, the subject is asked to recall the pattern again. The score corresponds to the total number of correct responses for the three trials (total score = 30) and the total number of correct responses in the delay recall trial (total score = 10).

Table 1. Demographic and clinical characteristics of parkinson's disease (PD) and healthy controls (HC) participants.

	PD Patients ($n = 43$)		Healthy Controls ($n = 45$)		
Variable	M (SD)	Range	M (SD)	Range	*p*
Age (years)	64.93 (7.59)	44.83-78.25	64.43 (8.36)	44.17-78.67	.768
Sex (%male/female)	62.8/37.2	–	51.1/48.9	–	.274
Education (years)	8.09 (4.42)	4-17	8.44 (4.56)	4-17	.714
BSI (PSDI)	1.65 (.51)	0-2.89	1.42 (.32)	1-2.24	.011
%TD/%AR*	48.8/51.2	–	–	–	-
Hoehn & Yahr Stage	2.10 (.67)	1-4	–	–	–
UPDRS part III	24.11(15.39)	8-58	–	–	–
Age at onset	55.95 (8.26)	35-70	–	–	–
Disease duration (years)	8.40 (4.15)	0-22	–	–	–

Note. M: mean. SD: standard deviation. BSI (PSDI), Brief Symptom Inventory (Positive Symptom Distress Index). All statistical analyses were considered significant as $p < .05$.
*Motor Phenotype = TD: Tremor-Dominant vs. AR: Akinetic-Rigid.

Participants were also evaluated with the Brief Symptom Inventory (BSI; Canavarro, 1999), to identify self-reported clinically relevant psychological symptoms (e.g., anxiety, depression). The global index of distress considered was the Positive Symptom Distress Index (PSDI). The cutoff considered was 1.70, indicating the presence of emotional distress.

The neuropsychological protocol was administered in a single 45-minute session. Data collection occurred between November and March 2022 in the northern region of Portugal (Porto, Braga, and Viseu). The assessments' results were anonymized.

Statistical analyses

Data were analyzed using the software program IBM SPSS® software (version 27). Descriptive statistics were used for sample characterization. Statistical comparisons between groups regarding sociodemographic and clinical data were conducted using an independent sample Student *t* Test. Cohen's *d* was used to measure effect size and clinical relevance in these variables. For cognitive measures, it was used One-Way ANOVA to statistically compare the groups. To examine the relationship between cognitive functions regarding visuospatial memory, correlational analyses were performed using Pearson's correlation coefficient and linear regression analysis (stepwise method). For the visuospatial measures in which statistically significant differences were obtained, a discriminant analysis (enter method) was carried out to understand which of the tests allowed us to better distinguish the two groups.

For PD patients, a multiple linear regression (stepwise method) was conducted to examine the extent to which sociodemographic (age, sex, and education) and clinical variables (motor phenotype, disease duration, and emotional distress) influence the performance on the 10/36 SPART. Specifically for this test, cutoff scores were calculated using ROC curve analyses. A total of 72 healthy controls, from a previously collected sample used by Sousa et al. (2021) for the validation of the same instrument for MS, were added to the initial database. The level of statistical significance was established as $p < .05$.

Table 2. Mean (M) scores, standard–deviation (SD), and range in global cognition and visuospatial tests for parkinson's disease (PD) and healthy controls (HC) participants.

	PD Patients ($n = 43$)		Healthy Controls ($n = 45$)		
Cognitive Tests	*M (SD)*	Range	*M (SD)*	Range	*p*
MoCA	22.49 (4.45)	10-29	24.91 (2.49)	20-29	.002
Clock Drawing Test	12.79 (4.69)	2-18	15.56 (3.00)	2-18	.001
ACE-R	13.70 (2.60)	6-16	14.84 (1.73)	9-16	.016
10/36 SPART immediate	14.30 (5.01)	4-27	16.40 (4.52)	7-27	.042
10/36 SPART delay	5.37 (2.13)	2-10	5.40 (2.34)	1-10	.954
VR immediate	52.95 (23.42)	9-104	62.98 (19.73)	28-104	.032
VR delay*	30.55 (29.72)	0-104	37.51 (25.68)	0-102	.245
Spatial Span	11.84 (3.51)	3-20	12.60 (2.62)	8-18	.250

Note. All statistical analyses were considered significant as $p < .05$. *In this test, PD patients = 42.

Results

The results are organized to explore five key points: (1) Characterization of global cognition and visuospatial memory performance in the neuropsychological protocol: comparisons between groups (PD patients vs. HC and Tremor-Dominant vs. Akinetic-Rigid PD phenotypes); (2) Relationship between visuospatial memory, visuospatial perception, and visuospatial working memory; (3) The predictive value of the visuospatial measures for group membership (PD vs. HC); (4) 10/36 SPART performance: Analysis of sociodemographic and clinical predictors for PD patients; and (5) Sensitivity of the 10/36 SPART to differentiate PD patients from HC: ROC curve analysis.

Global cognition and visuospatial memory

Comparisons between PD patients and HC

The results obtained by PD patients and HC on global cognition (MoCA) and visuospatial measures (Clock Drawing Test, ACE-R's Visuospatial Cognitive Domain, 10/36 SPART, WMS's Visual Reproduction—VR –, and Spatial Span subtests) can be seen in Table 2. Mean raw scores significantly differed between PD patients and HC in all these measures, with controls obtaining better scores than patients.

In terms of global cognition (MoCA), we found statistically significant differences between groups ($F(1,86) = 10.05$, $p = .002$, $\eta 2 = .105$), with PD patients scoring significantly lower than HC ($M = 22.49$, $SD = 4.45$ vs. $M = 24.91$, $SD = 2.49$, respectively). The HC data was normative

according to age and education for the Portuguese population ($M = 25.58$, $SD = 2.25$). Analyzing the cognitive domains evaluated by MoCA, statistically significant differences were observed between the two groups in visuospatial/executive, attention, language, and abstraction domains with PD patients scoring significantly lower than HC. Nevertheless, the visuospatial/executive domain showed the highest effect size among all MoCA's cognitive domains ($t(86) = 3.15$, $p = .002$, $d = .672$).

Regarding visuospatial perception, statistically significant differences between groups were found in the Clock Drawing Test ($F(1,86) = 10.95$, $p = .001$, $\eta 2 = .113$), with HC performing better than PD patients ($M = 15.56$, $SD = 3.00$ vs. $M = 12.79$, $SD = 4.69$, respectively), and ACE-R's Visuospatial Cognitive Domain ($F(1,86) = 5.99$, $p = .016$, $\eta 2 = .065$) with HC performing better than patients ($M = 14.84$, $SD = 1.73$ vs. $M = 13.70$, $SD = 2.60$, respectively). Concerning visuospatial learning and memory, we found that PD patients performed significantly worse than controls ($M = 14.30$, $SD = 5.01$ vs. $M = 16.40$, $SD = 4.52$, respectively) on the immediate task of the 10/36 SPART ($F(1,86) = 4.27$, $p = .042$, $\eta 2 = .047$). Also, on the VR's immediate task, it was found a statistically significant difference between groups ($F(1,86) = 4.73$, $p = .032$, $\eta 2 = .052$), with PD patients ($M = 52.95$, $SD = 23.42$) performing significantly worse than controls ($M = 62.98$, $SD = 19.73$). No statistically significant differences were found between groups on the delayed recall tasks of the 10/36 SPART ($p = .954$) and VR ($p = .245$). In addition, no statistically significant differences were found between groups in the Spatial Span subtest ($p = .250$).

Comparisons between Tremor-Dominant (TD) and Akinetic-Rigid (AR) patients' phenotypes. According to Kehagia et al. (2013), there are two different profiles of cognitive deficits, each one associated with a different PD's motor phenotype (TD and AR), with AR patients having a faster cognitive decline, especially regarding visuospatial abilities. However, no differences between the two phenotypes were found in all the applied tests.

Relationship between visuospatial memory, visuospatial perception, and visuospatial working memory

A linear regression analysis was conducted to explore the nature of the relationship between visuospatial learning memory (10/36 SPART and VR immediate tasks), visuospatial perception (ACE-R's visuospatial cognitive domain), and spatial working memory (Spatial Span). The analysis resulted in a statistically significant model ($F(2,85) = 34.23$; $p = <.001$, $R^2 = .445$), including both Spatial Span and ACE-R's visuospatial cognitive domain as predictive factors explaining 45% of the visuospatial learning variance for the entire sample. Spatial Span was the strongest predictor ($\beta = .409$, $t = 4.564$, $p = <.001$), followed by ACE-R's visuospatial cognitive domain ($\beta = .379$, $t = 4.233$, $p = <.001$). According to Pearson's correlation coefficient, visuospatial learning presents a statistically significant moderate positive correlation with spatial working memory ($r = .57$; $n = 88$; $p = <.001$) and, also, with visuospatial perception ($r = .56$; $n = 88$; $p = <.001$). Regarding PD patients, Spatial Span and ACE-R's visuospatial cognitive domain accounted for 47% of visuospatial learning variance ($R^2 = .47$; $F(1,41) = 36.05$; $p = <.001$). In the HC group, 35% of visuospatial learning variance was explained by Spatial Span and ACE-R's visuospatial cognitive domain ($R^2 = .35$; $F(1,43) = 23.24$; $p = <.001$).

The predictive value of the visuospatial measures for group membership

The predictive value of the visuospatial measures was assessed using a direct discriminant function analysis (DFA) to predict group membership. In the model, were only included the visuospatial measures in which statistically significant differences were found between groups. Significant mean differences were observed for all the predictors (Clock Drawing Test, $F(1, 86) = 10.95$, $p = .001$; Wilks Lambda = .887; ACE-R's Visuospatial Cognitive Domain, $F(1, 86) = 5.99$, $p = .016$; Wilks Lambda = .935; Visual Reproduction immediate task, $F(1, 86) = 4.73$, $p = .032$; Wilks Lambda = .948; 10/36 SPART immediate task, $F(1, 86) = 4.27$, $p = .042$; Wilks Lambda = .953). The discriminant function revealed a significant association between groups and all predictors ($p = .011$). Table 3 displays the standardized canonical coefficients and the structure coefficients. The Clock Drawing Test emerged as the strongest discriminator between groups.

The classification results, shown in Table 4, reveal that the discriminant function presents 77.8% of sensitivity and 58.1% of specificity, with 68.2% of the original grouped cases being correctly classified. Eighteen PD patients were misclassified into the HC group and 10 healthy subjects were misclassified into the PD patients' group.

10/36 SPART performance: Analysis of sociodemographic and clinical predictors for PD patients

To understand which sociodemographic and clinical factors predicted the performance of PD patients on the 10/36

Table 3. Standardized discriminant function and structure coefficients for the two groups.

Function 1	Coefficients	r_s	r_s^2
Clock Drawing Test	1.169	.873	76.2%
ACE-R (visuospatial cognitive domain)	−.533	.646	41.7%
VR immediate	.106	.574	32.9%
10/36 SPART immediate	.483	.545	29.7%

Table 4. Classification results.

			Predicted group membership	
		Group	HC	PD Patients
Original	Count	HC (n= 45)	35	10
		PD Patients (n= 43)	18	25
	%	HC	77.8	22.2
		PD Patients	41.9	58.1

Percentage of originally grouped cases correctly classified: 68.2%.

Table 5. Pearson's correlation coefficients (r) and point-biserial correlation (rpb) between PD patients' global cognition (MoCA), visuospatial performance, and demographic variables.

Tests	Age *r* (*p*)	Sex[a] *rpb* (*p*)	Education *r* (*p*)
MoCA	**−.414** ** **(.006)**	−.129 (.409)	**−.656** ** **(<.001)**
Clock Drawing Test	**−.302** * **(.049)**	−.059 (.709)	.271 (.079)
ACE-R (visuospatial cognitive domain)	−.265 (.086)	−.097 (.537)	**.411** ** **(.006)**
10/36 SPART immediate	**−.340** * **(.026)**	**−.319** * **(.037)**	**.367** * **(.016)**
10/36 SPART delay	**−.429** ** (.004)	**−.342** * **(.025)**	**.490** ** **(<.001)**
VR immediate	**−.507** ** **(<.001)**	−.127 (.416)	**.582** ** **(<.001)**
VR delay	−.189 (.231)	−.135 (.395)	**.463** ** **(.002)**
Spatial Span	**−.453** ** **(.002)**	−.130 (.405)	**.458** ** **(.002)**

Note. [a]0 – masculine, 1 – feminine. *Correlation is significant at $p < .05$. **Correlation is significant at $p < .01$.

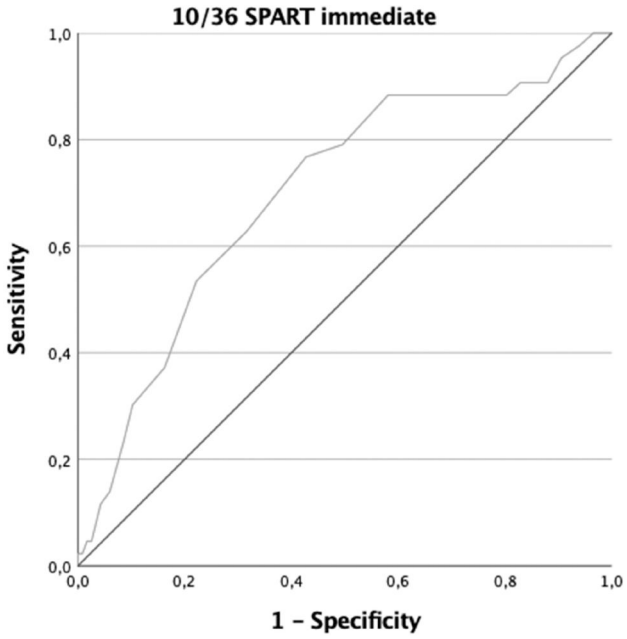

Figure 1. Receiver operating characteristic (ROC) curves of the 10/36 SPART immediate task differentiating between HC and PD patients (AUC = 0.70, CI = 0.61–0.79).

SPART, two multiple linear regression analyses (stepwise method) were performed for the immediate and delayed recall tasks. The factors included in the model were chosen based on the literature regarding clinical and demographic variables that influence cognition in PD, as well as on performed correlation analyses. No significant correlations were found between global cognition, visuospatial performance, and clinical factors (disease duration, motor phenotype, stage of the disease, and emotional distress). However, based on the literature, the clinical factors included were motor phenotype (TD vs. AR; dichotomous variable), disease duration, and emotional distress evaluated by BSI's PSDI (continuous variables). As can be observed in Table 5, statistically significant correlations were found between global cognition, visuospatial performance, and demographic variables. As such, the demographic factors included were age, education (continuous variables), and sex (dichotomous variable).

These six variables were entered in the model as predictors and the 10/36 SPART's immediate and delayed recall trials as dependent variables. Considering the 10/36 SPART immediate task, the analysis resulted in a statistically significant model ($F(3,39) = 7.33$; $p = <.001$, $R^2 = .360$), including sex, age, and emotional distress as predictive factors explaining 36% of the performance variance. Age was the strongest predictor ($\beta = -.508$, $t = -3.752$, $p = <.001$), followed by gender ($\beta = -.350$, $t = -2.545$, $p = .015$) and emotional distress ($\beta = -.290$, $t = -2.089$, $p = .043$). Neither the disease duration, motor phenotype nor education were significant predictors ($p = .844$, $p = .560$, and $p = .105$, respectively).

Concerning the 10/36 SPART delayed recall, the results showed that the model was statistically significant and explained approximately 50% of the performance variance on this task ($F(3,39) = 12.79$; $p = <.001$, $R^2 = .496$). This model included sex, age, and education as predictive factors. The strongest predictor was age ($\beta = -.443$, $t = -3.593$, $p = <.001$), followed by gender ($\beta = -.421$, $t = -3.534$, $p = .001$) and education ($\beta = .330$, $t = 2.752$, $p = .009$). Neither the disease duration, motor phenotype nor emotional distress were significant predictors ($p = .293$, $p = .171$, and $p = .751$, respectively).

Sensitivity of the 10/36 SPART to differentiate PD patients from HC: ROC curve analysis

ROC curve analyses were performed to evaluate the diagnostic accuracy of the 10/36 SPART (Figure 1), allowing to determine cutoff scores and distinguish between HC and PD patients. This analysis was only possible to execute for the 10/36 SPART immediate task for which statistically significant differences between the two groups were found. No significant differences were observed between groups in the delayed recall trial; therefore, no cutoff scores were calculated for this task.

We added to the initial database of HC, 72 healthy subjects from a previously collected sample. Regarding the discrimination between HC and PD patients in the 10/36 SPART immediate task, this analysis generated an optimal cutoff score of 19 points, with 88% sensitivity and 58% specificity (AUC of 0.70, CI = 0.61–0.79).

Discussion

One of the main goals of this study was to characterize the visuospatial memory profile of PD patients since few studies focus on this cognitive domain and it has been pointed out as a possible predictor of cognitive decline toward dementia

(Kehagia et al., 2013). The results have confirmed significant differences between groups in visuospatial memory performance, with PD patients performing lower than HC in most of the applied tests.

Patients obtained an overall poor performance in global cognition (MoCA) compared to HC ($M = 22.49$ vs. 24.91, respectively), a result consistent with those observed by Del Pino et al. (2021) and Kawashima et al. (2021). Moreover, the significant difference in the performance of the two groups in MoCA's visuospatial/executive domain showed the highest effect size ($d = .672$), strengthening the idea that these skills are especially impaired in this population.

Patients presented a significantly lower performance than HC in immediate visuospatial memory, however, no differences between groups were observed in delayed memory, reinforcing the results found by Galtier et al. (2014). These findings emphasize that visuospatial memory impairment in PD may be more related to visuospatial encoding—and consequently with short-term memory (STM)—than to the retention and retrieval of information in memory—long-term memory (LTM). In this regard, the information remembered by PD patients in delayed memory tasks was retained far beyond the life of STM even though the processing capacity of STM operations showed to be reduced (Sullivan & Sagar, 1991). These results can also provide experimental evidence for the clinical manifestation of bradyphrenia in PD (Sullivan & Sagar, 1991), which refers to a slowness in mental information processing. If it is given sufficient time for the subjects to respond, as in the delayed recall tasks, they can perform accurately. Though, if the task is limited by time (e.g., 10/36 SPART and VR immediate tasks), it can become harder to perform correctly. These findings, however, do not exclude the possibility of a LTM deficit in PD dependent on the clinical severity of the disease (e.g., demented PD patients) and dependent on the tests applied. In fact, Havlík et al. (2020) applied BVMT-R to a sample of HC, PD-NC (PD with normal cognition), and PD-MCI (PD with mild cognitive impairment) and found both memory and learning deficits in PD-MCI.

The literature highlights differences in cognition between TD and AR motor phenotypes, with AR patients being associated with a faster cognitive decline (Wojtala et al., 2019) especially concerning semantic fluency and visuospatial abilities (Kehagia et al., 2013). In this study, no significant differences were found in the applied tests, suggesting similar visuospatial performance between motor phenotypes. Despite our results being distinct from previous studies (Verbaan et al., 2007; Wojtala et al., 2019), it is noteworthy that the visuospatial measures used were not the same. Thus, a direct comparison between the results is not possible. Also, our findings do not support the Dual Syndrome Hypothesis (Kehagia et al., 2013), which can be due to the fact that our sample did not include patients with dementia and/or with a significant cognitive decline. Perhaps with a sample of patients with dementia (PD-D), we could observe other results.

The extent to which visuospatial perception and spatial working memory could predict visuospatial learning was analyzed. These variables had considerable predictive power (PD patients: 47%; HC: 35%), suggesting that subjects who perform better in Spatial Span and ACE-R's visuospatial cognitive domain will also perform better in visuospatial learning (10/36 SPART and VR immediate tasks). These results are in accordance with Galtier et al. (2014), allowing us to assume that visuospatial perception and spatial working memory play a relevant role in explaining visuospatial learning impairment. Therefore, visuospatial perception and spatial working memory measures should be included in the neuropsychological protocol for PD patients.

Focusing on the neuropsychological protocol, the discriminant analysis showed that the four visuospatial measures allowed for correctly classifying 68.2% of the original grouped cases. The Clock Drawing Test was the strongest discriminator between groups, surpassing the 10/36 SPART. Hence, our results propose the Clock Drawing Test as a useful screener of visuoperceptive and spatial impairment. Since this task is already included in MoCA, we suggest using the 18-point clock drawing scoring system by Babins et al. (2008) to have more robust information. As stated, different visuospatial measures have been used in research. It is of distinct interest to achieve a consensus about a standardized protocol to evaluate the visuospatial domain, and consequently, compare PD patients worldwide. According to the Movement Disorder Society's (Litvan et al., 2012) guidelines for PD patients' evaluation, two measures are needed to comprehensively assess each domain. Thus, we suggest the inclusion of the ACE-R's visuospatial cognitive domain and the 18-point clock drawing scoring system by Babins et al. (2008) to assess visuospatial perception. Regarding visuospatial memory, the performance on tests that imply visual function can be affected by visual dysfunctions and by the loss or reduction of fine motor skills (Uc et al., 2005). One example is the WMS's Visual Reproduction (already frequently used in clinical practice) which requires drawing. Once motor dysfunctions are frequent in PD, it is of clinical interest to have tests requiring less use of motor skills. Dujardin et al. (2016) recommended the 10/36 SPART. The current study is the first to provide empirical evidence regarding its utility in the PD patients' assessment, as well as cutoff scores (19 points for the immediate task), so it can be added to the protocol. Still, the area under the ROC curve was 0.70, revealing modest discrimination (Hosmer et al., 2013) between PD patients and HC. Therefore, it would benefit from further studies to become more revealing for clinical practice in terms of accurate classification.

The significant predictors of PD patients' performance on the 10/36 SPART were age, sex, education, and emotional distress. Age and education are the main factors that influence test scores. Increased age was associated with poorer performance in both immediate and delayed recall trials. This fact is not surprising as it is expected that younger individuals encode and retrieve better than older ones due to a reduction in the capacity of working memory that might limit older adults' ability to encode information and limit long-term memory (Hara & Naveh-Benjamin, 2015). Furthermore, it was found that the higher the education

level, the better the delayed visuospatial performance. The fact that education supports improved performance on a variety of cognitive tests in PD is expected and in line with the concept of cognitive reserve (Hindle et al., 2014). Sex also plays an important role in PD cognitive performance and was a significant predictor of both immediate and delayed recall trials, revealing that males perform better than females. While women tend to outperform men on verbal learning tasks, men show high-level performances on subtests measuring visuospatial processing (Pauls et al., 2013). Emotional distress was another predictor of 10/36 SPART immediate performance suggesting that the higher the level of emotional distress, the poorer the visuospatial learning. Even though anxiety has not been related to worse visuospatial abilities (Ehgoetz Martens et al., 2018), depression has been shown to worsen, in general, cognitive abilities (Lin et al., 2018).

Potential limitations of our study must be mentioned. A common limitation in PD research, also present in this study, is the relatively small sample size, which must be considered when generalizing the results. One example was the inclusion of 12 patients with MoCA scores below 22 points (cutoff score for MCI) and 4 patients with scores below 17 points (cutoff score for AD), not allowing to perform statistical analysis with different cognitive impairments (PD-MCI and PD-D). Also, MoCA is used in several studies as a useful screening tool to differentiate PD patients with and without cognitive impairment (e.g., Hoops et al., 2009), in this study it was not possible to perform such an analysis. Another limitation lies with our assessment protocol as we did not include tasks recommended by the Movement Disorder Society's (Litvan et al., 2012) guidelines for PD patients' evaluation, such as Benton's Judgment of Line Orientation (JoLO) and BVMT-R, which should be used to continue this study or similar future studies. Due to the lack of knowledge and studies about the application of JoLO in Portugal, we suggested the inclusion of ACE-R's visuospatial cognitive domain, although in future studies these two tasks should be applied and explored since JoLO can be a more useful and sensitive tool and is already recommended by Litvan et al. (2012). Similarly, although, in our study, the 18-point clock drawing scoring system by Babins et al. (2008) was revealed as a useful screening tool between patients and HC, we did not use CLOX (Royall et al., 1998). In future studies, it should be used this task as it is recommended by the Movement Disorder Society (Litvan et al., 2012). Another limitation lies with the scale used to measure emotional distress—BSI. Despite being a composite measure that provides information about the level of emotional distress, it does not clearly distinguish the prevalence of anxiety and/or depression, separately. In future work, we suggest using scales like the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) to evaluate the impact of each independent variable on visuospatial learning. Another limitation refers to the fact that the applied tests, except the Clock Drawing Test, don't have ecological validity. Therefore, it would be important to design assessment tools that resemble daily living activities related to visuospatial memory (e.g., driving simulators).

The visuospatial memory profile in PD must be interpreted within a broader framework of deficits that are present from the early stages of the disease, such as executive dysfunction, sensory impairment, and motor symptoms, suggesting that visuospatial defects are multi-determined in PD (Papagno & Trojano, 2018). For example, executive dysfunction (e.g., control of attention, working memory, planning, inhibitory control) is also a prominent and early cognitive symptom with a significant impact across the PD timeline affecting visuospatial and memory performance. Regarding this, in future studies, with larger sample sizes and a more comprehensive neuropsychological protocol, it would be important to consider and better understand other factors that also affect visuospatial memory, such as executive dysfunction (e.g., working memory, visual organization, planning), and motor symptoms. Also, it will be important to conduct longitudinal studies with larger sample sizes and different types of PD patients (non-demented, with mild cognitive impairment, and with dementia) to help unravel the fluctuations of visuospatial skills through disease duration and their ability to predict cognitive decline toward dementia. Furthermore, our results do not clarify to what extent the visuospatial STM deficit is produced by executive dysfunction or by damage in the visuospatial storage. Further studies should address this topic by conducting neuroimaging studies to clarify the neural mechanisms underlying these cognitive deficits (i.e., visuospatial and executive). Moreover, it is of great interest to keep exploring the 10/36 SPART's potential to provide useful information about the visuospatial outcomes of PD patients, and consequently determine cutoff scores based on variables such as age, sex, and education. Additionally, and specifically for the Portuguese population, more work is needed to include in the evaluation protocol tests like Benton's Judgment of Line Orientation (JoLO) and BVMT-R widely used in international studies (e.g., Del Pino et al., 2021; Galtier et al., 2014; Uc et al., 2005) and both recommended by Litvan et al. (2012).

Conclusions

We provided a visuospatial memory profile of PD highlighting visuospatial STM deficits. This is the first study providing clinical data for PD patients without dementia in the 10/36 SPART, a test requiring few materials and reduced motor skills. Lower levels of education, being female, advanced age, and higher levels of emotional distress predicted lower performances. Furthermore, two useful tools with high discriminant values were suggested to evaluate visuoconstructive and visuospatial perception, namely the Clock Drawing Test (Babins et al. (2008); 18 points classification) and the ACE-R's visuospatial cognitive domain.

Given the high prevalence of cognitive impairment in PD, particularly in the visuospatial memory and its association with a faster cognitive decline to dementia, it is of distinct interest to keep investigating this domain and

fluctuations through disease duration. Future studies should focus on longitudinal investigations of PD patients with mild cognitive impairment progressing to dementia and the impact of visuospatial impairments. Moreover, it is of high interest, for clinical and research purposes, to obtain an internationally validated neuropsychological test battery to compare PD patients worldwide, following the assessment protocol guidelines proposed by the Movement Disorder Society (Litvan et al., 2012).

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References

Aarsland, D., Creese, B., Politis, M., Chaudhuri, K. R., Ffytche, D. H., Weintraub, D., & Ballard, C. (2017). Cognitive decline in Parkinson's disease. *Nature Reviews. Neurology*, *13*(4), 217–231. https://doi.org/10.1038/nrneurol.2017.27

Babins, L., Slater, M. E., Whitehead, V., & Chertkow, H. (2008). Can an 18-point clock-drawing scoring system predict dementia in elderly individuals with mild cognitive impairment? *Journal of Clinical and Experimental Neuropsychology*, *30*(2), 173–186. https://doi.org/10.1080/13803390701336411

Cabreira, V., & Massano, J. (2019). Doença de Parkinson: Revisão clínica e atualização. *Acta Médica Portuguesa*, *32*(10), 661–670. https://actamedicaportuguesa.com/revista/index.php/amp/article/view/11978 https://doi.org/10.20344/amp.11978

Canavarro, M. C. (1999). Inventário de sintomas psicopatológicos: BSI. In M. R. Simões, M. Gonc¸alves & L. S. Almeida (Eds.), *Testes e provas psicológicas em Portugal* (Vol. II, pp. 87–109). SHO-APPORT.

Del Pino, R., Acera, M., Murueta-Goyena, A., Lucas-Jiménez, O., Ojeda, N., Ibarretxe-Bilbao, N., Peña, J., Reyero, P., Cortés, J., Tijero, B., Galdós, M., Gómez-Esteban, J. C., & Gabilondo, I. (2021). Visual dysfunction is associated with cognitive impairment in Parkinson's disease. *Parkinsonism & Related Disorders*, *92*, 22–25. https://doi.org/10.1016/j.parkreldis.2021.10.005

Dujardin, K., Auzou, N., Lhommée, E., Czernecki, V., Dubois, B., Fradet, A., Maltete, D., Meyer, M., Pineau, F., Schmitt, E., Sellal, F., Tison, F., Vidal, T., Azulay, J.-P., Welter, M.-L., Corvol, J.-C., Durif, F., & Rascol, O, NS-Park network. (2016). French consensus procedure for assessing cognitive function in Parkinson's disease. *Revue Neurologique*, *172*(11), 696–702. https://doi.org/10.1016/j.neurol.2016.05.001

Ehgoetz Martens, K. A., Silveira, C. R., Intzandt, B. N., & Almeida, Q. J. (2018). State anxiety predicts cognitive performance in patients with Parkinson's disease. *Neuropsychology*, *32*(8), 950–957. https://doi.org/10.1037/neu0000478

Fahn, S., & Elton, R. L. (1987). UPDRS program members. Unified Parkinsons' disease rating scale. *Recent Developments in Parkinson's Disease*, *2*, 153–163.

Fernandez-Baizan, C., Garcia, M. P. F., Diaz-Caceres, E., Menendez-Gonzalez, M., Arias, J. L., & Mendez, M. (2020). Patients with Parkinson's disease show alteration in their visuospatial abilities and in their egocentric and allocentric spatial orientation measured by card placing tests. *Journal of Parkinson's Disease*, *10*(4), 1807–1816. https://doi.org/10.3233/JPD-202122

Firmino, H., Simões, M. R., Pinho, M. S., Cerejeira, L., & Martins, C. (2008). *O Exame Cognitivo de Addenbrooke–Revisto [The Addenbrooke's Cognitive Examination–Revised]*. Serviço de Avaliação Psicológica da Faculdade de Psicologia e de Ciências da Educação da Universidade de Coimbra.

Freitas, S., Simões, M. R., Santana, I., Martins, C., & Nasreddine, Z. (2013). *Montreal cognitive assessment (MoCA): Versão 3*. Laboratório de Avaliação Psicológica, Faculdade de Psicologia e de Ciências da Educação da Universidade de Coimbra.

Galtier, I., Nieto, A., Lorenzo, J. N., & Barroso, J. (2014). Cognitive impairment in Parkinson's disease: More than a frontostriatal dysfunction. *The Spanish Journal of Psychology*, *17*, E68. https://doi.org/10.1017/sjp.2014.69

Galtier, I., Nieto, A., Mata, M., Lorenzo, J. N., & Barroso, J. (2021). Analyses of visuospatial and visuoperceptual errors as predictors of dementia in Parkinson's disease patients with subjective cognitive decline and mild cognitive impairment. *Journal of the International Neuropsychological Society : JINS*, *27*(7), 722–732. https://doi.org/10.1017/S1355617720001216

Goldman, J. G., Holden, S., Ouyang, B., Bernard, B., Goetz, C. G., & Stebbins, G. T. (2015). Diagnosing PD-MCI by MDS task force criteria: How many and which neuropsychological tests? *Movement Disorders : official Journal of the Movement Disorder Society*, *30*(3), 402–406. https://doi.org/10.1002/mds.26084

Hara, Y., & Naveh-Benjamin, M. (2015). The role of reduced working memory storage and processing resources in the associative memory deficit of older adults: Simulation studies with younger adults. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology and Cognition*, *22*(2), 129–154. https://doi.org/10.1080/13825585.2014.889650

Havlík, F., Mana, J., Dušek, P., Jech, R., Růžička, E., Kopeček, M., Georgi, H., & Bezdicek, O. (2020). Brief Visuospatial Memory Test-Revised: normative data and clinical utility of learning indices in Parkinson's disease. *Journal of Clinical and Experimental Neuropsychology*, *42*(10), 1099–1110. https://doi.org/10.1080/13803395.2020.1845303

Hayes, M. T. (2019). Parkinson's disease and parkinsonism. *The American Journal of Medicine*, *132*(7), 802–807. https://doi.org/10.1016/j.amjmed.2019.03.001

Hindle, J. V., Martyr, A., & Clare, L. (2014). Cognitive reserve in Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism & Related Disorders*, *20*(1), 1–7. https://doi.org/10.1016/j.parkreldis.2013.08.010

Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: onset, progression, and mortality. *Neurology*, *17*(5), 427–442. https://doi.org/10.1212/wnl.17.5.427

Hosmer, D. W., Jr, Lemeshow, S., & Sturdivant, R. X. (2013). *Applied logistic regression* (Vol. 398). John Wiley & Sons.

Hoops, S., Nazem, S., Siderowf, A. D., Duda, J. E., Xie, S. X., Stern, M. B., & Weintraub, D. (2009). Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson's disease. *Neurology*, *73*(21), 1738–1745. https://doi.org/10.1212/WNL.0b013e3181c34b47

Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery, and Psychiatry*, *55*(3), 181–184. https://doi.org/10.1136/jnnp.55.3.181

Kawashima, S., Shimizu, Y., Ueki, Y., & Matsukawa, N. (2021). Impairment of the visuospatial working memory in the patients with Parkinson's Disease: an fMRI study. *BMC Neurology*, *21*(1), 335. https://doi.org/10.1186/s12883-021-02366-7

Kehagia, A. A., Barker, R. A., & Robbins, T. W. (2013). Cognitive impairment in Parkinson's disease: The dual syndrome hypothesis. *Neuro-Degenerative Diseases*, *11*(2), 79–92. https://doi.org/10.1159/000341998

Lazaruk, L. (1994). Visuospatial impairment in persons with idiopathic Parkinson's disease: A literature review. *Physical & Occupational Therapy In Geriatrics*, *12*(2), 37–48. https://doi.org/10.1080/J148V12N02_04

Levin, B. E., Llabre, M. M., Reisman, S., Weiner, W. J., Sanchez-Ramos, J., Singer, C., & Brown, M. C. (1991). Visuospatial impairment in Parkinson's disease. *Neurology*, *41*(3), 365–369. https://doi.org/10.1212/WNL.41.3.365

Lin, S. J., Baumeister, T. R., Garg, S., & McKeown, M. J. (2018). Cognitive profiles and hub vulnerability in Parkinson's disease. *Frontiers in Neurology*, *9*, 482. https://doi.org/10.3389/fneur.2018.00482

Litvan, I., Goldman, J. G., Tröster, A. I., Schmand, B. A., Weintraub, D., Petersen, R. C., Mollenhauer, B., Adler, C. H., Marder, K., Williams-Gray, C. H., Aarsland, D., Kulisevsky, J., Rodriguez-Oroz, M. C., Burn, D. J., Barker, R. A., & Emre, M. (2012). Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. *Movement Disorders : official Journal of the Movement Disorder Society*, *27*(3), 349–356. https://doi.org/10.1002/mds.24893

Luvizutto, G. J., Brito, T. S. S., Neto, E. M., & Souza, L. A. P. S. (2020). Altered visual and proprioceptive spatial perception in individuals with Parkinson's disease. *Perceptual and Motor Skills*, *127*(1), 98–112. https://doi.org/10.1177/0031512519880421

Papagno, C., & Trojano, L. (2018). Cognitive and behavioral disorders in Parkinson's disease: an update. I: cognitive impairments. *Neurological Sciences : official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *39*(2), 215–223. https://doi.org/10.1007/s10072-017-3154-8

Pauls, F., Petermann, F., & Lepach, A. C. (2013). Gender differences in episodic memory and visual working memory including the effects of age. *Memory (Hove, England)*, *21*(7), 857–874. https://doi.org/10.1080/09658211.2013.765892

Rao, S. M., Leo, G. J., Bernardin, L., & Unverzagt, F. (1991). Cognitive dysfunction in multiple sclerosis.: I. Frequency, patterns, and prediction. *Neurology*, *41*(5), 685–691. https://doi.org/10.1212/WNL.41.5.685

Royall, D. R., Cordes, J. A., & Polk, M. (1998). CLOX: an executive clock drawing task. *Journal of Neurology, Neurosurgery & Psychiatry*, *64*(5), 588–594. DOI: https://doi.org/10.1136/jnnp.64.5.588

Simon, D. K., Tanner, C. M., & Brundin, P. (2020). Parkinson disease epidemiology, pathology, genetics, and pathophysiology. *Clinics in Geriatric Medicine*, *36*(1), 1–12. https://doi.org/10.1016/j.cger.2019.08.002

Sousa, C., Rigueiro-Neves, M., Passos, A. M., Ferreira, A., & Sá, M. J, Group for Validation of the BRBN-T in the Portuguese MS Population. (2021). Assessment of cognitive functions in patients with multiple sclerosis applying the normative values of the Rao's brief repeatable battery in the Portuguese population. *BMC Neurology*, *21*(1), 170. https://doi.org/10.1186/s12883-021-02193-w

Sullivan, E. V., & Sagar, H. J. (1991). Double dissociation of short-term and long-term memory for nonverbal material in Parkinson's disease and global amnesia: A further analysis. *Brain : a Journal of Neurology*, *114 (Pt 2)*(2), 893–906. https://doi.org/10.1093/brain/114.2.893

Tysnes, O. B., & Storstein, A. (2017). Epidemiology of Parkinson's disease. *Journal of Neural Transmission (Vienna, Austria: 1996)*, *124*(8), 901–905. https://doi.org/10.1007/s00702-017-1686-y

Uc, E. Y., Rizzo, M., Anderson, S. W., Qian, S., Rodnitzky, R. L., & Dawson, J. D. (2005). Visual dysfunction in Parkinson disease without dementia. *Neurology*, *65*(12), 1907–1913. https://doi.org/10.1212/01.wnl.0000191565.11065.11

Verbaan, D., Marinus, J., Visser, M., van Rooden, S. M., Stiggelbout, A. M., Middelkoop, H. A., & van Hilten, J. J. (2007). Cognitive impairment in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *78*(11), 1182–1187. https://doi.org/10.1136/jnnp.2006.112367

Wechsler, D. (2008). *Escala de Memória de Wechsler (3a Edição): Manual Técnico*. Cegoc-TEA.

Wojtala, J., Heber, I. A., Neuser, P., Heller, J., Kalbe, E., Rehberg, S. P., Storch, A., Linse, K., Schneider, C., Gräber, S., Berg, D., Dams, J., Balzer-Geldsetzer, M., Hilker-Roggendorf, R., Oberschmidt, C., Baudrexel, S., Witt, K., Schmidt, N., Deuschl, G., … Reetz, K. (2019). Cognitive decline in Parkinson's disease: the impact of the motor phenotype on cognition. *Journal of Neurology, Neurosurgery, and Psychiatry*, *90*(2), 171–179. https://doi.org/10.1136/jnnp-2018-319008

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, *67*(6), 361–370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x