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Art therapy for Parkinson's disease

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ABSTRACT

Objective: To explore the potential rehabilitative effect of art therapy and its underlying mechanisms in Parkinson's disease (PD).
Methods: Observational study of eighteen patients with PD, followed in a prospective, open-label, exploratory trial. Before and after twenty sessions of art therapy, PD patients were assessed with the UPDRS, Pegboard Test, Timed Up and Go Test (TUG), Beck Depression Inventory (BDI), Modified Fatigue Impact Scale and PROMIS-Self-Efficacy, Montreal Cognitive Assessment, Rey-Osterrieth Complex Figure Test (RCFT), Benton Visual Recognition Test (BVRT), Navon Test, Visual Search, and Stop Signal Task. Eye movements were recorded during the BVRT. Resting-state functional MRI (rs-fMRI) was also performed to assess functional connectivity (FC) changes within the dorsal attention (DAN), executive control (ECN), fronto-occipital (FOC), salience (SAL), primary and secondary visual (V1, V2) brain networks. We also tested fourteen age-matched healthy controls at baseline.
Results: At baseline, PD patients showed abnormal visual-cognitive functions and eye movements. Analyses of rs-fMRI showed increased functional connectivity within DAN and ECN in patients compared to controls. Following art therapy, performance improved on Navon test, eye tracking, and UPDRS scores. Rs-fMRI analysis revealed significantly increased FC levels in brain regions within V1 and V2 networks.
Interpretation: Art therapy improves overall visual-cognitive skills and visual exploration strategies as well as general motor function in patients with PD. The changes in brain connectivity highlight a functional reorganization of visual networks.

1. Introduction

The diagnosis of Parkinson's disease (PD) rests on clinical evidence of motor signs [1]. However, non-motor features such as mood changes, cognitive deficits, psychosis, and behavioral and perceptual abnormalities are common in PD [2,3], reducing functional independence and

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promoting social withdrawal as well as quality of life decrement. Current pharmacological treatments target symptom management and, while generally effective for motor and some non-motor manifestations of the disease, certain motor and perceptual problems, such as visual and visuospatial abnormalities, do not respond to dopaminergic treatment or other interventions [2]. Visual problems, though often under-recognized, are frequent in patients with PD at all stages and may include reduced contrast sensitivity, abnormal dark-light adaptation and color discrimination, irregular eye movements, restricted visual exploration, impaired motion perception, reduced visual recognition, and altered perception of extra-personal space [4]. Additionally, systematic perceptual biases may affect motor function, in particular locomotion and balance: visual impairment in PD has been linked to navigational veering, freezing of gait, and recurrent falls [5,6]. Disability arising from impaired visuospatial function may have a negative effect on activities of daily living such as reading, walking independently, driving, and maintaining overall physical fitness. While art therapy has been used in patients affected by dementia, post-traumatic stress disorder, chronic anxiety, major depression and other neuropsychiatric conditions, leading to improvement of physical, mental, and emotional wellbeing, only anecdotal and uncontrolled studies have reported benefit in patients with PD [7]. While intriguing, the putative mechanisms that underpin such improvements remain undetermined. Recent studies suggest that artistic activities depend on neural functions related to attention, creativity, abstraction, symbolic language, and associative ideation [8]. In particular, the process of visual art making relies on several aspects of visual function, such as visual perception, processing, imagery, and recognition [8,9]. Here, we aim to determine whether proctored art therapy induces a neural re-organization of visual-related networks with effects on visual exploration and therefore perception. In addition, we hypothesized that the effect of art therapy in the visual domain may extend more broadly, including motor function and clinical symptoms.

2. Subjects/materials and methods

2.1. Study design and participants

The was an open-label, prospective, exploratory trial to determine the effects of art therapy in PD patients (clinicalTrial.gov identifier: NCT03178786). The study was conducted at the Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, NYU Langone Health, New York, and at the NYU Steinhardt School. We recruited 18 PD patients (mean age ± SD: 68.4 ± 6) and 14 age-matched controls (mean age of 66.1 ± 11.7). The diagnosis of PD was based on published criteria [3]. Inclusion criteria for PD patients included: a) Hoehn and Yahr stage 2–3 in the ON state; b) Beck Depression Inventory II (BDI-II) < 20; c) Montreal Cognitive Assessment (MoCA) > 22. Dopaminergic regimen was kept unchanged throughout the duration of study. Patients were assessed during the ON state for all study evaluations. The control group of age-matched subjects without neurological or psychiatric disorders was tested to provide normative ranges for the ocular motor and fMRI analyses. This group did not undergo art therapy intervention. Two control subjects and two PD patients did not complete the fMRI studies. One patient with PD withdrew from the study because of cataract surgery, unrelated to the study. The study protocol was approved by the Institutional Review Board of NYU School of Medicine. All participants provided written informed consent.

2.2. Art therapy intervention

The experimental protocol was previously published [10]. Briefly, the art therapy intervention consisted of twenty sessions lasting approximately 90 min each, twice a week, for ten consecutive weeks. Sessions took place at the NYU Steinhardt Department of Arts and Art Professions. Patients were divided in groups of eight and ten participants respectively, allowing for each group to be followed by three credentialed art therapists, thus resulting on an average therapist/client ratio of approximately 1:3. For each patient, the art therapists developed a tailored study plan, while encouraging the expression of emotional and artistic connotations. Adjustments were made across sessions, based on patients' responses. Nine different art projects were administered, with a new project introduced every two sessions. These projects were designed to meet the physical limitations of PD patients and to improve potentially dysfunctional visuospatial functions. Art therapy involved exposure to a broad range of visual art forms and techniques. The intervention included basic elements of clay manipulation, painting on canvas, collage, drawing, as well as more advanced figurative arts techniques such as murals. All participants were asked to complete the same art therapy projects, but the level of technical engagement was tailored based on the therapists' guidance and the ability and experience of the patients. Art activities were mostly individual, with a group project in the last two sessions. Art therapy was preferred over other forms of visual rehabilitation, as it has a high compliance and retention, and it is appealing to most patients.

2.3. Clinical assessments

Clinical assessment included: all sections of the MDS UPDRS [11]; the Timed Up and Go Test (TUG) [12] during regular walking, with serial subtractions, and during a quick walk; the Pegboard Test with both the dominant and non-dominant hand [13]. All subjects also underwent MoCA [14] and BDI-II [15]. Clinical evaluations were performed by two neurologists specialized in movement disorders (A.C. and M.B.). Subjects with PD were evaluated by the same rater pre- and post-intervention in order to minimize inter-rater variability. Assessors did not take part in the art therapy process and were unaware of the individualized plan of treatment developed by the art therapist for each subject. The following scales were administered exclusively to patients: the Modified Fatigue Impact Scale (MFIS) [16]; the Scale for the Assessment of Positive Symptoms in PD (SAPS-PD) [17]; the PROMIS Self-Efficacy Questionnaire for Chronic Conditions [18]; the PD Questionnaire (PDQ-39) to assess the overall impact of the disease on daily quality of life [19].

2.4. Visuospatial assessments

Three tests, Navon Test, Visual Search and Simple Visual-Motor Reaction Time (PsyToolkit Software Tools, https://www.psytoolkit.org/), were administered to test visual discrimination and reaction time; subjects were comfortably seated on a chair 50 cm from a computer screen with a keyboard in front of them in a well-lit and quiet environment. After a few practice trials for familiarization, subjects were encouraged to perform the tasks to the best of their capabilities. Subjects' gaze was recorded during the Benton Visual Recognition Test (BVRT) [20] with a head-mounted, infrared eye-tracking device (500 Hz sampling rate, 0.5° spatial accuracy, Eyelink 2, SR Research, Ontario Canada). After calibration, on a 27.0″ Dell LED monitor, we display first, the digitized BVRT. For eye tracking analyses, raw eye position traces were initially median-filtered to remove speckle noise, and blinks were removed from all traces. After this initial pre-processing stage, an adaptive algorithm following Nystrom [21] was used to detect the timing and positions of saccades and fixations. Saccadic detection enables the analysis of the spatial scatter of fixations as well as the rate of saccades performed during BVRT. Exploration path lengths (overall distance traveled by gaze during the test) as well as horizontal fixation variance (average spread of fixation position across all fixations) were measured. Subjects were also asked to perform the Rey-Osterrieth Complex Figure Test (RCFT) to the best of their ability; two investigators (A.C. and D.M.) independently rated all the RCFT drawings; in addition, 10% of the drawings were inspected by a third rater (H. B.). Since both BVRT and RCFT were not administered according to their standardized procedures, only raw scores are being reported. Of the 14

controls, two were unable to maintain head stability per instructions during the eye tracking and were not considered for analysis, leaving 12 controls. Of the 18 PD, 14 presented for visuospatial assessments; during examinations, four were not considered for analysis due to either dyskinesias or somnolence, leaving 10 patients.

2.5. MRI acquisition

MRI brain scans were acquired at the Center for Biomedical Imaging, NYU Langone Health, with a 3 T MR scanner with 32-channels phased-array head coil (Prisma, Siemens Healthineers). The MRI protocol included: a high resolution 3D T1-weighted magnetization-prepared 180° radio-frequency pulses and rapid gradient-echo (MP RAGE) (TR/TE/TI = 11.56/5.048/500 ms; FA = 8°, voxel size = 1 × 1 × 1 mm^3), axial T2-weighted (TR/TE = 6000/109 ms; FA = 150°; voxel size = 0.6 × 0.66 × 5 mm^3), and 400 vol eyes-closed resting-state fMRI datasets using single-shot echo-planar imaging (EPI) sequence (TR/TE = 854/37 ms; FA = 52°, voxel size = 2 × 2 × 2 mm^3). PD patients underwent MRI during the ON therapeutic state.

2.6. MR image processing

Rs-fMRI datasets were pre-processed using SPM12 (https://www.fil.ion.ucl.ac.uk/spm/) with the following steps: slice time correction, re-alignment to the first volume image in order to correct for head movement, normalization to MNI using the parameters obtained during the segmentation procedure, and smoothing using an 8 mm FWHM kernel. The de-noising and filtering of pre-processed rs-fMRI data sets were then processed with CONN (v.17) toolbox (McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge; https://web.conn-toolbox.org/), where temporal de-spiking, band-pass filtering (0.08 Hz–0.1 Hz), as well as scrubbing of physiological noise and subject-movement effects were performed. Independent component analysis (ICA) was performed based on datasets of all participants. Networks of interest (NOIs) were obtained by back-reconstruction and converted into calibrated z-maps. The following NOIs were identified based on ICA: dorsal attention network (DAN), executive control network (ECN), frontal-occipital network (FOC), salience network (SAL), primary visual network (V1), and secondary visual network (V2).

2.7. Statistics

2.7.1. Visuospatial and clinical tests

Statistical analyses were performed using SPSS statistical software (version 25; SPSS, Inc., Chicago, IL). Data were normally distributed, as assessed with normality tests (Shapiro-Wilk test). We used two-tailed T-tests for unequal variance to compare patients with PD and Controls. To assess the outcomes of art therapy in patients with PD, paired t-tests were used for normally distributed variables. The threshold for statistical significance was set at $\alpha = 0.05$.

2.7.2. Resting state functional connectivity

Second level analysis of the MRI data was performed using SPM12. Two-sample T-test was conducted to assess between-group differences in FC within the NOIs at baseline between HCs and PD. The following contrasts were of interest: Controls > PD; Controls < PD. Age and gender were entered as covariates in the design metrics. In order to assess the overtime changes in FC following AT intervention in the PD group, a repeated-measures T-test was carried out. Significance threshold for all between-groups statistical comparisons of interest was set to $p < 0.001$, corrected for cluster size based on AlphaSim calculation (clusters with size > 50).

2.7.3. Correlation analyses

Partial correlations were performed, with age and gender as covariates, between clinical, visuospatial and FC outcomes in both PD and control groups together, and in each group separately (PD-baseline, PD-follow-up, and controls). A bivariate regression model was applied to account for age and gender variability. Variables showing a Pearson coefficient $\geq \pm 0.75$ were considered strongly correlated [22].

3. Results

3.1. Visuospatial and clinical outcomes

The characteristics in terms of age, gender, education, cognition, and depression scores were similar in the patient group at baseline and the control group (Table 1). Differences between the two groups at baseline were mostly in visual tests. RCFT performance indices were worse in patients with PD (N = 14) than in controls (N = 11; independent two-sample *t*-test: t (24) = 1.853; p = 0.0383), and errors during the Navon Test were greater in patients (N = 7) than in controls (N = 6; t (11) = 2.734; p = 0.019). Similarly, we found that during BVRT, exploration path lengths were longer and horizontal fixation variance was greater in patients than in controls (Figs. 1 and 2).

After the twenty sessions of art therapy in patients with PD, the most striking findings were decreases in visual exploration path length, horizontal fixation variance, and in the number of saccades made during the BVRT (Fig. 2). The PD group initially showed a larger number of saccades (25.0 ± 1.1) relative to controls (20.6; ± 0.9, two-tailed unpaired *t*-test: t (20) = 3.35; p = 0.0016) that decreased after art therapy (19.9 ± 1.0, two-tailed paired T-test: t (9) = 14.8; p = 6.2e-08) reaching the controls' levels. Similarly, before art therapy, saccadic path lengths were larger in PD (2511 ± 140) compared to controls (1817 ± 117, t (20) = 4.06; p = 0.00030) and decreased after the intervention (1621 ± 113; t (9) = 20.9; p = 3.1e-09) to the controls' levels. Although slightly higher, the saccade spatial variance in the PD group at baseline (7.0 ± 0.21) showed only a trend toward significance when compared to the controls' values (6.6 ± 0.20; t (20) = 1.4; p = 0.085). Nevertheless, it significantly decreased post art-therapy (6.8 ± 0.25; t (9) = 2.5; p = 0.017).

The outcomes of other visuospatial tests and clinical scales in PD also improved following art therapy (Fig. 3). Briefly, the Navon test errors were lower than baseline although not significantly so (two-tailed paired samples *t*-test: t (10) = −1.185; p = 0.289). However, the number of errors for patients with PD after art therapy did not differ from those of control subjects (one-tailed independent samples *t*-test with unequal variance: t (10) = 1.601; p-value = 0.138). Similarly, after the treatment, RCFT mean values in PD group improved (two tailed paired samples *t*-test: t (13) = 2.0295, p = 0.0634), reaching the range of the controls' (one-tailed independent samples *t*-test: t (23.5) = -0.387, p = 0.703). In addition, we found significant decreases of the scores of both UPDRS-III (two-tailed paired samples *t*-test: t (13) = - 6.16; p = 0.0063) and total UPDRS t (13) = -6.93; p = 0.0368). We did not find any effect of art therapy for all the other outcome measures. The main changes observed on visuospatial and clinical outcomes following art therapy are also summarized in Supplemental table 1 (see: supplemental materials).

Table 1
Demographics and main characteristics of study population.

	PD Group	HC Group	P value
Age, mean (SD)	68.4 (6.0)	66.1 (11.7)	0,55*
Sex, F:M	10:5	9:3	0.96**
Years of Education, mean (SD)	16.9 (2.7)	16.2 (4.0)	0,59*
MOCA, mean (SD)	27.2 (1.5)	26.2 (2.9)	0,27*
BDI-II, mean (SD)	7.6 (4.4)	3.8 (4.8)	0,52*
Disease Duration, mean (SD)	6.2 (4.6)	n/a	n/a
Hoehn and Yahr, mean (SD)	2.3 (0.5)	n/a	n/a
LEDD, mean (SD)	501.9 (369.1)	n/a	n/a

Abbreviations: PD, Parkinson's disease; HC, Healthy Controls; LEDD, Levodopa Equivalent Daily Dose; MOCA, Montreal Cognitive Assessment; UPDRS, BDI-11, Beck Depression Inventory-II; *By 2-tailed *t*-test; ** By $\chi 2$ test with Yates correction.

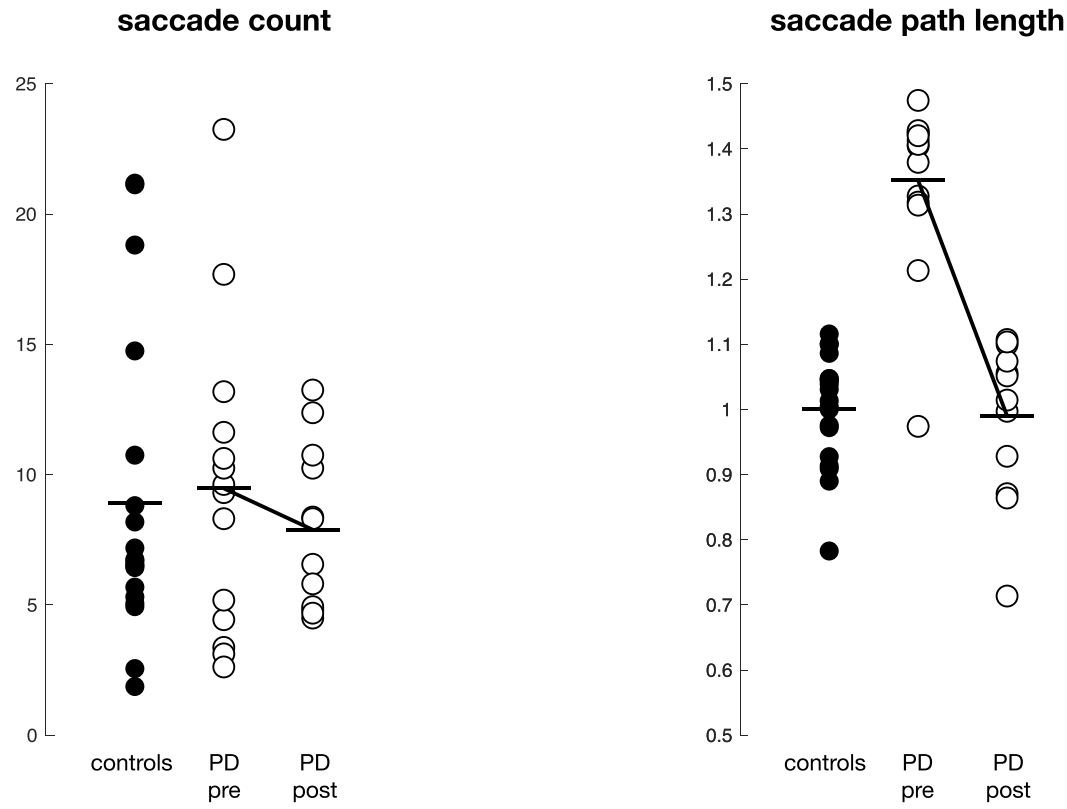

Fig. 1. Visual Exploration Patterns on BVRT

3.2. Resting state functional connectivity

At baseline, FC values of patients with PD before art therapy were significantly greater than those of controls within the DAN, ECN, FOC, V1, and SAL ($p < 0.001$, adjusted for cluster size, Fig. 4). Specifically, the areas with greater FC levels were: the right inferior frontal gyrus, left middle frontal gyrus, and right inferior parietal lobule in the DAN; the left fusiform gyrus, posterior cingulate cortex, and left superior temporal gyrus in the ECN; in the right inferior frontal gyrus within the SAL network; and the left middle occipital gyrus in V1. Interestingly, performances on MoCA in the combined patient and control group showed correlations with FC in multiple regions included in the DAN, FOC and ECN, in that the greater the MoCA score the higher was the FC. In the control group, the number of errors during Navon Test positively correlated with FC in left and right cuneus within the FOC. In the PD group at baseline, performance in TUG while performing serial subtractions positively correlated with FC in the left inferior frontal gyrus within the ECN.

Following art therapy in patients with PD, we found increases of FC in regions within the V1 and V2 networks: left paracentral lobule within V1 ($p < 0.001$, adjusted for cluster size); the left middle temporal gyrus in V2 ($p < 0.001$, adjusted for cluster size). Increased FC was also found in the right superior frontal gyrus and left lenticular nucleus (Fig. 4).

4. Discussion

The main result of this study is that art therapy in patients with PD ameliorated visual exploration and visuospatial dysfunction, as measured by significant changes in fMRI visual connectivity networks and in some measures of the eye-tracking tests, while also improving motor function as measured by the UPDRS part III. Patients with PD may experience a wide array of visual disturbances at different disease stages, and among these, visual exploration and visuospatial abnormalities may have important implications in visuomotor integration. Prior investigations have reported abnormal patterns of visual exploration with smaller saccades, mainly resulting in restricted ocular scanning [23]. Our results further suggest the overarching pre-therapy strategy for visual exploration in PD was inefficient, since it appears that the generation of additional saccades with an overall longer path length was necessary to complete the BVRT. Patients with PD may also exhibit impaired performance on tasks relying on visuospatial processing, inclusive of pattern recognition, mental rotation, and figure ground segregation [24,25]. Our study demonstrated impaired function on RFCT and increased errors on the Navon Test, confirming impairments in visual constructional ability in patients with PD.

Following art therapy treatment, patients improved their visual exploration patterns and values approached the levels of the control group, suggesting that art-based visual training can lead to the use of more efficient visual exploration strategies. Improvements were also found in higher-order visual processing, as indicated by the results of the Navon Test and RCFT without changes in simple visual-motor reaction tasks. In fact, the Navon Test assesses the allocation of attentional resources during the processing of visual information with neural correlates that include extrastriate visual areas [26]. Overall, our findings suggest that art therapy may enhance visuoperceptual skills in patients with PD, in agreement with previous results in healthy subjects [8]. Indeed, the process of making visual art involves visuo-spatial abilities and thus, the engagement of diffuse anatomic and functional networks that support contrast coding, depth perception, visual transience, organization of 3-D texture, spatial reasoning and other functions. The extended recruitment of these networks may partly explain the specific benefits on visuo-spatial exploration. Future studies in which PD subjects are randomly assigned to art therapy versus another structured regular activity will help to determine if the potential benefits of art therapy are specific to this intervention.

In parallel to the behavioral results, the imaging results showed

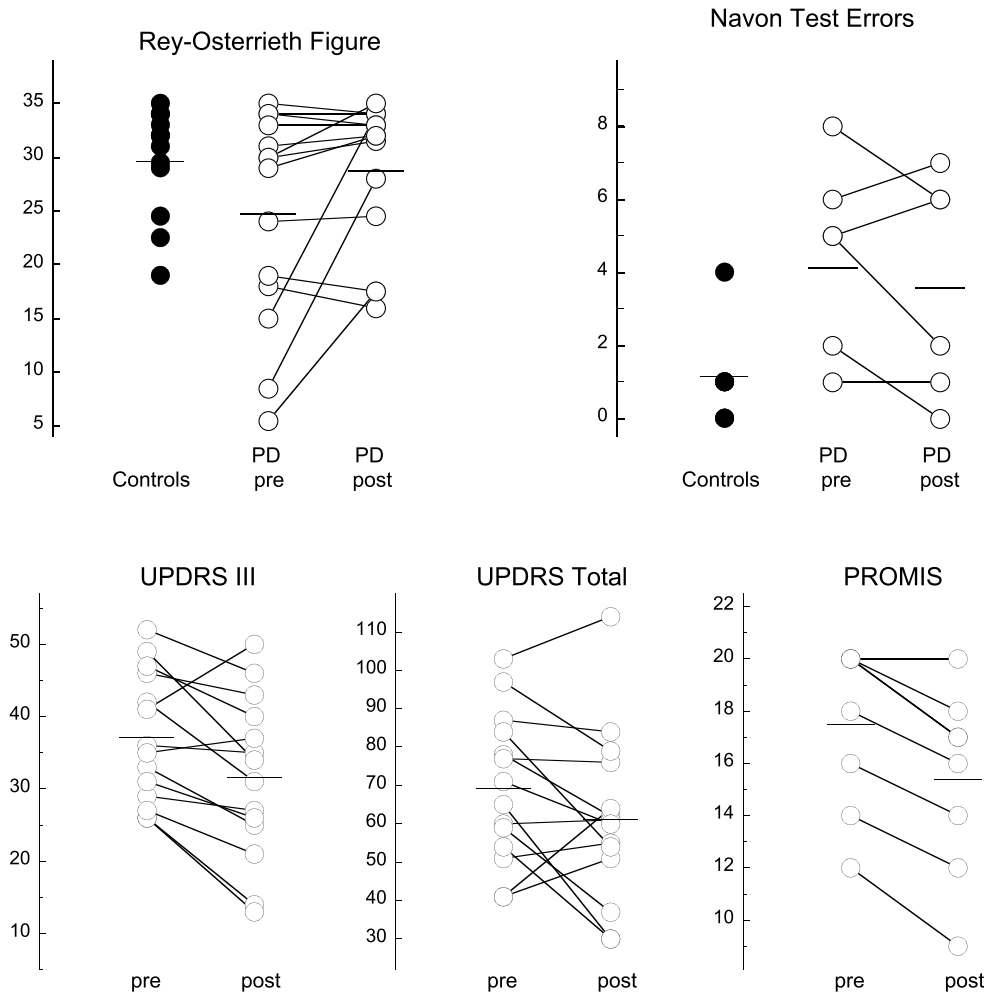

Fig. 2. Visuospatial and clinical outcomes.

stronger FC at baseline in patients with PD within the DAN and the ECN, networks involved in goal-directed action during attentional tasks. Stronger connectivity in areas involved in attention and working memory has been found during resting-state in PD [27,28], a finding that can be interpreted as a compensation mechanism, particularly relevant in that concordance was noted between performance and symptoms scores. Indeed, we found that FC values in those areas were correlated with scores of MoCA and TUG while performing serial subtractions, tasks requiring attentional and cognitive engagement. Following art therapy, we found an increase of FC within the visual networks that could be interpreted as a functional reorganization involved in the perceptual processing of afferent visual information. It is possible that this reorganization has been induced by visuospatial practice during the art therapy sessions and is the basis of the performance improvements in the visual exploration task.

Finally, our results show that art therapy also had positive effects on motor function performance, in agreement with a few exploratory studies in geriatric populations [7,29]. Beside a potential placebo effect, it is plausible that visual abnormalities may impact a broad range of motor and non-motor behaviors, including perception of extrapersonal space and gait function. Whether the small effect on motor function is clinically meaningful will need to be determined in future studies.

We acknowledge that there are some limitations that are inherent to the exploratory nature of this study. These include the lack of an intervention control group and long-term follow-up. The art therapy intervention, although structured and standardized in its application, had to be adapted to individual patients, with some variability in its practical application to individual subjects. Also, this study did not assess a dose-dependency for the observed effects. Indeed, longer and/or more intense treatments could have resulted in better and/or more sustained benefits, although the high prevalence of fatigue, sensory discomfort, and motor disability in PD patients may challenge tolerability and adherence over time. Another limitation is about the eye movement study: the high sensitivity of the eye tracking device to motion limited the data sample as the high occurrence of involuntary movements in a number of these patients created data fidelity constraints. Indeed, these results need to be confirmed in a larger population with the use of technology that allows for the elimination of artifacts induced by head and neck motion mostly occurring during the ON-state. In addition, future studies will include assessments in the OFF state, potentially removing this confound. Finally, the lack of assessments blinding could have biased the clinical scores, leading to overestimation of the effects. Indeed, these results are promising but they need to be confirmed by future studies with larger number of subjects, appropriate control groups and with examiners blind to participant status.

In summary, we found that art therapy in mild to moderately impaired PD patients produced significant improvements in visuospatial skills, visual exploration strategies, and motor function. These improvements were accompanied by changes in FC highlighting a

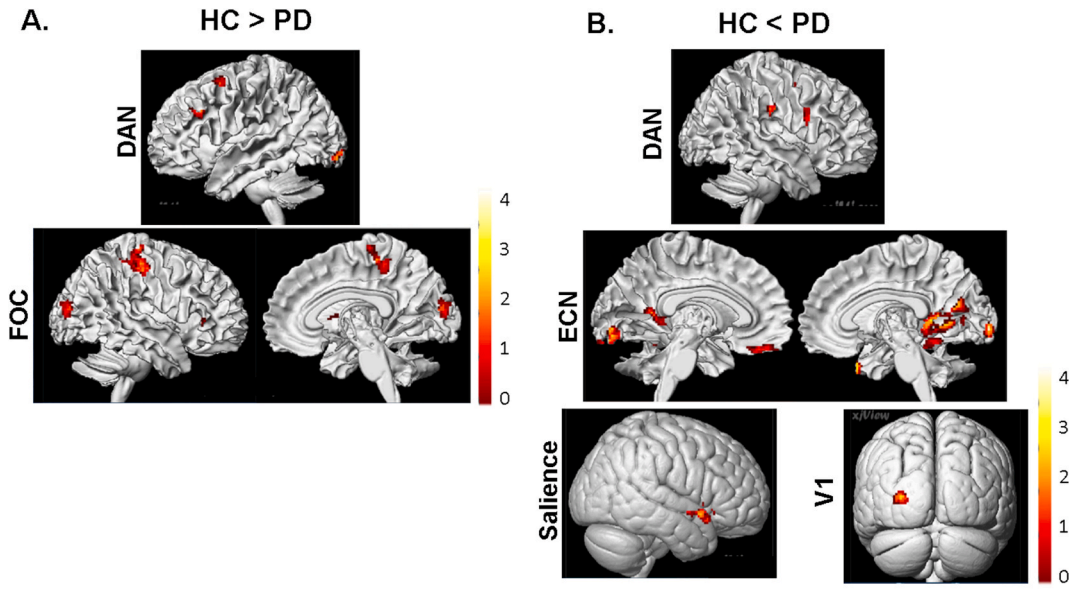

Fig. 3. Between group differences in functional connectivity levels.

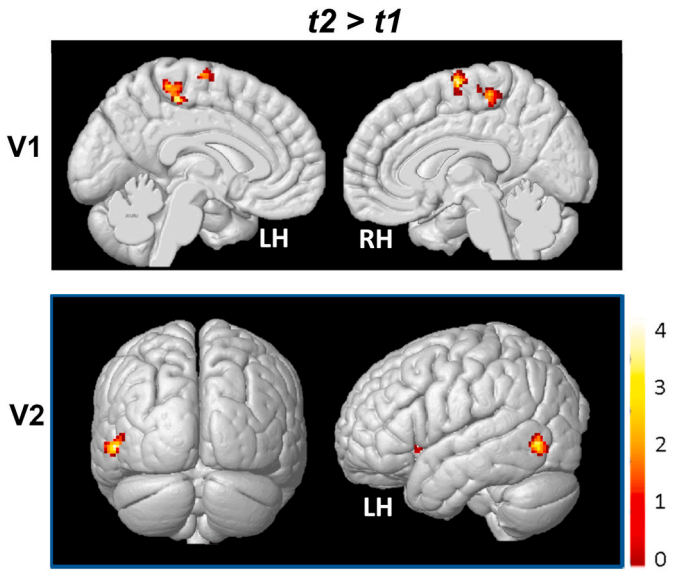

Fig. 4. Overtime changes in functional connectivity levels after art therapy.

functional reorganization of primary and associative visual networks, suggesting that art therapy could be an appealing adjuvant to current pharmacological treatment. Further studies are needed to corroborate these preliminary findings, and to verify the precise mechanisms of such improvements.

Author contribution statement

Alberto Cucca: Organization of Research Project; Execution of Research Project; Design and Execution of Data Analysis; Writing of the first manuscript draft. Alessandro Di Rocco: Conception of the Research Project; Study design; Review and Critique.

Ikuko Acosta: Design, organization and execution of Art Therapy; Review and Critique.

Mahya Beheshti: Execution of Research Project; Review and Critique.

Marygrace Berberian: Design, organization and execution of Art Therapy; Review and Critique.

Hilary C. Bertisch: Execution of Research Project; Review and Critique.

Amgad Droby: rs-fMRI Data Analysis; Review and Critique. Tom Ettinger: Director, art therapy assessment; author, House-Tree-Person Parkinson's Disease Rating Scale.

Todd E. Hudson: Execution of Research Project; Review and Critique.

Matilde Inglese: Design of rs-fMRI Protocol and rs-fMRI data analysis; Review and Critique.

Yoon J. Jung: Execution of Research Project; Review and Critique.

Daniella Mania: Execution of Research Project; Review and Critique. Angelo Quartarone: Conception of Research Project, Study design; Execution of Research Project; Review and Critique.

John-Ross Rizzo: Conception of Research Project; Execution of Research Project; Review and Critique.

Kush Sharma: Execution of Research Project; Review and Critique.

Andrew Feigin: Organization of Research Project; Execution of Research Project; Review and Critique.

M. Felice Ghilardi: Conception of Research Project, Study design; Review and Critique.

Milton C. Biagioni: Organization of Research project; Execution of research Project; Design and Execution of Data Analysis; Review and Critique.

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Declaration of competing interest

None to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2021.01.013.

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