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Preliminary evidence from a Line-Bisection Task for visuospatial neglect in Parkinson's disease

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Dears Sirs,

Neurodegenerative diseases cause atrophy in several brain networks, affecting visuo-spatial cognition [1]. Nonetheless, this kind of impairment is sometimes not assessed by standard clinical evaluation. Visuospatial dysfunctions negatively impact everyday functioning in Parkinson's disease [PD].

It has been shown that in more than half of the patients with PD, the onset of motor symptoms presents primarily or exclusively unilaterally [2], allowing to classify patients with right side onset motor symptoms (RPD) or with left side onset (LPD). Importantly, the unilateral predominance of symptoms may persist throughout the span of the disease progression [3].

Given the hemispheric specialisation of several cognitive functions, we might expect differential effects of the asymmetric basal ganglia (BG) degeneration on visuospatial abilities in PD, similar to other asymmetric diseases such as unilateral stroke. To date, the impairments in orienting of attention in patients with lateralised PD are still under investigation, although visuo-spatial deficits seem to be more prominent in patients whose motor symptoms arise on the left than the right body side [4]. Previous studies [5,6] have shown the hand used to perform the task affected the overall performance in line bisection, and patients with Focal Cervical Dystonia deviated more to the left of true center than healthy participants when using their left hand rather than right one. Since this aspect it has never been investigated in LPD and RPD patients, here we performed a piloting case-controls study (2 vs 10) to test: a) the usefulness of introducing in clinicians' daily routine a Line-Bisection task for the assessment of the visuospatial domain; b) if the hand used to perform the task could affect the performance.

To this aim, two cognitively non-impaired right-handed PD patients, presenting motor fluctuations and dyskinesias, and 10 matched normal controls [NC] were recruited. We excluded patients exhibiting disorders of anterior visual pathways that may confound visuospatial function.

Motor features and disease severity were evaluated in on-/off-

conditions and scored using the revised Italian version of the "Movement Disorder Society - Unified Parkinson's Disease Rating Scale" (MDS-UPDRS) part III and MDS-UPDRS total scores, respectively. Hoehn & Yahr Scale was used to stage the disease. Levodopa equivalent daily dose (LEDD) was calculated for each patient. Last pharmacological administration was performed 3 hours before the experimental session (LPD = 600 mg; RPD = 625 mg). Subjects underwent a neuropsychological-neuropsychiatric assessment, in line with previous studies [7,8].

The PD participants had the datscan altered predominantly to the right/left and contralateral asymmetry of motor symptoms [1 LPD: male, 66 years, on UPDRS-III = 4, on Hoehn & Yahr = 2, LEDD mg = 937.5; 1 RPD: female, 60 years, on UPDRS-III = 4, on Hoehn & Yahr = 2.5, LEDD mg = 625]. Both the PD patients exhibited a normal global cognitive profile [1 LPD: Mini-mental State Examination = 30, Frontal Assessment Battery = 15; 1 RPD: Mini-mental State Examination = 29, Frontal Assessment Battery = 15]. The neuropsychiatric assessment revealed no behavioral alterations [1 LPD: Beck Depression Inventory = 9, Beck Anxiety Inventory = 19; 1 RPD: Beck Depression Inventory = 4, Beck Anxiety Inventory = 5].

Visuospatial attention was assessed using a Line-Bisection Task, in which participants had to bisect 200 mm long and 1 mm thick horizontal black lines, centered on an A4 white sheet of paper [9]. Participants were asked to mark the middle of 40 lines, using their right or left hand. The stimuli were centered on the participants' sagittal midplane, at a distance of approximately 50 cm. Twenty lines were bisected using the right hand and twenty lines using the left hand. The deviation from the lines true center was calculated and errors to the right or to the left of the line's midpoint were measured to the nearest millimeter. Rightward errors were preceded by + and leftward errors by – [6,10]. The patients comparisons were performed with a modified *t*-test for individual scores versus a control sample [11]. The patients signed a written informed consent to participate to the study, which was approved by the Local Ethical Committee.

Patients' and NC's performance on the visuospatial task are reported in Fig. 1.

Both the PD patients produced a significant ($p < 0.001$) greater leftward deviation than controls when the task was performed with the more affected hand (i.e. the right hand for the RPD [mean = -4.60 ± 3.61 ; NC: mean = -0.15 ± 0.68] and the left hand for the LPD [mean = -8.80 ± 4.70 ; NC: mean = -4.24 ± 0.79]). For the other hand condition, results are heterogeneous. The RPD patient produced a significant ($p < 0.001$) greater rightward deviation than controls when performing the task with the left hand (mean = 0.85 ± 3.30 ; NC: mean = -4.24 ± 0.79). Conversely, the LPD patient produced a significant ($p < 0.001$) greater leftward

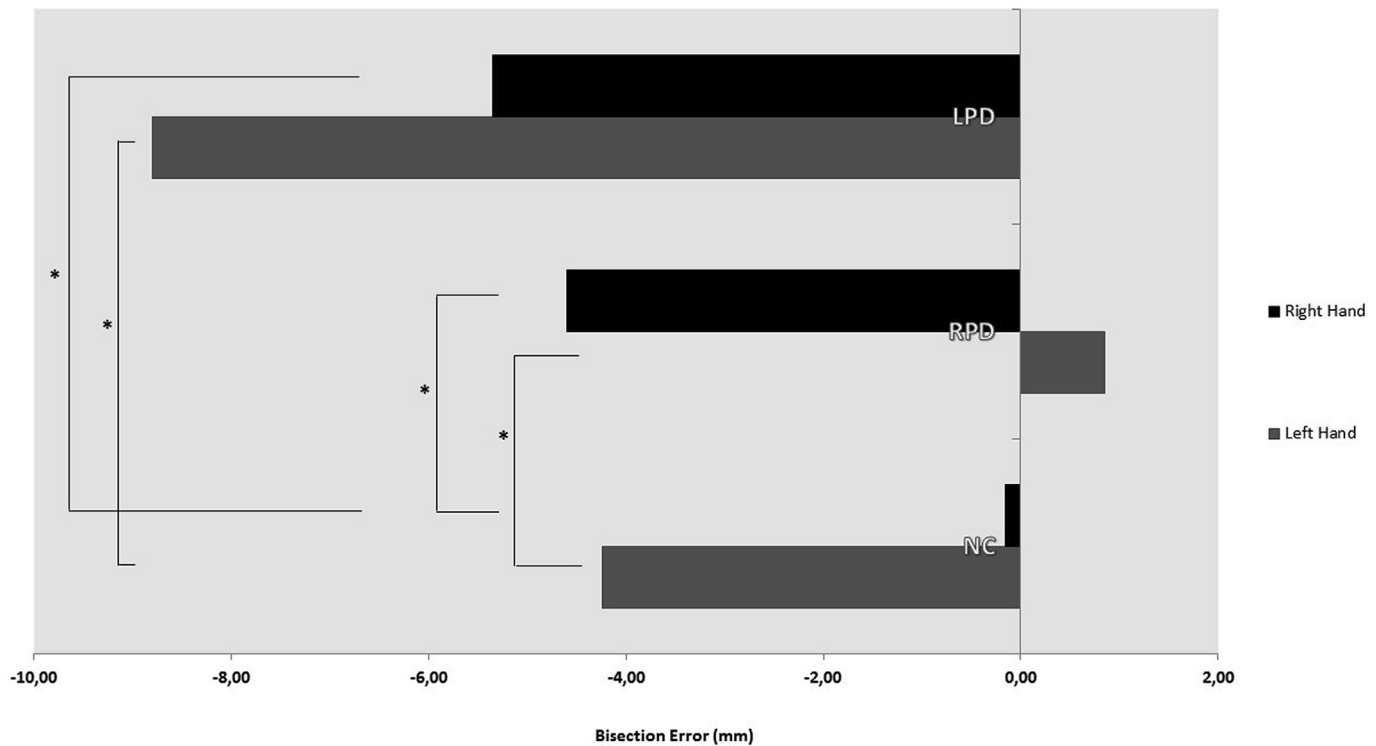


Fig. 1. Mean bisection error for the two patients (LPD, RPD) and for the normal controls (NC). Asterisks indicate significant differences between patients and the control groups. The LPD patient produced a significant greater leftward deviation than controls when the task is performed with the right hand and with the left hand ($p < 0.001$). The RPD patient produced a significant greater leftward deviation than controls when the task is performed with the right hand ($p < 0.001$) and a significant ($p < 0.001$) greater rightward deviation than controls when performing the task with the left hand, according to a modified t -test for individual scores versus a control sample.

deviation than controls when he performed the task with the right hand (mean = -5.35 ± 4.24 ; NC: mean = -0.15 ± 0.68).

At the Line-Bisection Task, healthy participants usually show the phenomenon called “*pseudoneglect*”, i.e. the tendency to bisect horizontal lines toward the left [12]. The hand used to perform manual bisection tasks modulates performance, where use of the left hand leads to greater leftward deviation than those obtained using the right hand [5]. The “*pseudoneglect*” is viewed as reflecting right hemisphere specialization for processing spatial information, resulting in orienting toward the contralateral hemispace [12,13]. This bias is usually reduced in older adults [6,14]. Although previous signs of visuospatial neglect in LPD and RPD patients have been reported [4,15–18], those studies used to not reported information on individual patients with neglect according to standardized “paper-and-pencil” visuospatial tests [4,15–18]. Furthermore, results could derive from the side from which the target line initially appeared [18] or the response modality (verbal versus motor) [4]. Finally, important bias in the evaluation must be considered due to difficulty in correctly use the ICT-IoT devices, such as the PC mouse [4]. Indeed, it could be necessary to improve mouse controlling using adaptive path smoothing technique via B-spline to ensure the correctness of the detected data.

Interestingly, for the left-hand condition, the RPD demonstrated rightward attentional bias, whereas the LPD patient showed the leftward bias, showing that motor/attentional asymmetries could not occur on the same side [19] and that in PD patients the affected hand, rather than other one, when used to perform the task affected the performance differently with respect to healthy subjects. Indeed, the right and the left BG lesions can induce left neglect [20]. In particular, horizontal and vertical orienting of attention can be affected in Parkinson's disease [20]. This suggests that ipsi- and contralateral pathways exist which may predispose

leftward asymmetry independent of the BG side affected [21]. Finally, these data are congruent with research in humans supporting the idea that dopamine plays an important role in spatial orienting [21].

Line-Bisection is an effective task to detect visuospatial disorder in PD. Moreover, it is preparatory to an in-depth neuropsychological evaluation of this cognitive domain that could severely affect patients' daily living.

A major limitation of our study is the small sample size. Therefore, the ability to draw generalizable conclusion is severely hindered by its small sample size. Secondly, standard deviations for line bisections were greater for both people with PD than the control group. This may affect the ability to compare the two individuals with PD to the control group. Future studies are needed to shed light on the neuropsychological mechanisms underlying attentional asymmetry in PD.

Moreover, increased leftward bias during line bisection with the left hand for the individual with left hemibody PD may reflect a type of akinesia or decreased ability to move the left hand in the left hemispace [22]. Specific experiments would be necessary to test this hypothesis.

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