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Floating door sign does not differentiate Parkinson’s disease from essential tremor

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Parkinson’s disease (PD) is known to be associated with micrographia, presented as decreased letter size in written text. A previous reported, potentially important observation suggested that when PD patients are instructed to draw a house, patients undershoot the drawing of the vertical lines of the door of the house and fail to connect the lines with the house floor. This ‘floating door sign’ would be a result of shortened stroke size and hypometric hand movements in PD and, importantly, no similar findings were reported in patients with essential tremor (ET). Thus, the sign could represent a simple qualitative test for PD vs ET differential diagnostics.

In this study, we evaluated the usefulness of the floating door sign as a bedside test in early PD diagnostics compared to ET patients and healthy controls (HC). We advised the subjects (XX PD patients, XX ET patients and XX healthy controls) to draw a house with windows and a door. We then measured the distance between the horizontal floorline of the house to the vertical doorlines.

The results showed that there was no difference in the presence of the floating door sign between PD and ET patients, as 47% of PD patients and 37% of ET patients presented the sign ($p=0.26$). Compared to healthy controls, PD patients showed more floating door sign (PD: 47% vs. HC: 24% $p<0.05$) but there were no differences between ET patients and healthy controls.

In conclusion, the floating door sign does not differentiate PD from ET and is not a valid bedside test for clinicians.

Floating door sign does not differentiate Parkinson's disease from essential tremor

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Abstract

Diagnostic usefulness of the floating door sign was tested in 144 PD patients, 41 essential tremor patients and 38 controls. There were no differences in the presence of floating door sign between PD and ET patients. The sign does not seem to be a reliable differential diagnostic tool.

Main text

Parkinson's disease (PD) is associated with micrographia, as reflected in globally decreasing letter size throughout written text (consistent micrographia), or in gradually decreasing letter size while writing (progressive micrographia). [1] In 2013, Kulkarni et al. [2] reported a potentially important observation related to micrographia in PD. They suggested that when PD patients are instructed to draw a house, patients undershoot the drawing of the vertical lines of the door of the house and fail to connect the lines with the house floor. This 'floating door sign' would be a result of shortened stroke size and hypometric hand movements in PD and, importantly, no similar findings were reported in patients with essential tremor (ET). Thus, the sign could represent a simple qualitative test for PD vs ET differential diagnostics. However, the initial observation by Kulkarni et al. was limited by the sample size (81 PD patients, 19 ET patients) and lack of motor, cognitive or imaging measurements [2]. Here, we aimed to replicate and expand the previous findings with a considerably larger sample size and detailed clinical and imaging characteristics of the patients.

Altogether 144 PD patients, 41 ET patients, and 38 healthy controls were included in this study. The sample was a subsample of a previously described larger cohort [3], involving patients with valid drawing samples. 19.4% of PD patients were de novo levodopa-unmedicated and the remaining patients on levodopa were examined when their motor state was ON or partially ON. On the day of the brain dopamine tranporter (DAT) imaging, each participant was clinically examined 2-4 hours prior to imaging. The examinations included the floating door sign, a clinical interview, the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease

Rating Scale (MDS-UPDRS) part III, the Mini-Mental State Examination (MMSE) and the Beck Depression Inventory (BDI). Symptom severity also in ET patients was evaluated using the MDS-UPDRS, without ET-specific evaluation tools (e.g. TETRAS). Writing and drawing micrographia were also evaluated as described earlier.[3] For the floating door sign, we used the same protocol and cut-offs as in the original study describing the test [2]: subjects were instructed to draw a house with door and windows and the distance between the horizontal floor line and vertical door lines was measured. The test was considered positive if the vertical lines were more than 1 mm apart from the floor line. Groups were compared using one-way ANOVA with Tukey's method for pairwise comparisons, Kruskall-Wallis test with Dunn-Bonferroni method for pairwise comparisons or Chi-Square test as appropriate. P-values were corrected for multiple comparisons. The level of statistical significance was set at corrected $p<0.05$. The study was approved by the local ethics committee and the participants gave their informed consent.

The results showed that there was no difference in the presence of the floating door sign between PD and ET patients (Table 1), as 47% of PD patients and 37% of ET patients presented the sign ($p=0.26$). Compared to healthy controls, PD patients showed more floating door sign (PD: 47% vs. HC: 24% $p<0.05$) but there were no differences between ET patients and healthy controls. There were no differences between floating door sign positive (n=67) and negative (n=77) PD patients in consistent (Median [IQR] area of handwriting sample: 3.7 [2.9] cm^2 vs 4.1 [3.1] cm^2, $p=0.12$) or progressive micrographia (mean [SD] β-value of regression line: -0.15 [0.22] vs -0.13 [0.20], $p=0.72$). MDS-UPDRS motor scores were higher in PD patients who had the floating door sign as compared to those who did not (mean

[SD] = 38.9 [13.3] vs. 33.6 [15.9], p=0.03), but motor scores did not differ between ET patients with and without the sign (p=0.56).

Our results demonstrate that the floating door sign is a prevalent finding in both PD and ET patients and thus it does not represent a diagnostically useful specific marker for PD. The differential diagnosis between tremor-dominant PD and ET can be potentially challenging at early stages. Therefore, a simple bedside clinical test, such as the floating door sign, would have been a useful addition to the current diagnostic battery of tests. However, we revisited this issue and combined a large sample size with other clinical tests and brain functional dopamine transporter (DAT) imaging to verify the clinical PD and ET diagnoses. The results show that 1) the floating door sign is common in both PD and ET and 2) the sign is not related to PD micrographia. Micrographia, as evaluated using simple writing samples, may be more useful in a clinical setting as it may show diagnostic value in early and cognitively normal tremulous patients [3], particularly if combined with digital tablet technology and kinematic analyses [4]. Other paper and pen drawing tasks, such as Archimedes spiral and line drawing, may also provide better objective evidence of abnormal neurological function and aid differential diagnosis oftremor syndromes [5].

Author contribution

VR: data management, statistical analysis and drafting manuscript. ME: data collection, data management, manuscript revision and editing, SN, EJ: data collection, data management, manuscript revision and editing, EM: data collection, data management, manuscript revision and editing ,KM: data collection and

manuscript revision, TN, RL, TM: data collection and manuscript revision, JJ, FS: data collection and manuscript revision. VK: study concept design, data collection, statistical analysis and drafting manuscript. All authors critically revised the manuscript and approved the final version of the manuscript.

Declaration of competing interest

None.

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Table 1. Demographic and clinical characteristics of studied subjects. Values are mean (SD), median [IQR] or n.

	PD	**ET**	**HC**	**p-value**[1]	**p-value**[2] PD vs ET	**p-value**[2] PD vs HC	**p-value**[2] ET vs HC
n	144	41	38	-	-	-	-
Age, years	64.6 (10.2)	64.4 (10.2)	67.0 (9.2)	0.39	ns	ns	ns
Sex, male/female	71/73	19/22	19/19	0.93	ns	ns	ns
MMSE	28.0 [3.0]	28.0 [3.0]	28.0 [2.0]	0.19	ns	ns	ns
BDI	5.3 [7.0]	6.6 [9.2]	1.0 [6.0]	<0.001	ns	***	***
LEDD, mg	0.00 [100]	0.00 [0.0]	0.00 [0.0]	<0.001	**	***	ns
Levodopa, yes/no	28/116 (19%)	1/40 (2%)	0/38 (0%)	<0.001	**	**	ns
MDS-UPDRS III motor score	34.0 [21.3]	34.0 [21.0]	5.5 [7.3]	<0.001	ns	***	***
Mean striatum DAT SBR	1.58 (0.53)	2.99 (0.61)	2.41 (0.32)	<0.001	***	***	ns
Drawing micrographia, cm^2	23.0 [25.4]	27.1 [23.6]	25.8 [28.0]	0.457	ns	ns	ns
Writing micrographia (consistent), cm^2	3.98 [3.0]	5.36 [3.9]	5.48 [2.9]	<0.001	***	**	ns
Writing micrographia (progressive), β-value	-0.14 [0.25]	-0.06 [0.17]	-0.06 [0.32]	0.01	*	ns	ns
Floating door, yes/no	67/77 (47%)	15/26 (37%)	9/29 (24%)	0.03	ns	*	ns

[1] One-way ANOVA with Tukey's method for pairwise comparisons, Kruskall-Wallis with Dunn-Bonferroni method for pairwise comparisons or Chi-Square test as appropriate
[2] P-values after correction for multiple comparisons. ***p<0.001, **p<0.01, *p<0.05
PD = Parkinson disease, ET = Essential tremor, HC = Healthy control, SBR = specific binding ratio ([region/reference]-1), ns = non-significant
MMSE = Mini-mental state examination score, BDI = BDI questionnaire score, LEDD = levodopa equivalent daily dose, UPDRS = Unified Parkinson's Disease Rating Scale, SBR = specific binding ratio