

Digitalized spiral drawing in Parkinson's disease: A tool for evaluating beyond the written trace

Jérémy Danna, Jean-Luc Velay, Alexandre Eusebio, Lauriane Véron-Delor, Tatiana Witjas, Jean-Philippe Azulay, Serge Pinto

▶ **To cite this version:**

Jérémy Danna, Jean-Luc Velay, Alexandre Eusebio, Lauriane Véron-Delor, Tatiana Witjas, et al.. Digitalized spiral drawing in Parkinson's disease: A tool for evaluating beyond the written trace. Human Movement Science, 2019, 65, pp.80-88. 10.1016/j.humov.2018.08.003 . hal-01862959

HAL Id: hal-01862959
https://hal.science/hal-01862959

Submitted on 10 Apr 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Full Length Article

Digitalized spiral drawing in Parkinson's disease: A tool for evaluating beyond the written trace

Jérémy Danna[a,*], Jean-Luc Velay[a], Alexandre Eusebio[b,c], Lauriane Véron-Delor[a,d], Tatiana Witjas[b,c], Jean-Philippe Azulay[a,b], Serge Pinto[d]

[a] Aix-Marseille Univ, CNRS, LNC, UMR 7291, FR 3C 3512, Marseille, France
[b] Department of Neurology and Movement Disorders, APHM Timone University Hospital, France
[c] Aix-Marseille Univ, CNRS, INT, UMR 7289, Marseille, France
[d] Aix-Marseille Univ, CNRS, LPL, UMR 7309, Aix-en-Provence, France

ARTICLE INFO

Keywords:
Parkinson's disease
Motor assessment
Graphonomics
Digitizer

ABSTRACT

One of the current scientific challenges is to propose novel tools and tasks designed to identify new motor biomarkers in Parkinson's disease (PD). Among these, a focus has placed on drawing tasks. Independently from clinical ratings, this study aimed to evaluate the pen movement and holding in digitalized spiral drawing in individuals with PD without and with medical treatment and in healthy controls. A three-step data-driven analysis was conducted. First, the effects of spatial and temporal constraints on several variables were determined. Second, the relationship between handedness and dominance of PD symptoms was investigated for the most relevant variables. Finally, a third analysis was conducted to assess the occurrence of changes associated with PD. The first analysis revealed that the number of velocity peaks and pen altitude variations were the most relevant variables in spiral drawing for evaluating the effect of the disease and medication. The second analysis revealed that the effect of medication was present for the movement fluency only, when spirals with spatial constraints were produced at a spontaneous speed by the hand on the side of dominant PD signs. Finally, the third analysis showed that the effect of medication was greater at the beginning of drawing than at the end. Digitalized spiral drawing makes it possible to observe precisely when the kinematic changes related to the disease occur during the task. Such a simple and quick task might be of great relevance to contribute to the diagnosis and follow-up of PD.

1. Introduction

The diagnosis and follow-up of Parkinson's disease (PD) are very often based on a clinical-motor assessment of tremor at rest, rigidity, akinesia (or bradykinesia) and postural instability (Jankovic, 2008). Proposing novel tools and tasks in order to improve motor evaluation and to identify new motor biomarkers is one of the challenges facing scientists (Wu, Le, & Jankovic, 2011). Among these biomarkers, increasing attention is being paid to handwriting and drawing tasks (Ponsen, Daffertshofer,

* Corresponding author at: CNRS/Aix-Marseille Université, Laboratoire de Neurosciences Cognitives, LNC, UMR 7291, FR 3C 3512, 3 place Victor Hugo, 13331 Marseille cedex 3, France.
E-mail address: Jeremy.danna@univ-amu.fr (J. Danna).

Wolters, Beek, & Berendse, 2008; Rosenblum, Samuel, Zlotnik, Erikh, & Schlesinger, 2013; Sadikov et al., 2017; San Luciano et al., 2016; Saunders-Pullman et al., 2008; Stanley et al., 2010; Westin et al., 2010). Moving a pen requires a fine distal motor ability with a strong accuracy constraint. Interestingly, handwriting deterioration seems to be one of the earliest neurobehavioral biomarkers of PD (Sharma et al., 2013): micrographia, a specific abnormal reduction in writing size, is one of the first signs that may alert the patient (McLennan, Tyler, Schwab, & Nakano, 1972). Handwriting in PD is assessed routinely via the Unified Parkinson's Disease Rating Scale (UPDRS; part 1, item 8 – Fahn, Elton, & UPDRS Development Committee, 1987). However, it is not directly and systematically evaluated by the neurologist, who can, at best, check the written trace on paper to objectify micrographia.

Thanks to the development of graphic tablets and advanced techniques for the assessment of pen movements, it has been reported that beyond the written trace, kinematic aspects of movements (including speed, acceleration, force amplitude and stroke duration) are affected in PD (Longstaff et al., 2003; Teulings & Stelmach, 1991; Tucha et al., 2006; Van Gemmert, Adler, & Stelmach, 2003). Consequently, several kinematic variables have been made available to better investigate the behavioral manifestation of the redefined *PD dysgraphia*, a new term that encompasses the whole spectrum of disorders that affect the writing of PD patients (Letanneux, Danna, Velay, Viallet, & Pinto, 2014; Pinto & Velay, 2015). The main issue is that handwriting involves linguistic processes that can be influenced in PD by cognitive impairments, and in general by sociocultural factors, contrary to drawing tasks that involve exclusively sensorimotor processes. A drawing task, validated and standardized by the international scientific and medical communities, is of great importance in order to assess and manage the motor control of both hands related to PD. Even if the relevance of drawing must be confirmed compared to handwriting (Drótar et al., 2016), the Archimedean spiral drawing is the most well-known and widely used task for evaluating fine motor performance in various movement disorders, including Essential Tremor (Fahn, Tolosa, & Marin, 1993; Haubenberger et al., 2011; Kraus & Hoffmann, 2010), ataxia (Trouillas et al., 1997), dystonia (Comella, Leurgans, Wuu, Stebbins, & Chmura, 2003), and even PD (Adler, Van Gemmert, Teulings, & Stelmach, 2003; Liu, Carroll, Wang, Zajicek, & Bain, 2005; Memedi et al., 2015; Sadikov et al., 2017; San Luciano et al., 2016; Saunders-Pullman et al., 2008; Stanley et al., 2010; Wang et al., 2008; Zham, Arjunan, Raghav, & Kumar, 2017).

Independently from clinical ratings, this study aimed to determine "hidden" variables of drawing movement, which are not visible from the visual inspection of the written trace but observable from a kinematic and dynamic analyses of pen movement and holding, in individuals with PD without and with medical treatment and in healthy controls. For this purpose, a three-step data-driven analysis was conducted.

1) A series of previous experiments suggested that performance deterioration in PD can be maximized when adding temporal constraints (to draw more quickly than normal; e.g. Dounskaia, Van Gemmert, Leis, & Stelmach, 2009), and/or spatial constraints (to write larger than normal; e.g. Van Gemmert, Teulings, Contreras-Vidal, & Stelmach, 1999). To our knowledge, how both temporal (to draw at spontaneous speed vs. as quickly as possible) and spatial (to draw small vs. big spirals with borders) constraints affect PD patients' performance with and without treatment, when compared to healthy controls, remains an unanswered question. In the first analysis, the effects of spatial and temporal constraints on several kinematic and dynamic variables were evaluated in order to identify which variable(s) and which constraint(s) should be the most relevant for objectifying changes in drawing movement in PD sufferers and their response to medical treatment.
2) The asymmetry of PD symptoms at the onset of the disease persists during the disease progression (for a review, see Djaldetti, Ziv, & Melamed, 2006) and makes motor evaluation of both hands necessary to better identify fine motor deficits related to pathology (San Luciano et al., 2016). In the second analysis, the relationship between handedness and dominance of PD symptoms was investigated for the variables determined in the first step.
3) Digitalized spiral drawing makes it possible to observe precisely when the kinematic changes related to the disease occur during the task. Consequently, a third analysis was conducted for the most relevant experimental task and kinematic variable identified by the previous analyses for assessing more precisely the occurrence of changes associated with PD.

2. Methods

2.1. Participants and clinical assessment

Twenty right-handed (Edinburgh test > 80% – Oldfield, 1971) patients with PD (59.6 years ± 8.7; nine females) and twenty controls (61:11 years ± 4:4, 10 females) volunteered for the experiment. The controls were age- ($t(38) = 1.00$, $p = 0.32$, NS), handedness-, and gender-matched. Patients were clinically examined using the motor section (part III) of the Unified Parkinson's Disease Rating Scale (UPDRS, Fahn et al., 1987), without (*OFF*, treatment withdrawn for at least 12 h) and with (*ON*, about 45 min after treatment) medical treatment. The demographics and clinical information of the patients are summarized in Table 1. The patients included in the present study had all akinetic-rigid symptoms and tremor was an exclusion criterion. Note that on the basis of the lack of difference in the total motor score of the UPDRS between the two treatment states, one patient was not retained for the analyses (see Table 1).

Table 1
Demographics and clinical information of the PD patients.

	Age (years)	Gender	Handedness score	DD (years)	UPDRS-III ON-med	UPDRS-III OFF-med	LEDD (mg)	Symptom dominance	MG	order
01	68	F	19	10	15	26	775	Left	Yes	1
02	69	F	19	10	10	11	600	Right	No	1
03	65	F	18	6	2	39	1500	Right	No	1
04	54	M	18	10	2	23	1500	Left	Yes	1
05	58	F	20	10	6	26	400	Right	No	1
06	65	F	20	10	18	39	600	Right	Yes	1
07	64	M	20	10	4	12	1500	Left	No	2
08	59	M	15	6	11.5	19	600	Left	Yes	2
09	60	M	14	9	6	13	1150	Right	No	1
10	59	M	20	8	7	26	1310	Left	Yes	1
11	65	M	16	12	4	17	1100	Right	Yes	2
12	60	M	18	10	1	8	1085	Right	Yes	2
13	70	F	20	11	9	38	850	Left	No	1
14	63	F	20	13	12	21	1200	Left	Yes	2
15	52	M	20	6	7	20	1230	Left	Yes	2
16	48	F	20	11	1	11	860	Right	Yes	2
17	40	M	20	3	1	10	700	Left	No	2
18	69	M	20	10	3	19	1100	Left	No	1
19	41	M	14	5	1	32	950	Right	Yes	2
20	64	F	20	6	14	33	1150	Left	Yes	1
Mean	***59.6***		***18.5***	***8.8***	***6.5***	***22***	***1000***			

Abbreviations: DD: disease duration; F: female; L: left; LEDD: Levodopa equivalent daily dose; M: male; MG: Micrographia reported by the patient; R: right. Order 1: OFF then ON and order 2: ON then OFF. Subject 02 was not retained for the analyses.

Based on both UPDRS score and patient's anamnesis, eleven patients had left-sided dominance of PD symptoms, the remaining eight patients experienced predominantly right-sided signs. Both patients and control participants had normal or corrected-to-normal vision. In order to prevent any possible repetition effect related to double recording (OFF and ON), the order of the medication states was counterbalanced. Ten patients were first evaluated OFF then ON the same morning, after at least 45 min; the remaining nine patients were evaluated ON first, and the OFF evaluation was carried out the morning of the following day. This study was conducted in accordance with the Declaration of Helsinki (World Medical Association, 2013), and approved by the local Ethics Committee Review Board (project n° 2012-A00460-43, Comité de Protection des Personnes [CPP], Sud-Méditerranée 1, France). The patients were included after providing informed written consent.

2.2. Experimental procedure

Each participant was required to draw Archimedean spirals from predefined templates (models illustrated in Supplementary material 1) and under several experimental conditions. The design included eight experimental conditions, according to: two temporal constraints (spontaneous vs. as quickly as possible); two spatial constraints (small vs. big); and the handedness (dominant vs. non-dominant hand). Participants were comfortably seated in front of a table upon which the graphic tablet was placed and they drew the spirals using an ink pen on a sheet of paper (A4 format: 21.0 29.7 cm) affixed to a graphic tablet (Wacom, Intuos3 A4, sampling frequency 200 Hz and resolution 5080 lpi). The instruction was to draw the spiral according to the defined condition (for example, as fast as possible with the left hand), starting from the center and ending at the periphery, without touching the edges of the spiral. The experimental condition order was counter-balanced, except for the handedness condition, for which all subjects started first with the right (dominant) hand, and then with the left hand. The drawing task was performed twice, OFF and ON, and as mentioned above each patient was also evaluated with the UPDRS in both medication states, prior to the task.

2.3. Dependent variables

Several variables were considered:

- The trace length (mm) that corresponds to the total length of the written trace;
- The movement duration (s) that correspond to the total time that the participant put to perform the spiral;
- The mean velocity (mm/s) that corresponds to the ratio between the trace length and the movement duration (without taking into account the "in-air" movement duration during pen lifts);

- The number of pen lifts, determined from the axial pressure directly measured by the tablet;
- The number of pen stops, determined from the periods during which the pen is in contact with the paper (tablet) and does not vary its position for at least 30 ms. This period allows us to discard the normal stops and to conserve only the abnormal ones (Paz-Villagrán, Danna, & Velay, 2014);
- The number of velocity peaks, determined after filtering the data with a 4th order low-pass Butterworth filter with a cutoff frequency of 10 Hz;
- The mean pen altitude, corresponding to the inclination of the pen in contact with the tablet. This altitude was between 0 (horizontal) and 90 degrees (vertical).
- The mean pen azimuth, corresponding to the angle between the pen and the y-axis of the tablet when the pen is in contact with the tablet (between 0 and 360 degrees);
- The variability (standard deviation) of pen altitude;
- The variability (standard deviation) of pen azimuth.

Note that the pen position (x and y), its altitude, and its azimuth were directly measured by the tablet Wacom.

2.4. Statistical analyses

A three-step analysis was conducted using general linear models (ANOVA). Results highlighting disease or medication effects, as well as relevant interactions, were considered in the main text (other results are summarized and provided in Supplementary material 2). The level of significance was set to $p \leq 0.05$. For all ANOVAs, Fisher's LSD post-hoc tests with Bonferroni's correction were applied when necessary.

The aim of the first-step of the analysis was to determine which variables were the most relevant for identifying changes in drawing movement associated with PD (comparison between OFF patients and controls) and for highlighting medication effects (comparison between OFF and ON). All variables were submitted to analyses of variance (ANOVA) with the 'Hand' condition (left vs. right), 'Temporal' condition (spontaneous vs. fast), and the 'Spatial' condition (big vs. small) as repeated measures. The 'Disease' (patients OFF vs. controls) was added as a group factor in the first ANOVA, and the 'Medication' state (OFF vs. ON) as repeated measures were considered in the second ANOVA.

On the basis of the findings reported in the first analysis, the most discriminatory variables were selected for the second-step analysis. The aim of this second-step was to compare performance between the two hands, according to handedness and side-dominance of PD symptoms. An ANOVA with the 'Hand' condition (left vs. right) and the 'Medication' state (OFF vs. ON) as repeated measures, and with the 'Side-dominance' of PD symptoms (left vs. right) as a group factor, was conducted in each spatial and temporal condition. To highlight the clinical potential of evaluating the most discriminatory variable in the most relevant condition, a correlation test (Spearman rank correlation coefficient) between the OFF-ON medication difference of performance for this variable and the OFF-ON medication difference in the motor score (part III) of the UPDRS was carried out.

Finally, based on this second analysis, the most discriminatory variable and the most relevant condition were selected for the third analysis on the temporal distribution of movement dysfluency. Four temporal areas were created by dividing each spiral production into four equal quarter-times (see Fig. 2.A. for an illustration). These areas were defined as Q1 (first quarter-time), Q2 (second

Table 2
Summary of statistical significances and test power ($\eta 2_p$). *$p < .05$; **$p < .01$; ***$p < .001$. A) Comparison between PD patients (OFF) and controls. B) Comparison between the two medication states (OFF vs. ON). In white and bold, the two most relevant variables based on the two statistical analyses.

	A) PD-Off vs. controls				B) Off vs. On medication			
	D	*H × D*	*T × D*	*S × D*	*M*	*M × H*	*M × T*	*M × S*
Trace length								
Movement duration	*; 0.16							
Mean velocity	*; 0.13		**; 0.20					
Lifts								
Stops	**; 0.17							
Velocity peaks	**; 0.22**				*; 0.24**			
Mean pen altitude								
Altitude variations	**; 0.17**				*; 0.28**	*; 0.24**		
Mean pen azimuth	***; 0.28**	*; 0.16**				*; 0.22**		
Azimuth variations					*; 0.29			**; 0.34

Abbreviations: D: Disease effect (PD patients off-medication vs. Controls); H: Hand; T: Temporal constraint effect (Spontaneous vs. Fast); S: Spatial constraint (Big vs. Small); M: Medication effect (OFF vs. ON).

quarter-time), Q3 (third quarter-time), and Q4 (last quarter-time). Only the performance with the right hand was considered. An ANOVA was conducted with the 'Quarter-time' condition (Q1, Q2, Q3, and Q4) and the 'Medication' state (OFF vs. ON) as repeated measures, and with the 'Side-dominance' of PD symptoms (left vs. right) as group factor.

3. Results

3.1. General analysis

Results of the first-step analysis are summarized in Table 2. The ANOVA revealed that the number of velocity peaks, the pen altitude variations, and to a lesser extent, the mean pen azimuth, were the most relevant variables in spiral drawing: both the effects of Disease (Table 2.A) and medication (Table 2.B) were revealed for these variables. In other words, OFF patients produced more peaks, held the pen differently, and surprisingly, were less variable in pen holding than controls and ON patients.

3.2. Handedness and side-dominance of PD symptoms

A second-step detailed analysis was conducted, for PD patients only, on the three variables identified in the first-step (velocity peaks, altitude variations and pen azimuth), which included the handedness and side-dominance of PD symptoms as factors. All statistical results of this second-step analysis are reported as Supplementary material 3. On the basis of the hypothesis that performance between the two hands was differently affected by the side-dominance of PD symptoms, only significant results on the double interaction (Medication × Hand × Side-dominance) are reported here.

The ANOVA revealed a double interaction on the mean azimuth in the production of big spirals at a spontaneous speed ($F(1, 17) = 7.74, p < 0.05$), but the post-hoc analysis did not show any significant difference functions of medication state (OFF vs. ON) in either 'Hand' nor any 'Side-dominance'. The analysis also revealed a double interaction in the number of velocity peaks in the production of small spirals at a spontaneous speed ($F(1, 17) = 9.18, p < 0.01$). The post-hoc test showed that the medication effect was present when spirals were produced by the left hand in the left-sided dominance group, and when spirals were produced by the right hand in the right-sided dominance group (Fig. 1).

The correlation between the OFF-ON medication difference of velocity peaks in drawing small spirals at a spontaneous speed and the OFF-ON medication difference in the UPDRS – Part III score was significant (Spearman's rho = 0.57, p = 0.01).

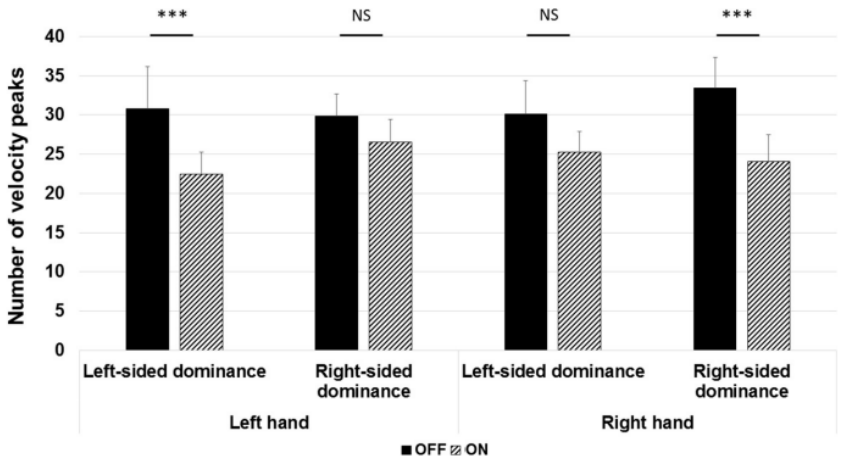


Fig. 1. Number of velocity peaks in the production of small spirals at a spontaneous speed by the PD patients off- (OFF) and on- (ON) medication functions of sided dominance of symptoms in spirals produced with the non-dominant (left) and dominant (right) hand.

3.3. Temporal distribution of velocity peaks

The analysis revealed that the main effect of Medication tends to be significant ($F(1, 19) = 4.19, p = 0.06$). The analysis also revealed a main effect of Quarter-time ($F(3, 51) = 4.58, p < 0.01$). Post-hoc tests of the Quarter-time effect showed that velocity peaks were less numerous in Q4 than in Q3. Interestingly, the post-hoc analysis revealed significant differences between the two medication states only in the first two quarter-times for patients with right-sided dominance (Fig. 2.B).

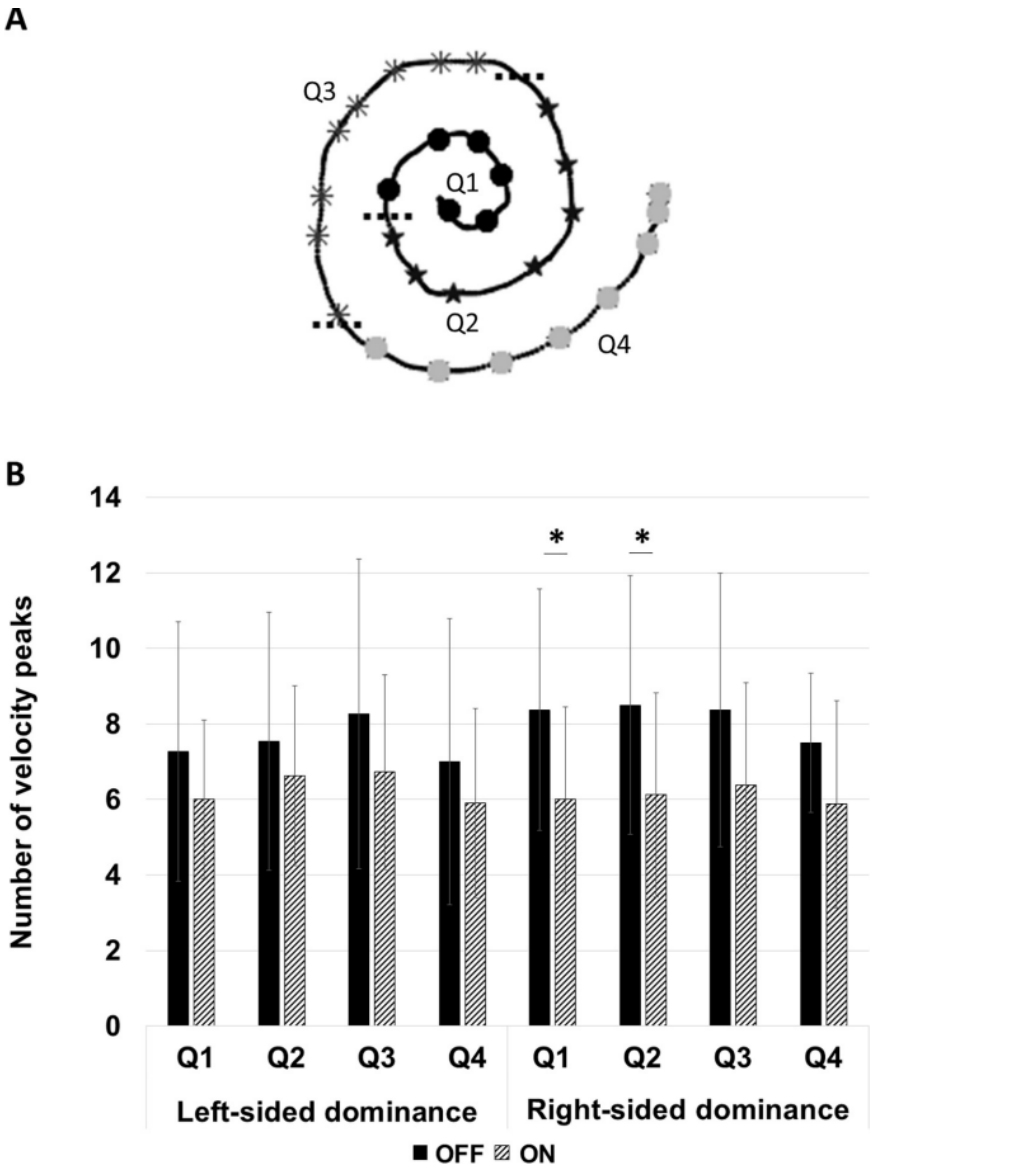


Fig. 2. (A) Illustration of temporal decomposition of movement dysfluency (number of velocity peaks) on spiral drawing by an individual with PD (ON). The dotted lines mark out the four temporal areas (Q1, Q2, Q3, and Q4). The velocity peaks in each temporal area are illustrated with different symbols. (B) Number of velocity peaks produced by the PD patients (OFF and ON) in production of big spirals at spontaneous speed, according to the four temporal areas and the sided dominance of pathology.

4. Discussion

Spiral drawing is a quick and non-invasive test validated and commonly performed by neurologists. Thanks to the development of graphic tablets, the visual inspection of the written trace and of the patient's movements can be completed with several objective and finer indexes on pen kinematics and holding. For 15 years, a growing attention has been paid to digitalized spiral drawing in order to better characterize fine motor impairments in PD (Adler et al., 2003; Groznik et al., 2014; Liu et al., 2005; Memedi et al., 2015; Pereira et al., 2018; Sadikov et al., 2017; San Luciano et al., 2016; Saunders-Pullman et al., 2008; Stanley et al., 2010; Wang et al., 2008; Zham et al., 2017). Using a data-driven analysis, the present study aimed at identifying "hidden" kinematic and/or dynamic changes in pen movement and holding for parkinsonian patients ON and OFF medication and for healthy controls by evaluating their performance under different experimental constraints and produced by both hands.

Which variables are the most relevant for identifying differences in performance? The results of analysis 1 revealed that the

number of velocity peaks and the pen altitude were the most relevant variables in spiral drawing for evaluating the effects of the disease and medication. Deficits in drawing movement fluency were previously shown in PD by means of an increased normalized jerk (Teulings, Contreras-Vidal, Stelmach, & Adler, 1997), increased acceleration peaks (Adler et al., 2003) or increased velocity fluctuations (Sadikov et al., 2017). However, to the best of our knowledge, changes in pen holding observed with pen altitude variations have never been reported until now. The decrease in pen variations when patients were OFF medication can be discussed in the light of a shift of distal control of the hand and fingers to a more proximal control of the arm, leading to a freezing of the hand articulations. This hypothesis is corroborated by Weiss, Dafotakis, Metten, and Noth (2009) who demonstrated that distal and proximal prehensions are differentially affected by PD, probably due to a different somatotopic organization of subloops between proximal and distal upper limb movements in the cortico-basal ganglia motor circuits (Tamás et al., 2016).

This first analysis did not provide a clear conclusion on the optimal condition that maximized the effects of dopaminergic treatment. Unexpectedly, general performance was not impacted by handedness. This might be explained by the *side*-dominance of PD symptoms. The relationship between the asymmetry of the disease and the handedness is not clearly established in the literature (see Stochl et al., 2009; Barrett, Wylie, Harrison, & Wooten, 2011 for opposite results). We thus investigated the relationship between handedness and dominance of PD symptoms on the number of velocity peaks and on the pen altitude variation and we observed that the number of velocity peaks was more relevant than the pen altitude variation for evaluating the medication effect in the follow-up of PD. For this variable only, the medication effect was present when spirals were produced by the hand corresponding to the sided dominance of pathology. The asymmetry of PD symptoms in spiral drawing was previously investigated by San Luciano et al. (2016). These authors computed the absolute value of the difference between dominant and non-dominant hand indices, accordingly to Barrett et al. (2011) who observed a significant association between handedness and the side of the initial symptom of PD. In the present study, we did not observe such association and we observed that the side-dominance of PD symptoms prevail over the handedness. It is well known that the localization of electrophysiological changes relates to the laterality of symptoms in PD due to the asymmetry of dopaminergic deficit (Tamás, Szirmai, Pálvölgyi, Takáts, & Kamondi, 2003). The clinical applications of this finding are thus potentially significant for the follow-up of PD because this variable could be a biomarker relevant to motor asymmetry of symptoms in PD (Djaldetti, Ziv, & Melamed, 2006; Stochl et al., 2009).

A spatial constraint (e.g., the small spiral drawing) requires a greater level of on-line visual control, compared to a temporal constraint (e.g., high speed execution). It is thus reasonable to think that when adding a spatial constraint, PD patients would benefit from additional visual cues for the task performance. However, our results showed that the spatial constraint was more relevant than the temporal constraint in the highlighting of performance differences between PD patients and healthy subjects and between the two medication states. Such an opposite effect was reported recently by Nackaerts et al. (2016) who stated that adding spatial constraints when writing small loops would conflict with the potential benefit provided by the visual cueing. They argued that the activation of the dorsolateral network underlying the control of externally-cued movements (including the parietal and premotor cortices and cerebellum; Nieuwboer, Rochester, Muncks, & Swinnen, 2009) may be precluded by an overly demanding visual constraint or by visuospatial skills that are impaired in individuals with PD (Cronin-Golomb & Braun, 1997).

Finally, our results showed that the effects of medication state on movement fluency were greater in the first two quarter-times of the spiral drawing. In other words, Parkinsonian patients OFF medication were much less smooth in the acceleration phase from the starting point than in the deceleration phase, when the pen was close to the end point. Such an increase of dysfluency may result from an effect of akinesia that would not only affect the movement initiation but maybe also the early movement production.

5. Conclusions

This study showed that spiral drawing can distinguish between patients with PD and healthy controls, and between patients ON and OFF medication. In line with previous studies assessing spiral drawing in PD (San Luciano et al., 2016; Saunders-Pullman et al., 2008; Stanley et al., 2010; Zham et al., 2017), our findings highlight the relevance of the digitalized drawing of a small spiral with high spatial constraints, completed by analysis of movement fluency and, if possible, pen holding. The correlation between the difference of movement fluency in the most relevant condition of the task and in the UPDRS –III score suggests that it may well complement the motor assessment of PD for the follow-up.

One possibility would be to develop and validate a simple digitalized spiral drawing test that could be implemented with a commercially available tablet in order to evaluate more precisely the upper limb motor deficits across a large population of PD patients, with the aim of including this test in the follow-up and diagnosis of PD. Note however that a fine evaluation of such movements requires high (temporal and spatial) resolutions (for instance superior to 10 Hz, Memedi et al., 2015; Sadikov et al., 2017). Actually, in order to highlight its potential in the early diagnosis of PD (Adler et al., 2003; Pereira et al., 2018; Ponsen et al., 2008; Rosenblum et al., 2013; San Luciano et al., 2016), it would be interesting to consider *de novo* PD patients and patients with parkinsonism symptoms in a longitudinal study to observe if these behavioral signs are already present in the early stages and change under medication as the disease progresses. Moreover, such a simple drawing task may be proposed with a simple handwriting task, as writing a word or signing, in order to evaluate the fine motor deficits as functions of the level of movement automation.

More generally, the exponential development of new digitalized tools, including tablets with camera, touch screen and stylus, with high temporal and spatial resolutions and data storage, led to the possibility of developing applications that record and analyze in real-time the quality of diverse human movements, as for example gait (e.g., Salarian et al., 2004), tapping (e.g., Shribman, Hasan, Hadavi, Giovannoni, & Noyce, 2018), and fine (grapho-)motor skills of both hands (e.g., Sadikov et al., 2014). The aim is not to replace the assessment made by the neurologist but to complete it with quantitative measurements of movement disorders.

Acknowledgment

We thank David Wood (English at your Service, www.eays.eu) for revising the English of the manuscript.

Funding

This work, carried out within the Labex BLRI (ANR-11-LABX-0036) and the Institut Convergence ILCB (ANR-16-CONV-0002), has benefited from support from the French government, managed by the French National Agency for Research (ANR) and the Excellence Initiative of Aix-Marseille University (A*MIDEX).

Conflict of interest

The authors state that they have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.humov.2018.08.003.

References

Adler, C. H., Van Gemmert, A. W. A., Teulings, H.-L., & Stelmach, G. E. (2003). A quantitative analysis of the production of the Archimedes spiral in Parkinson's disease patients and controls. In H. L. Teulings, & A. W. A. Van Gemmert (Eds.). *Proceedings of the 11th conference of the International Graphonomics Society (IGS2003), 2-3 November 2003, Scottsdale, Arizona, USA* (pp. 119–122). ISBN 0-9746365-0-9.

Barrett, M. J., Wylie, S. A., Harrison, M. B., & Wooten, G. F. (2011). Handedness and motor symptom asymmetry in Parkinson's disease. *Journal of Neurology Neurosurgery & Psychiatry, 82*(10), 1122–1124.

Comella, C. L., Leurgans, S., Wuu, J., Stebbins, G. T., & Chmura, T. (2003). Rating scales for dystonia: A multicenter assessment. *Movement Disorders, 18*, 303–312.

Cronin-Golomb, A., & Braun, A. E. (1997). Visuospatial dysfunction and problem solving in Parkinson's disease. *Neuropsychology, 11*, 44–52.

Djaldetti, R., Ziv, I., & Melamed, E. (2006). The mystery of motor asymmetry in Parkinson's disease. *Lancet Neurology, 5*, 796–802.

Dounskaia, N., Van Gemmert, A. W. A., Leis, B. C., & Stelmach, G. E. (2009). Biased wrist and finger coordination in Parkinsonian patients during performance of graphical tasks. *Neuropsychologia, 47*, 2504–2514.

Drótar, P., Mekyska, J., Rektorova, I., Masarová, L., Smékal, Z., & Faundez-Zanuy, M. (2016). Evaluation of handwriting kinematics and pressure for differential diagnosis of Parkinson's disease. *Artificial Intelligence in Medicine, 67*, 39–46.

Fahn, S., Elton, R. L., & UPDRS Development Committee (1987). The unified Parkinson's Disease Rating Scale. In S. Fahn, C. D. Marsden, D. B. Calne, & M. Goldstein (Vol. Eds.), *Recent developments in Parkinson's disease: Vol. 2*, (pp. 153–163). New York: Raven Press.

Fahn, S., Tolosa, E., & Marin, C. (1993). Clinical rating scale for tremor. In J. Jankovic, & E. Tolosa (Eds.). *Parkinson's disease and movement disorders* (pp. 271–280). (2nd ed.). Baltimore: Williams and Wilkins.

Groznik, V., Sadikov, A., Mozina, M., Zabkar, J., Georgiev, D., & Bratko, I. (2014). Attribute visualisation for computer-aided diagnosis: A case study. *Proceedings of the IEEE international conference on healthcare informatics* (pp. 294–299). .

Haubenberger, D., Kalowitz, D., Nahab, F. B., Toro, C., Ippolito, D., Luckenbaugh, D. A., ... Hallett, M. (2011). Validation of digital spiral analysis as outcome parameter for clinical trials in Essential Tremor. *Movement Disorders, 26*, 2073–2080.

Jankovic, J. (2008). Parkinson's disease: Clinical features and diagnosis. *Journal of Neurology Neurosurgery, and Psychiatry, 79*, 368–376.

Kraus, P. H., & Hoffmann, A. (2010). Spiralometry: Computerized assessment of tremor amplitude on the basis of spiral drawing. *Movement Disorders, 25*, 2164–2170.

Letanneux, A., Danna, J., Velay, J. L., Viallet, F., & Pinto, S. (2014). From micrographia to Parkinson's disease dysgraphia. *Movement Disorders, 29*, 1467–1475.

Liu, X., Carroll, C. B., Wang, S. Y., Zajicek, J., & Bain, P. G. (2005). Quantifying drug-induced dyskinesia in the arms using digitized spiral-drawing tasks. *Journal of Neuroscience Methods, 144*, 47–52.

Longstaff, M., Mahant, P., Stacy, M., Van Gemmert, A. W. A., Leis, B., & Stelmach, G. E. (2003). Discrete and dynamic scaling of the size of continuous graphic movements of parkinsonian patients and elderly controls. *Journal of Neurology, Neurosurgery, and Psychiatry, 74*, 299–304.

McLennan, J. E., Tyler, H. R., Schwab, R. S., & Nakano, K. (1972). Micrographia in Parkinson's disease. *Journal of the Neurological Sciences, 15*, 141–152.

Memedi, M., Sadikov, A., Groznik, V., Žabkar, J., Možina, M., Bergquist, F., ... Nyholm, D. (2015). Automatic spiral analysis for objective assessment of motor symptoms in Parkinson's disease. *Sensors, 15*, 23727–23744.

Nackaerts, E., Nieuwboer, A., Broeder, S., Smits-Engelsman, B. C., Swinnen, S. P., Vandenberghe, W., & Heremans, E. (2016). Opposite effects of visual cueing during writing-like movements of different amplitudes in Parkinson's disease. *Neurorehabilitation and Neural Repair, 30*, 431–439.

Nieuwboer, A., Rochester, L., Muncks, L., & Swinnen, S. P. (2009). Motor learning in Parkinson's disease: Limitations and potential for rehabilitation. *Parkinsonism & Related Disorders, 15*, S53–S58.

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9*, 97–113.

Paz-Villagrán, V., Danna, J., & Velay, J.-L. (2014). Lifts and stops in proficient and dysgraphic handwriting. *Human Movement Science, 33*, 381–394.

Pereira, C., Pereira, D. R., Rosa, G. H., Albuquerque, V. H. C., Weber, S. A. T., Hook, C., & Papa, J. P. (2018). Handwritten dynamics assessment through convolutional neural networks: An application to Parkinson's disease identification. ***Artificial Intelligence in Medicine, 87*****, 67–77.** https://doi.org/10.1016/j.artmed.2018.04.001.

Pinto, S., & Velay, J. L. (2015). Handwriting as a marker for PD progression: A shift in paradigm. *Neurodegenerative Disease Management, 5*, 367–369.

Ponsen, M. M., Daffertshofer, A., Wolters, E. C., Beek, P. J., & Berendse, H. W. (2008). Impairment of complex upper limb motor function in de novo Parkinson's disease. *Parkinsonism & Related Disorders, 14*, 199–204.

Rosenblum, S., Samuel, M., Zlotnik, S., Erikh, I., & Schlesinger, I. (2013). Handwriting as an objective tool for Parkinson's disease diagnosis. *Journal of Neurology, 260*, 2357–2361.

Sadikov, A., Groznik, V., Možina, M., Žabkar, J., Nyholm, D., Memedi, M., ... Georgiev, D. (2017). Feasibility of spirography features for objective assessment of motor function in Parkinson's disease. *Artificial Intelligence in Medicine, 81*, 54–62.

Sadikov, A., Groznik, V., Žabkar, J., Možina, M., Georgiev, D., Pirtošek, D., & Bratko, I. (2014). Parkinson check smart phone app. In T. Schaub, G. Friedrich, & O'Sullivan (Eds.). *Proceedings of ECAI 2014, frontiers in artificial intelligence and applications, 263* (pp. 1213–1214). Amsterdam: IOS Press.

Salarian, A., Russmann, H., Vingerhoets, F. J. G., Dehollain, C., Blanc, Y., Burkhard, P. R., & Aminian, K. (2004). Gait assessment in Parkinson's disease: Toward an ambulatory system for long-term monitoring. ***IEEE Transactions on Biomedical Engineering, 51*****(8),** https://doi.org/10.1109/TBME.2004.827933.

San Luciano, M., Wang, C., Ortega, R. A., Yu, Q., Boschung, S., Soto-Valencia, J., ... Saunders-Pullman, R. (2016). Digitized spiral drawing: A possible biomarker for early Parkinson's disease. *PLoS One, 11*(10), e0162799.

Saunders-Pullman, R., Derby, C., Stanley, K., Floyd, A., Bressman, S., Lipton, R. B., ... Pullman, S. L. (2008). Validity of spiral analysis in early Parkinson's disease. *Movement Disorders, 23*, 531–537.

Sharma, S., Moon, C. S., Khogali, A., Haidous, A., Chabenne, A., Ojo, C., ... Ebadi, M. (2013). Biomarkers in Parkinson's disease (recent update). *Neurochemistry International, 63*, 201–229.

Shribman, S., Hasan, H., Hadavi, S., Giovannoni, G., & Noyce, A. J. (2018). The BRAIN test: A keyboard-tapping test to assess disability and clinical features of multiple sclerosis. *Journal of Neurology, 265*(2), 285–290.

Stanley, K., Hagenah, J., Brüggemann, N., Reetz, K., Severt, L., Klein, C., ... Saunders-Pullman, R. (2010). Digitized spiral analysis is a promising early motor marker for Parkinson disease. *Parkinsonism & Related Disorders, 16*, 233–234.
Stochl, J., Hagtvet, K. A., Brozová, H., Klempír, J., Roth, J., & Ruzicka, E. (2009). Handedness does not predict side of onset of motor symptoms in Parkinson's disease. *Movement Disorders, 24*, 1836–1847.
Tamás, G., Kelemen, A., Radics, P., Valálik, I., Heldman, D., Klivényi, P., ... Erőss, L. (2016). Effect of subthalamic stimulation on distal and proximal upper limb movements in Parkinson's disease. *Brain Research, 1648*, 438–444.
Tamás, G., Szirmai, I., Pálvölgyi, L., Takáts, A., & Kamondi, A. (2003). Impairment of post-movement beta synchronisation in Parkinson's disease is related to laterality of tremor. *Clinical Neurophysiology, 114*, 614–623.
Teulings, H. L., Contreras-Vidal, J. L., Stelmach, G. E., & Adler, C. H. (1997). Parkinsonism reduces coordination of fingers, wrist, and arm in fine motor control. *Experimental Neurology, 146*, 159–170.
Teulings, H. L., & Stelmach, G. E. (1991). Control of stroke size, peak acceleration, and stroke duration in Parkinsonian handwriting. *Human Movement Science, 10*, 315–334.
Trouillas, P., Takayanagi, T., Hallett, M., Currier, R. D., Subramony, S. H., Wessel, K., ... Manyam, B. (1997). International Cooperative Ataxia Rating Scale for pharmacological assessment of the cerebellar syndrome. *Journal of the Neurological Sciences, 145*, 205–211.
Tucha, O., Mecklinger, L., Thome, J., Reiter, A., Alders, G. L., Sartor, H., ... Lange, K. W. (2006). Kinematic analysis of dopaminergic effects on skilled handwriting movements in Parkinson's disease. *Journal of Neural Transmission, 113*, 609–623.
Van Gemmert, A. W. A., Adler, C. H., & Stelmach, G. E. (2003). Parkinson's disease patients undershoot target size in handwriting and similar tasks. *Journal of Neurology, Neurosurgery, and Psychiatry, 74*, 1502–1508.
Van Gemmert, A. W. A., Teulings, H. L., Contreras-Vidal, J. L., & Stelmach, G. E. (1999). Parkinson's disease and the control of size and speed in handwriting. *Neuropsychologia, 37*, 685–694.
Wang, H., Yu, Q., Kurtis, M. M., Floyd, A. G., Smith, W. A., & Pullman, S. L. (2008). Spiral analysis – Improved clinical utility with center detection. *Journal of Neuroscience Methods, 171*, 264–270.
Weiss, P. H., Dafotakis, M., Metten, L., & Noth, J. (2009). Distal and proximal prehension is differentially affected by Parkinson's disease. The effect of conscious and subconscious load cues. *Journal of Neurology, 256*, 450–456.
Westin, J., Ghiamati, S., Memedi, M., Nyholm, D., Johansson, A., Dougherty, M., & Groth, T. (2010). A new computer method for assessing drawing impairment in Parkinson's disease. *Journal of Neuroscience Methods, 190*, 143–148.
World Medical Association (2013). World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. *Journal of American Medical Association, 310*, 2191–2194. https://doi.org/10.1001/jama.2013.281053.
Wu, Y., Le, W., & Jankovic, J. (2011). Preclinical biomarkers of Parkinson disease. *Archives of Neurology, 68*, 22–30.
Zham, P., Arjunan, S. P., Raghav, S., & Kumar, D. (2017). Efficacy of guided spiral drawing in the classification of Parkinson's Disease. *IEEE Journal of Biomedical and Health Informatics*. https://doi.org/10.1109/JBHI.2017.2762008.