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Full Length Article

A paradigm for emulating the early learning stage of handwriting: Performance comparison between healthy controls and Parkinson's disease patients in drawing loop shapes

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ABSTRACT

We present a novel paradigm, aimed at emulating the early stage of handwriting learning in proficient writers, by asking them to produce a familiar shape through a novel (unfamiliar) motor plan. Handwriting of beginner writers is characterized by slower movements, reduced spatial precision, lower fluency and reduced force regulation compared to those observed in the handwriting production of proficient writers. Features observed in the ink trace obtained with the novel motor plan and performance comparison of the handwriting obtained by familiar and unfamiliar motor plan suggest that the proposed paradigm is able to elicit non-automated movements in proficient writers.

As that produced by beginner writers, handwriting of Parkinson's disease (PD) patients is characterized by lack of fluency, slowness and abrupt changes of direction. Furthermore, PD patients show impaired performance in learning novel motor behaviors, as well as in executing motor behaviors acquired before the onset of the disease. We used the proposed paradigm for comparing the performance achieved by healthy controls in writing a familiar shape through a novel motor plan with those obtained by PD patients performing a well-known motor plan for drawing the same shape. Our analysis points out some similarities between performance obtained by healthy controls and those obtained by PD patients, sustaining the hypothesis that the fine tuning of the motor plan parameters involved in the handwriting production is impaired by PD.

1. Introduction

Handwriting involves complex movements that can be seen as a composition of elementary movements, each corresponding to an elementary shape or stroke (Plamondon & Maarse, 1989). Studies on motor control (Kawato, 1999) suggested that an elementary movement is performed through a process of sensorimotor transformation (involving the activation and cooperation of several brain areas) in which the location of the target to reach, encoded in trajectory coordinates, is converted into information (the motor plan) suitable for the motor system. This process characterizes the first stage of learning, which is computational demanding and slower, since it relies on the visuo-proprioceptive feedback, which allows humans to correct, trial by trial, the trajectory and motor plan. As learning proceeds, the information provided by the visuo-proprioceptive feedback is exploited in the following trials for a more efficient execution of the task, leading to a coordination and control solution more accurate in terms of the motor production (so that the actual trajectory corresponds to the desired one), and more economical in terms of the metabolic energy expenditure (Sparrow &

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Newell, 1998). Lashley (1930) and Hebb (1949) observed that movements learned with one extremity could be executed by different effectors (this phenomenon is known as "motor equivalence"), and Raibert (1977) and Wing (2000) showed that writing movements learned through the dominant hand could be executed by using different body parts (such as the non-dominant hand, the mouth and the foot). They observed that, despite subjects had no previous experience writing with any of the other effectors and even though the movements were not smooth, the writing production followed the same trajectory in all conditions. Taken together, these studies suggest that the sequence of movements composing a motor task is stored in the brain in two ways: in an abstract form (effector independent) related to the spatial sequence of points representing the trajectory plan, and as a sequence of motor commands (effector-dependent) directed to obtain particular muscular contractions and articulatory movements. It has been shown that when the untrained hand is used to perform a given sequence, learned with long-term practice with the other hand, performance is poorer, but this is not true for a newly learned sequence (Rand, Hikosaka, Miyachi, Lu, & Miyashita, 1998), supporting the hypothesis that early in learning the execution of the motor task is more based upon the trajectory plan (effector independent), whereas late in learning upon the sequence of motor commands (effector-dependent). Accordingly, we suggested (Senatore & Marcelli, 2012) that handwriting learning follows two distinct phases, in which two different processes take place. Early in learning, handwriting is acquired as a sequence of spatial coordinates (target points) converted into motor commands; as learning proceeds and the sequence of motor commands is acquired, it comes to be executed as a single behavior, and is performed automatically, with no need of the sensorimotor transformation and the info provided by the visuo-proprioceptive feedback. Consequently, with training, the simple point-to-point movements become continuous, curved and smoother. Indeed, during the first phase of handwriting learning the elementary strokes are drawn one after the other, are quite straight and aimed at reaching a sequence of points. Further support to this view has been provided by the neural model proposed by Grossberg and Paine (that incorporates both the role of basal ganglia and cerebellum), which has shown that handwriting movements are initially straight and guided by the visual feedback, while are guided by memory and become smooth and continuous after learning (Grossberg & Paine, 2000).

Handwriting production of beginner writers is characterized by slower movements, reduced spatial precision, lower fluency and reduced force regulation compared to those observed in the handwriting production of proficient writers (Graham & Weintraub, 1996; Rosenblum, Weiss, & Parush, 2003; Smits-Engelsman, Niemeijer, & Van Galen, 2001; Wann, 1987). Moreover, it has been shown that conscious control of movements, which characterizes the early learning stage of handwriting, causes the reduction of fluency in handwriting (Tucha, Paul, & Lange, 2001). As the writer becomes familiar with a given sequence of strokes, the group of strokes is "embedded" into a single sequence, which is drawn without any feedback, as it was an "elementary" writing movement. Skilled writers know how long it takes to draw a stroke and where it will finish, so that the next stroke can be initiated before the current one is completed, movements becomes more automated and fluency emerges from the time superimposition of strokes (Plamondon & Maarse, 1989). According to these findings and observations, the execution of a novel sequence of handwriting movements for obtaining a specific trajectory should be characterized by novel target points (or, more in general, different target points) and reduced motor performance compared to the known handwriting movements commonly performed for drawing the same trajectory.

It has been shown that cortical and subcortical structures, including the basal ganglia, cerebellum, and cortical regions, are critical in different stages and aspects in the acquisition and/or retention of motor behaviors (Doya, 2000; Doyon et al., 2009). Parkinson's disease (PD) is characterized by the dysfunction of the basal ganglia, caused by the loss of dopaminergic neurons. Such dysfunction, eventually, impairs the initial learning (Doyon & Ungerleider, 2002; Krebs, Hogan, Hening, Adamovich, & Poizner, 2001; Packard & Knowlton, 2002). It has also been shown that reduced amount of dopamine, the neurotransmitter that modulates basal ganglia activity, correlates with reduced performance in the acquisition and expression of a behavior during the initial stage of learning (Horvitz, Won, Morvan, Eyny, & Balsam, 2007; Smith-Roe & Kelley, 2000).

In previous work (Senatore & Marcelli, 2012) we designed a neural network model incorporating the key biological features of basal ganglia, cerebellum and their cortical interactions. Looking at the neural network behavior, we found that early in learning task performance is more dependent on the interactions between the cortex and the basal ganglia, whereas, after long-term training, task performance is more dependent on the cortex-cerebellar interactions. Other studies showed that basal ganglia are more activated in the execution of internally-driven movements (Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2003; Jenkins, Jahanshahi, Jueptner, Passingham, & Brooks, 2000), whereas increased activation of the cerebellum was observed in the execution of externally driven movements (Debaere et al., 2003; Jueptner & Weiller, 1998). Furthermore, it has been shown that motor learning in PD patients benefits from the use of external cues (reference points for the execution of the task) or augmented feedback (knowledge about the results of the executed movement) (Nackaerts et al., 2013). All together, these studies support the view that basal ganglia are involved in the early phase of learning, which is mainly focused in the acquisition of the sequence of target points (the trajectory plan) and is based on the visuo-proprioceptive feedback. However, the study of Swett, Contreras-Vidal, Birn, and Braun (2010) reported that a novel sequence of movements is initially mapped to form an internal representation of the sequence that is progressively encoded and refined subcortically (in the basal ganglia and in the cerebellum) as performance improves (Swett et al., 2010), providing some evidence that the basal ganglia are also involved in the late stage of learning, in which fine tuning of motor plan parameters is achieved.

Several studies observed that, similar to beginner writers, handwriting of PD patients is characterized by lack of fluency, slowness, abrupt changes of direction and micrographia (Flash, Inzelberg, Schechtman, & Korczyn, 1992; Marsden, 1989; McLennan, Nakano, Tyler, & Schwab, 1972; Sheridan, Flowers, & Hurrell, 1987; Teulings & Stelmach, 1991; Van Gemmert, Teulings, Contreras-Vidal, & Stelmach, 1999). PD deficits have been ascribed to patients' impaired ability in controlling movement speed and amplitude (Broderick, Van Gemmert, Shill, & Stelmach, 2009; Teulings & Stelmach, 1991; Van Gemmert et al., 1999), coordinating fingers and wrist movements (Teulings, Contreras-Vidal, Stelmach, & Adler, 1997; Van Gemmert, Adler, & Stelmach, 2003), and modulating

force-production (Stelmach, Teasdale, Phillips, & Worringham, 1989; Stelmach & Worringham, 1988). An interesting question, which is still unanswered, is whether these observed impairments are closely related and could be ascribed to the same underlying deficit.

We hypothesize that reduced performance achieved by PD patients in executing both novel tasks and previously acquired task could be due to an impaired fine tuning of the motor plan parameters involved in the handwriting production. In line with this hypothesis, we expected that PD patients perform handwriting as they got stuck on the early stages of the learning process, in which fine tuning of the motor plan is not still acquired, and that their performance remains poor, due to their impaired learning abilities. Consequently, we expect to find some similarities between the performance achieved by healthy controls in executing novel handwriting movements and those measured in handwriting movements produced by PD patients.

Therefore, the goal of the proposed work is twofold. We present a novel experimental paradigm, and provide evidence that through its use we were able to elicit non-automated movements in healthy subjects, and therefore emulate the early learning stage of a stroke sequence. Furthermore, with the aim of evaluating our hypothesis, we exploited the proposed paradigm, and compared the kinematic features of the handwriting traces produced by the healthy controls using skilled and unskilled movements to those produced by the PD patients.

The investigation of the deficits underlying poor performance characterizing handwriting movements of PD patients can provide insights for the development of novel rehabilitation strategies that could be combined with the pharmacological treatments.

2. Method

2.1. Participants

Handwriting samples were acquired from sixty healthy volunteers that participated in the study, whereas handwriting samples from thirty PD patients were extracted from the PaHaW Parkinson's disease handwriting database (Drotár et al., 2015, 2016).

Both healthy participants and PD patients were right-handed, performed handwriting using Latin alphabet, and had completed their mandatory period of education (at least 8 years). It has been showed that schooling improves handwriting skills, but that a stable level of handwriting proficiency is acquired during their first years of school (Maeland, 1991; Marr & Cermak, 2003). Therefore, we supposed that all analyzed groups have reached a stable level of handwriting proficiency. Moreover, we found no significant differences between handwriting parameters (in terms of speed and fluency) of control groups of this study and those measured in the control group included in the PaHaW database.

The study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki); all participants were informed about the goal of the experiment and signed informed consent to participate in the study.

2.1.1. Healthy groups

Thirty young participants (13 men and 17 women) with a mean age of 22.3 (standard deviation: 3.5; range: 19–32) and thirty elderly participants (13 men and 17 women) with a mean age of 67.1 (standard deviation: 5.9; range: 57–77) were included in the analysis. Since PD group was composed only of right-handed patients we enrolled in the study only right-handed subjects (Edinburg Handedness Inventory (Oldfield, 1971); handedness score > 0.5). Participants showed no significant differences in education level (two tailed t-test, $p > 0.3$). All participants reported no history or presence of any neurological or muscular disease and had normal or corrected to normal vision. All participants reported Italian as their first language.

2.1.2. PD patients group

Handwriting samples of PD patients were extracted from the data collected in the study of (Drotár et al., 2015, 2016), which involved thirty-seven Czech PD patients. We included in the analysis the data of thirty out of thirty-seven patients in a way that improved both age and gender matching between the PD patients and the elderly group participating in our study. PD group was composed of 13 men and 17 women, with a mean age of 69.4 years (standard deviation: 6.6; range: 57–79).

All patients were taking L-dopa COMT (catechol-o-methyl transferase) inhibitor and/or a dopamine agonist, and they performed the task in their ON state (i.e. 1–2 h after taking their regular dose of dopaminergic medication). More detailed information about all patients (disease duration, modified Hoehn and Yahr score, and levodopa equivalent daily dose) is reported in (Drotár et al., 2015, 2016). Table 1 summarizes patients' characteristics, reporting their means and standard deviations.

2.2. Procedure

Handwriting samples of the healthy participants were acquired while they were seated, in comfortable position, in front of a desk

Table 1
Information of Parkinson's disease group.

Disease duration		Hoehn and Yahr score		Levodopa equivalent dose	
Mean	Std	Mean	Std	Mean	Std
8.73	4.93	2.28	0.85	1461.1	724.7

upon which a digitizer tablet was placed. Healthy subjects were required to write a sequence of cursive 'l-loops' in two different ways: 1) drawing the 'l' shape by performing the loop in counterclockwise order (i.e. as they are used to do), hereafter referred as *writing l-loop*; 2) drawing the 'l' shape by performing the loop in clockwise order (i.e. in a way they are not used to), hereafter referred as *novel l-loop*. Fig. 1 shows one example of writing l-loop drawn by young (1A) and elderly (1E) controls and one example of novel l-loop drawn by young (1C) and elderly (1G) controls. Participants were instructed to hold the pen with their dominant hand and to write at their preferred speed, with no constraints about the number of repetitions of loops. Handwriting samples were collected through a digitizer tablet (WACOM Intuos 2) designed to record the movements made by the tip of a pen (Intuos2 Ink Pen XP-110). The tablet was overlaid with paper on which patients performed the handwriting tasks. The tablet recorded the positions (x and y coordinates) and the pressure of the pen-tip with a sampling rate of 100 Hz and a spatial resolution of 0.001 cm. The experimental procedures were set-up in MovAlyzeR by NeuroScript (Teulings, 2010). We provided no time constraint for the tasks, but all participants completed both tasks in less than two minutes. For both tasks we included in the analysis the first seven handwriting samples produced by each participant (or, whenever the participant produced less than seven loops, we included all the samples). On average, we analyzed 6.3 samples of writing l-loops and 6.1 novel l-loops per participant.

In the study of (Drotár et al., 2016) the handwriting of the patients were acquired in the same conditions used in our study. Patients were seated, in comfortable position, in front of a desk upon which a digitizer tablet was placed. Patients were asked to perform eight handwriting tasks according to a pre-filled template shown to the subjects before starting the experiment. The tasks consisted in drawing cursive letters, n-grams, words, sentences and the Archimedean spiral. The patients were instructed to write with their dominant hand, at their preferred speed, and no constraints about the number of repetitions of letters or words were given.

Handwritten signals (in the x-y plane and pressure axis) were acquired through a digitizing tablet (WACOM Intuos 4M) with a sampling rate of 100 Hz. Since the tablet does not provide visual feedback, it was overlaid with a paper on which the patients performed the handwriting tasks while seeing the ink trace produced. For the purpose of our study, we analyzed only the data recorded in the first task, that is the handwritten samples representing cursive "l-loops". From five to six handwritten samples per patient were provided in the PaHaW database. Fig. 1I shows an example of a handwritten l-loop drawn by a PD patient.

2.3. Measurements

We measured handwriting features at different levels: trace level, stroke level and segmentation points (SPs) level.

At trace level we computed the mean absolute acceleration and the mean absolute velocity employed by each participant to draw the loop trace. At stroke level we computed mean normalized jerk and mean stroke duration and size. Normalized jerk is a measure of the rate of change of acceleration normalized for stroke size and duration (for more details, see Teulings et al., 1997). Therefore, high normalized jerk values highlights reduced handwriting fluency, indicating deficits in coordination and reduced ability of controlling force.

At segmentation points level we calculated the mean absolute acceleration in the proximity of SPs for each participant. We measured and analyzed handwriting features at segmentation points level since these points represent the starting/ending points of the elementary movements composing the handwriting. We supposed that drawing the 'l' shape by changing the way the loop is drawn corresponds to execute a novel handwriting task, especially in the proximity of the crossing point of the loop, where participants had to change the set of movements (and therefore the set of motor parameters) needed to draw the loop. Indeed, we observed that when participants drew the novel l-loops (performing the loop in clockwise fashion) then novel SPs appeared close to the start/end of the loop, as shown in Fig. 1C and 1G. Therefore, for the healthy groups, we computed mean absolute acceleration in the proximity of three different sets of SPs located in the handwriting traces:

1) SPs of the writing l-loop ink trace, hereafter referred as regular segmentation points;
2) SPs of the novel l-loop ink trace appearing also in the writing l-loop (i.e. the regular SPs);
3) Novel SPs of the novel l-loop ink trace appearing in the proximity of the start/end of the loop, hereafter referred as novel segmentation points.

Instead, for the PD group, we computed mean absolute acceleration in the proximity of the regular SPs of the writing l-loop ink trace written by the patients.

2.4. Data analysis

All handwriting signals used in the analysis were processed according to a procedure used in other studies (Teulings & Maarse, 1984). Position data of the handwriting signals were low pass filtered at 12 Hz to reduce noise. Filtered data were segmented into strokes by identifying as segmentation points the points of the ink trace corresponding to the zero crossings of the vertical velocity profile. Segmentation points spaced less than 0.05 cm or giving rise to stroke durations lower than 0.04 s were removed.

We first compared the features measured in the writing and novel l-loops performed by healthy participants (both young and elderly) and then compare healthy performance in both conditions with those measured in the writing l-loop condition performed by PD patients. Statistical analysis was performed using the analysis of variance (ANOVA). Post hoc analysis was performed using paired *t*-tests corrected with the FDR (false discovery rate) procedure of Benjamini and Hochberg (1995).

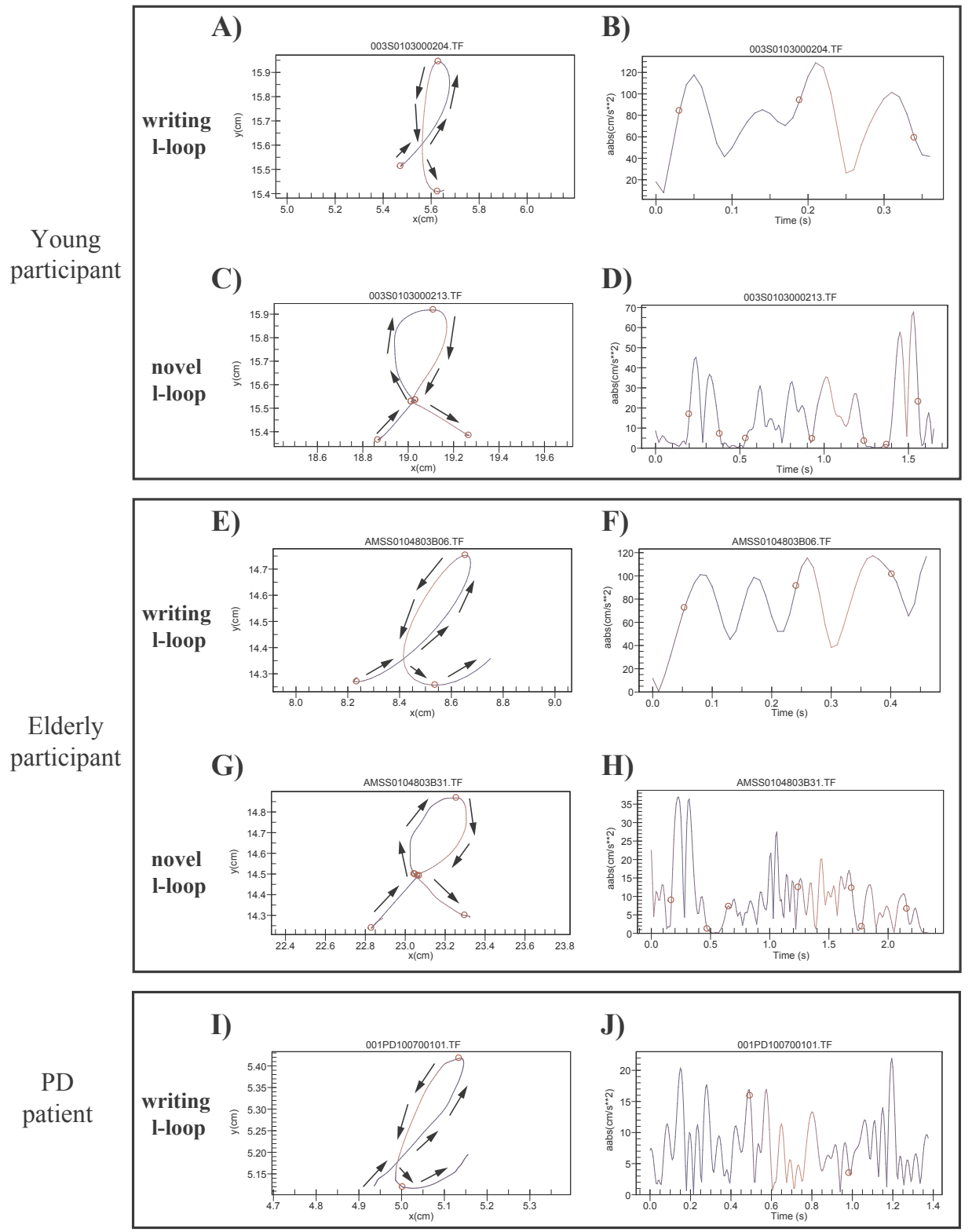

Fig. 1. Examples of the ink trace data and the corresponding acceleration profile of the pen-tip movements. A-B) Writing l-loop and C-D) Novel l-loop performed by a young subject. E-F) Writing l-loop and G-H) Novel l-loop performed by an elderly subject. I-J) Writing l-loop performed by a PD patient. Red circles reported in the ink traces and acceleration profiles represent the segmentation points. Black arrows close to the ink traces represent the writing order followed by the writer.

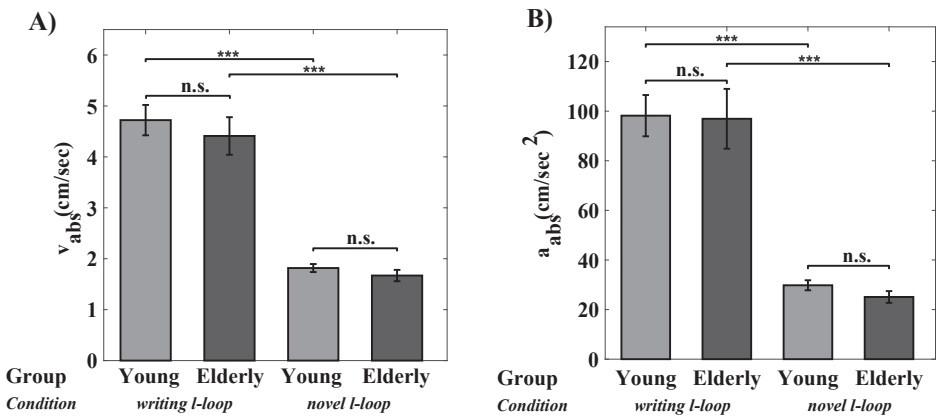

Fig. 2. Trace level features, measured from l-loops drawn by healthy groups in writing and novel conditions. A) Absolute velocity (mean ± SEM) across subjects. B) Absolute acceleration (mean ± SEM) across subjects. Stars represent the results of FDR (false discovery rate) corrected one tailed *t*-tests ($^{***}p < 0.001$; n.s. not significant).

3. Results

3.1. Writing vs novel l-loop performance in healthy writers

3.1.1. Features at trace level: Absolute velocity and acceleration

We found that drawing l-loops by using a novel motor plan produced a significant decrease ($p < 0.001$, one tailed *t*-test) in velocity and acceleration both in young and elderly group (Fig. 2). Young and elderly performing *novel l-loops* showed 60% and 40% decrease of their mean velocity, respectively. Similarly, we found a significant decrease of the mean absolute acceleration (70% both for young and elderly) when drawing *novel l-loops* compared to that measured when drawing the *writing l-loops*. In both conditions elderly performed slightly worse than young, although we found no significant differences between groups when performing the task in the same condition ($p > 0.6$ in writing l-loop condition; $p > 0.1$ in novel l-loop condition – two tailed *t*-test).

3.1.2. Features at stroke level: Normalized jerk, stroke duration and size

As for trace level features, we found significant worsening of stroke level features. In particular, we found significant increase of normalized jerk measured in handwriting of healthy groups when they wrote the *novel l-loop* ($p = 0.001$ for young group; $p = 0.015$ for elderly group - two tailed *t*-test), indicating reduced fluency and coordination (Fig. 3A). Elderly group showed higher normalized jerk than young controls, although we found no significant differences between groups ($p > 0.1$ in writing l-loop condition; $p > 0.2$ in novel l-loop condition – two tailed *t*-test). Mean stroke duration increased both for young and elderly groups when drawing the *novel l-loop*, with stroke duration of the elderly group becoming significantly longer than stroke duration of young group ($p < 0.01$, one tailed *t*-test) (Fig. 3B). Eventually, we found no significant differences between groups when drawing the loop in the same condition ($p > 0.3$, two tailed *t*-test) and a significant decrease in stroke size for both groups when drawing the *novel l-loop* ($p < 10^{-6}$, one tailed *t*-test) (Fig. 3C).

3.1.3. Features at segmentation points level: Absolute acceleration

We found that *novel l-loops* were characterized by greater trace decomposition, since their ink trace was composed of a higher number of elementary movements than the ink trace of *writing l-loops*. Indeed, both young and elderly participants performed on average 2.1 strokes for drawing the l-loop shape in writing conditions, whereas they performed on average 4.1 strokes for drawing the same shape in novel conditions. Therefore, the ink trace produced by healthy subjects using the familiar and novel motor plans were made up of different sets of segmentation points: *novel l-loops* contained both the segmentation points appearing in the ink trace of the *writing l-loop* and novel segmentation points (Fig. 1). As observed at trace level, we found that mean acceleration at regular segmentation points composing the *writing l-loops* was significantly higher than mean acceleration at regular segmentation points composing the *novel l-loops* ($p < 10^{-7}$, one tailed *t*-test). Furthermore, mean acceleration at regular segmentation points composing the *novel l-loops* was significantly higher than mean acceleration at novel segmentation points ($p < 10^{-4}$, one tailed *t*-test). We found no significant differences between groups under the same condition ($p > 0.2$, two tailed *t*-test). Measures and comparisons are reported in Fig. 4.

3.2. Performance comparison between healthy subjects and PD patients

3.2.1. Features at trace level: Absolute velocity and acceleration

The mean absolute velocity measured in the handwriting movements performed for drawing the *writing l-loop* showed a significant group effect ($F(2,87) = 70.08$, $p < 1\,0^{-5}$). Indeed, we observed that PD patients performing the *writing l-loop* task were significantly

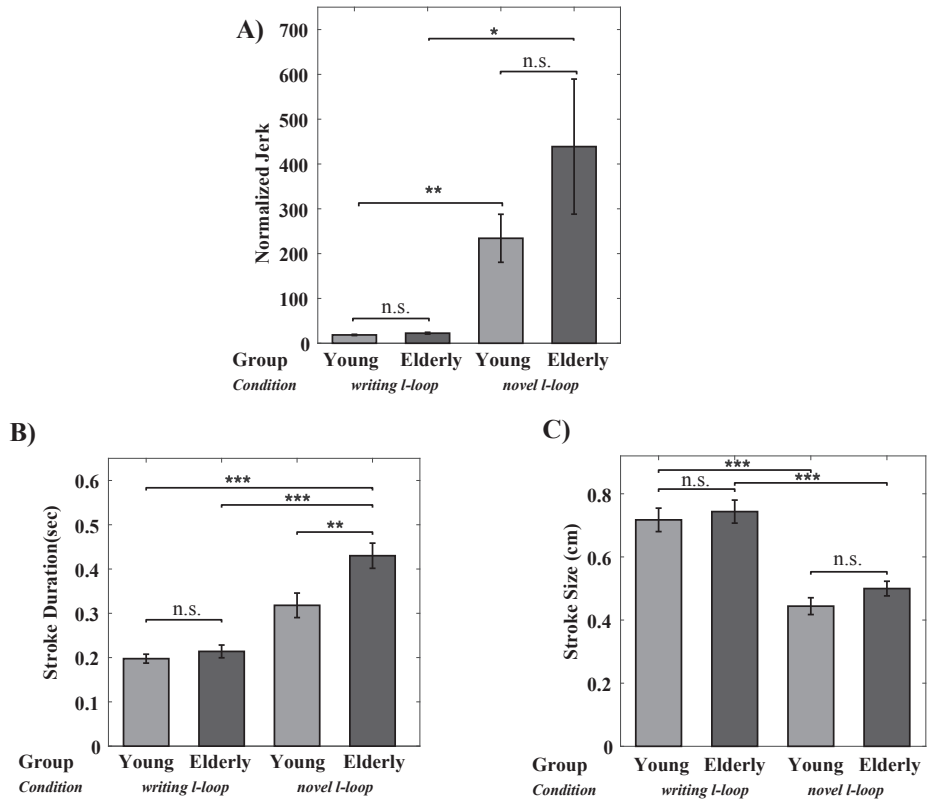

Fig. 3. Stroke level features, measured from l-loops drawn by healthy groups in writing and novel conditions. A) Normalized jerk (mean ± SEM) across subjects. B) Stroke duration (mean ± SEM) across subjects. C) Stroke size (mean ± SEM) across subjects. Stars represent the results of FDR (false discovery rate) corrected *t*-tests ($^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$; n.s. not significant).

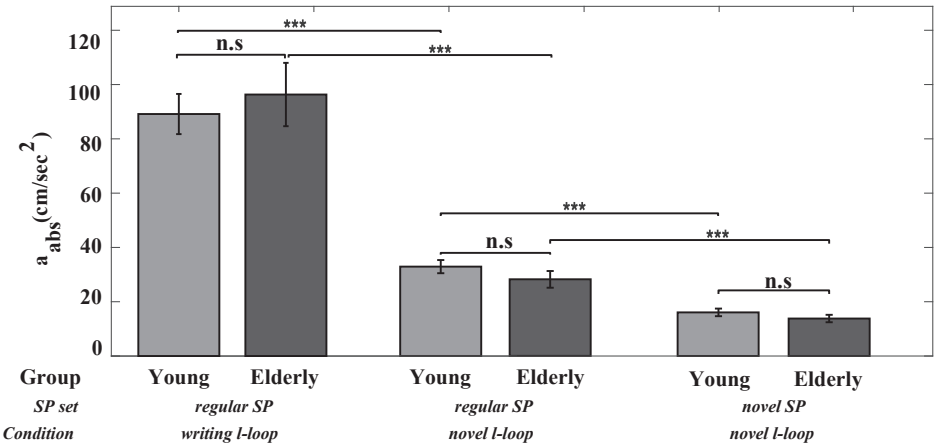

Fig. 4. Absolute acceleration (mean ± SEM) measured at different sets (regular and novel) of segmentation points composing the l-loops drawn by healthy groups in writing and novel conditions. Stars represent the results of FDR (false discovery rate) corrected *t*-tests ($^{***}p < 0.001$; n.s. not significant).

slower than young ($p < 0.001$, one tailed *t*-test) and elderly controls ($p < 0.001$, one tailed *t*-test) (Fig. 5A). However we also found that this statement still hold when comparing the mean absolute velocity of healthy controls drawing the *novel l-loop* and the mean absolute velocity of PD patients drawing the *writing l-loop* ($F(2,87) = 14.37$, $p < 10^{-5}$). Although healthy participants slow down their movements when drawing the *novel l-loop*, their mean velocity is still significantly higher than that mean absolute velocity of PD patients ($p < 0.001$, one tailed *t*-test).

Similarly, we found that the mean absolute acceleration measured in the handwriting movements performed for drawing the *writing l-loop* showed a significant group effect ($F(2,87) = 35.01$, $p < 10^{-5}$). PD patients drawing the *writing l-loop* showed

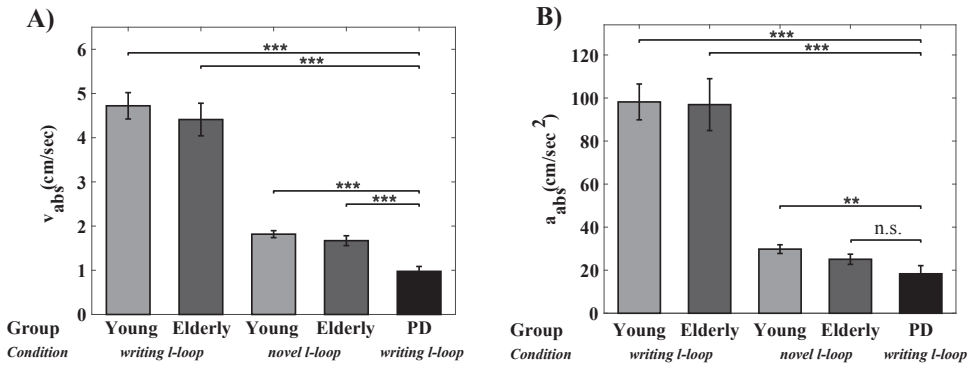

Fig. 5. Features at trace level. A) Absolute velocity (mean ± SEM) across subjects for each group and condition; comparison between mean absolute velocity of healthy controls drawing the writing l-loop and the novel l-loop and the mean absolute velocity of PD patients drawing the writing l-loop. B) Absolute acceleration (mean ± SEM) across subjects for each group and condition; comparison between mean absolute acceleration of healthy controls drawing the writing l-loop and the novel l-loop and the mean absolute acceleration of PD patients drawing the writing l-loop. Stars represent the results of FDR (false discovery rate) corrected one tailed *t*-tests ($^{**}p < 0.01$, $^{***}p < 0.001$, n.s. not significant).

significantly lower mean acceleration than healthy controls performing the same task ($p < 0.001$, one tailed *t*-test). As for the velocity, mean acceleration of healthy controls decreased when they drew the *novel l-loop*, and we found a significant difference among groups ($F(2,87) = 4.25$, $p < 0.05$). However, we found that young controls drawing the *novel l-loop* showed still higher acceleration than PD ($p < 0.01$, one tailed *t*-test), but elderly controls did not ($p > 0.05$, one tailed *t*-test). Measures and comparisons are reported in Fig. 5B. We found similar results when comparing the values of the acceleration peak measured for the three groups.

Previous work reported multiple accelerations and decelerations per stroke and multimodal speed patterns in PD handwriting (Teulings et al., 1997; Tucha et al., 2006; Van Gemmert et al., 2003). Looking at the acceleration profiles associated to the *novel l-loop* written by the healthy groups (Fig. 1D and 1H) we observed that they were characterized by multiple accelerations and decelerations, as observed in the acceleration profile of the handwriting performed by PD patients (Fig. 1J).

3.2.2. Features at stroke level: Normalized jerk, stroke duration and size

As reported in other works (Broderick et al., 2009; Teulings et al., 1997) we found that normalized jerk of PD patients significantly differs from that of the healthy controls ($F(2,87) = 10.62$, $p < 10^{-4}$) in drawing the *writing l-loops* (Fig. 6A). We found that mean normalized jerk of PD patients while drawing the *writing l-loop* is significantly higher than the mean normalized jerk of both young (one tailed *t*-test, $p < 0.01$) and elderly controls ($p < 0.01$, one tailed *t*-test) performing the same task. Normalized jerk of healthy controls increased when they wrote the *novel l-loop*, becoming higher than that measured in PD, but we found no significant difference between healthy controls and PD patients ($F(2,87) = 2.91$, $p > 0.05$).

Mean stroke duration of PD patients drawing the *writing l-loop* was significantly different from the mean stroke duration of healthy controls drawing the *writing l-loop* ($F(2,87) = 22.43$, $p < 10^{-5}$) (Fig. 6B). Indeed, we found that PD patients stroke duration was significantly higher than the mean stroke duration of young ($p < 0.001$, one tailed *t*-test) and elderly controls ($p < 0.001$, one tailed *t*-test) when drawing the *writing l-loops*. Mean stroke duration increased both for young and elderly controls when drawing the *novel l-loop*, and we found no significant difference between the mean stroke duration of healthy controls performing the *novel l-loop* and the mean stroke duration PD patients performing the *writing l-loop* ($p > 0.2$, two tailed *t*-test).

Eventually, mean stroke size of PD patients drawing the *writing l-loop* was significantly different from the mean stroke size of healthy controls drawing the *writing l-loop* ($F(2,87) = 68.77$, $p < 10^{-5}$) and the *novel l-loop* ($F(2,87) = 26.07$, $p < 10^{-5}$) (Fig. 6C). Indeed, although the mean stroke size produced by healthy controls decreased while they drew *novel l-loops*, the mean stroke size produced by PD patients was still significantly lower than the mean stroke size produced by young and elderly controls ($p < 0.001$, one tailed *t*-test).

3.2.3. Features at segmentation points level: Absolute acceleration

Focusing the analysis at the segmentation points level we found that, as for trace level, the mean absolute acceleration of PD patients drawing the *writing l-loop* is significantly lower than mean absolute acceleration of healthy controls ($F(2,87) = 36.15$, $p < 10^{-5}$) (Fig. 7A). Similarly, looking at the absolute acceleration measured at the *regular* segmentation points of the *novel l-loop* (i.e. the segmentation points that appears also in the *writing l-loop*) we found significant difference among groups ($F(2,87) = 11.99$, $p < 10^{-5}$) (Fig. 7B). Particularly, we found that PD patients had still significantly lower mean absolute acceleration than both young ($p < 0.001$, one tailed *t*-test) and elderly controls ($p < 0.01$, one tailed *t*-test). However, we found that the mean absolute acceleration of healthy controls measured at the *novel* SPs (i.e. those appearing close to the start/end of the l-loop) appearing in the *novel l-loops* was not significantly different from that measured at the regular SPs in PD ($F(2,87) = 0.59$, $p > 0.5$).

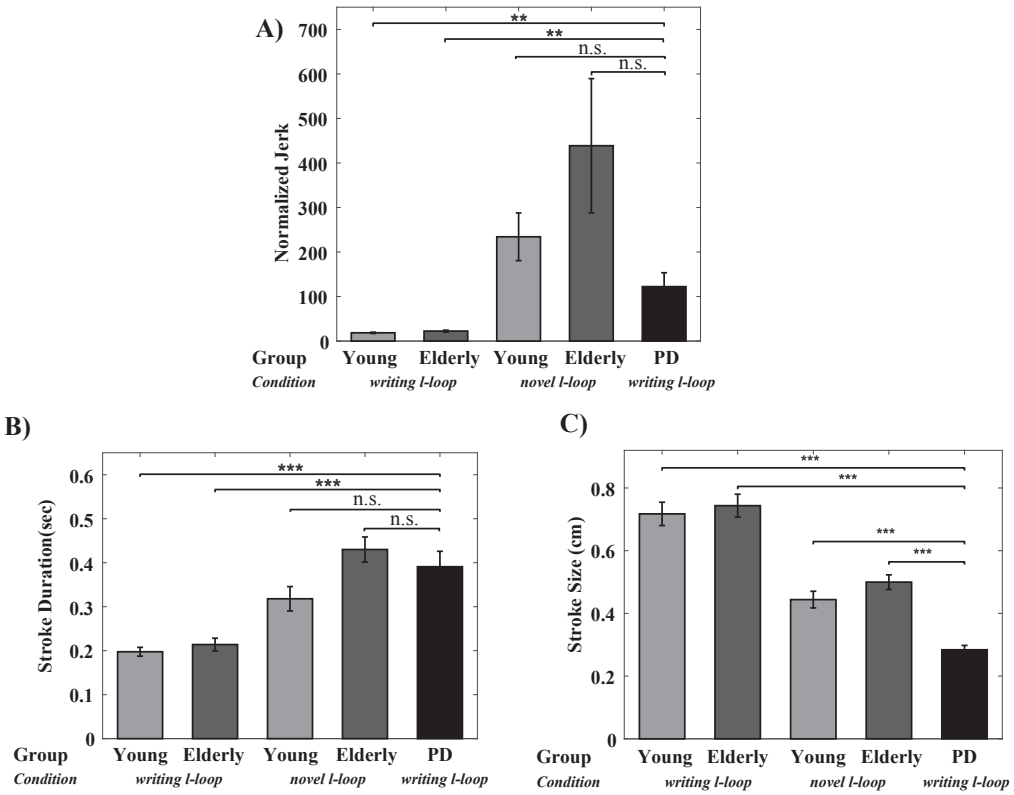

Fig. 6. Features at stroke level. Values are reported in terms of (mean ± SEM) across subjects for each group and condition. A) Comparison between mean normalized jerk of healthy controls drawing the writing l-loop and the novel l-loop and the mean normalized jerk of PD patients drawing the writing l-loop. B) Comparison between mean stroke duration of healthy controls drawing the writing l-loop and the novel l-loop and the mean stroke duration of PD patients drawing the writing l-loop. C) Comparison between mean stroke size of healthy controls drawing the writing l-loop and the novel l-loop and the mean stroke size of PD patients drawing the writing l-loop. Stars represent the results of FDR (false discovery rate) corrected *t*-tests ($^{**}p < 0.01$, $^{***}p < 0.001$, n.s. not significant).

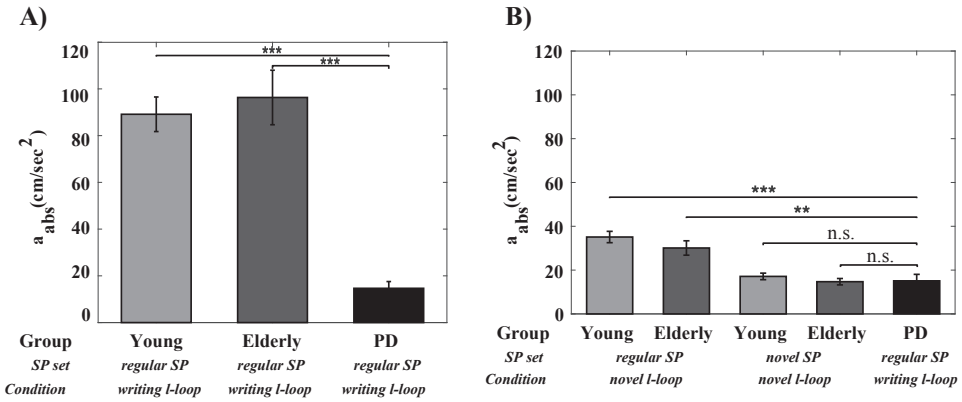

Fig. 7. Absolute acceleration (mean ± SEM) measured at different sets of segmentation points. A) Comparison among the absolute acceleration measured in the proximity of regular segmentation points appearing in the writing l-loop drawn by healthy controls and patients. B) Comparison between the absolute acceleration measured in the proximity of regular and novel segmentation points appearing in the novel l-loop drawn by healthy controls and the absolute acceleration measured in the proximity of regular segmentation points appearing in the writing l-loop drawn by patients. Stars represent the results of FDR (false discovery rate) corrected one tailed *t*-tests ($^{**}p < 0.01$, $^{***}p < 0.001$, n.s. not significant).

4. Discussion

We present a novel experimental paradigm, aimed at eliciting non-automated movements in proficient writers for emulating the early learning stage of a stroke sequence.

We asked to healthy writers to produce a sequence of strokes representing a familiar shape, but using a motor plan that is different from that they are used to, so that the writers had no knowledge of the fine-tuned parameters for modulating the force of the fingers and the wrist in order to obtain the same shape. We then compared, at trace, stroke and segmentation points level, the kinematic features of the handwriting traces produced by the writers using skilled and unskilled movements.

We supposed that drawing a familiar shape, such as a cursive 'l-loop', through an unfamiliar motor plan, that is changing the way the loop is drawn, corresponds to changing the learned set of movements commonly used for drawing the shape, and therefore acquire a novel sequence of target points to reach and, subsequently, achieve the fine-tuning of the motor plan parameters. Segmentation points represent the starting/ending points of the elementary movements composing the handwriting (Plamondon & Maarse, 1989), therefore can be considered a good approximation of the sequence of target points the writers reached for completing the task. Looking at the sequence of strokes composing the *writing l-loop* and the *novel l-loop* reported in Fig. 1, we observed that further segmentation points, and thus new strokes, appeared close to the start/end of the loop, where the writer had to change the sequence of movements needed to draw the shape. *Novel l-loops* were characterized by greater trace decomposition and, additionally, we found a significant decrease in healthy controls performance when executing the *novel l-loop* compared to the *writing l-loop*, indicating that writers had not still acquired the fine tuning of the motor program involved in the task. Indeed, the *novel l-loop* task negatively affected motor coordination in healthy writers and caused a significant decrease in the acceleration measured at the segmentation points in which the writer had to reacquire the fine-tuned parameters for producing the task. Taken together, these results show that the adopted paradigm, consisting in producing a familiar shape using a different motor plan, seems able to simulate the early learning stage of a sequence of strokes. These findings suggest that the proposed paradigm could be useful for evaluating the handwriting learning abilities in children, since it allows to compare long-term trained movements and novel movements. The detection of performance similarities in the two conditions would indicate deficits in handwriting learning abilities.

Based on the hypothesis that the fine tuning of the motor plan parameters involved in the handwriting production is impaired in PD patients, we expected that they perform handwriting as they were in the early stages of the learning process. Moreover, since learning is impaired in PD (Krebs et al., 2001; Roncacci, Troisi, Carlesimo, Nocentini, & Caltagirone, 1996; Worringham & Stelmach, 1990), their performance remain poor.

Therefore, we used the proposed paradigm for examining the differences and the similarities in the motor planning of loop shape between PD patients and healthy subjects. Looking at the difference in temporal and kinematic features between patients and controls when performing the familiar motor plan, we found that, in performing a familiar motor plan, controls showed better performance than patients, with elderly controls performing slightly worse than young controls. In particular, PD patients showed significantly lower mean velocity and acceleration both at trace and segmentation points level, significantly higher normalized jerk and stroke duration and significantly shorter stroke size. Our results are in accordance with previous works (Broderick et al., 2009; Teulings & Stelmach, 1991; Van Gemmert et al., 1999), which showed that PD patients have reduced capability in coordinating speed and amplitude of movements and controlling force production compared to healthy controls. However, performance of the healthy controls significantly decreased when they drew the *novel l-loop*, becoming similar to those observed in handwriting production of PD patients. We observed that the acceleration profile associated to the *novel l-loop* written by the healthy subjects was characterized by multiple accelerations and decelerations, as observed in the acceleration profile of the *writing l-loop* performed by the PD patients, and also reported by others (Teulings et al., 1997; Tucha et al., 2006; Van Gemmert et al., 2003).

Although we found a significant decrease in healthy controls performance when executing the novel motor plan, feature comparisons made at trace level showed that the mean velocity and acceleration of PD patients were still lower than the mean velocity and acceleration of healthy controls, as expected. We postulate that such a difference can be explained by considering that the novel motor plan we asked controls to adopt for drawing the same shape contained both known and novel movements, and the fine tuning of the former has already been learned and used when performing the novel task.

In order to separate the measure of the kinematic features associated to the ordinary and the novel parts composing the motor plan for drawing the *novel l-loop*, we compared the mean absolute acceleration measured in the proximity of two sets of segmentation points: regular segmentation points (those appearing both in the writing and novel l-loop ink trace) and novel segmentation points (those appearing only in the novel l-loop ink trace).

Looking at the regular SPs, we observed that, as for trace level, PD patients showed significantly lower mean absolute acceleration than controls, but the mean absolute acceleration measured at novel SPs in healthy controls traces was not significantly different from the mean absolute acceleration measured at regular SPs in PD patients' traces.

We used the normalized jerk for analyzing writer coordination: as it measures the rate of change of acceleration (normalized for stroke size and duration), higher normalized jerk corresponds to worst coordination and therefore reduced ability of controlling force. Healthy groups showed increased normalized jerk when performing the *novel l-loop* that did not significantly differ from the normalized jerk of PD patients.

We also observed that drawing the *novel l-loop* affects stroke size in healthy controls, but this could be simply due to the increased number of strokes needed to perform the same shape. Indeed, looking at the sequence of strokes adopted for drawing the same shape with two different motor plans, we observed that the mean number of strokes produced by healthy controls for drawing *novel l-loops* (young controls mean: 4.2; elderly controls mean: 4.1) was higher than that produced by the same groups for drawing *writing l-loops* (mean: 2.1 both for young and elderly controls) and higher than the mean number of strokes produced by the PD patients while drawing the *writing l-loops* (mean: 2.6). However, we found that the mean size of the strokes drawn by the healthy controls remains significantly higher than the mean size of the strokes drawn by the PD patients. Moreover, we observed that the mean stroke duration increased both for young and elderly controls when drawing the *novel l-loop*, and stroke duration of the elderly controls became longer than the stroke duration of the PD patients, even though we found no significant difference between stroke duration of healthy

controls and patients.

For providing some guidelines for future work, we conducted preliminary experiments on a small sample of PD patients, to whom we asked to write both writing and novel l-loops. We enrolled eight right-handed PD patients (Edinburg Handedness Inventory (Oldfield, 1971); handedness score > 0.5) in the early stage of the disease (disease duration ≤3 years, mean:1.8-sd:0.8), unilaterally affected by the disease (H&Y = 1). Preliminary results, obtained by comparing PD kinematic features to eight age and education matched healthy participants, extracted from those used in the main analysis, confirm the results of the main analysis, showing that healthy subjects perform better than PD in writing conditions, displaying both higher speed and acceleration ($p < 0.01$, one tailed *t*-test) and lower normalized jerk ($p < 0.05$, one tailed *t*-test). More important, for the novel writing task, we found no significant difference between performance of PD patients and age matched healthy participants in terms of speed ($p > 0.3$, two tailed *t*-test), acceleration ($p > 0.2$, two tailed *t*-test) and normalized jerk ($p > 0.8$, two tailed *t*-test).

Results obtained in the main analysis and preliminary results obtained from the ongoing study suggest that the fine tuning of the motor parameters is affected in PD, leading to the observed deficits in executing both novel tasks (reduced learning performance compared to controls) and previously acquired task (impaired motor coordination and force production compared to controls). Our conclusion is also consistent with the view that basal ganglia play an important role in learning, selection and temporal/spatial organization of group of motor commands (Hikosaka, 1991; Houk, 2005), and their dysfunction in PD patients could be related to impaired retention of the fine-tuned motor plan parameters involved in the execution of habitual motor tasks.

Further support to our conclusion is provided by the results of a recent study (Nackaerts et al., 2017) aimed at reducing micrographia in PD patients through amplitude training (with the help of visual cues). Several studies showed that amplitude training reduces micrographia in PD patients (Nackaerts et al., 2013). However, the study of Nackaerts et al. reported reduced micrographia, but invariant speed performance and deteriorated performance in terms of fluency and stroke duration. Our results suggest that rehabilitation techniques adopted so far were successful in reducing micrographia in PD patients since the correct sequence of target points for performing handwriting were externally provided, reducing the involvement of basal ganglia in the learning process and increasing the role of the cerebellum. On the other hand, these techniques failed in improving motor performance since PD patients are unable to achieve the fine-tuning of the motor parameters by exploiting only external visual cues.

Therefore, further investigation is needed for identifying novel rehabilitation procedures for improving writing performance in terms of speed and coordination, aimed at providing an alternative “learning root” of the fine-tuned motor parameters.

In order to provide some insights for the design of an effective rehabilitation strategy, our future work will be aimed at acquiring further handwriting data from PD patients, and evaluating the performance trend of PD patients in executing both the *writing* and *novel l-loop* tasks with and without target points to reach, with and without time constraints (through auditory cues), and comparing measured parameters in different conditions.

Furthermore, we consider to make a more in depth analysis, by investigating whether the results we got, using the proposed paradigm, still hold when the tasks are performed by PD patients at different disease stages (in terms of disease duration, H&Y index and UPDRS-III values), and with or without cognitive impairments.

Finally, in order to provide more evidence that the proposed paradigm emulates the early learning stage of handwriting, future work will be aimed at evaluating the performance of proficient writes in performing the novel task over time. We expected that, as the training of *novel l-loops* proceeds, performance of healthy controls will resemble those measured in the *writing l-loops*, since we have already observed an increasing trend in performance from the first to the last trial produced by the healthy groups, although the increase we found was not significant, possibly because of the reduced number of repetitions of the task.

5. Conclusion

We presented a novel paradigm, in which healthy proficient writers are given the task of producing a sequence of strokes representing a familiar shape, but using a motor plan that is different from the one they are used to. Measured performance (in terms of speed, acceleration and fluency) and ink trace features (presence of novel target points) showed that the proposed paradigm is able to elicit non-automated movements in healthy controls. By exploiting our paradigm, we found some similarities between performance achieved by healthy writers using a novel motor plan and those obtained by PD patients writing the same shape using the habitual motor plan. Furthermore, preliminary results, obtained from an ongoing study, showed no differences between older adults and PDs on performance of the novel-loop. Our analysis suggests that the fine tuning of the motor plan parameters involved in the handwriting production is impaired in PD.

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