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Original Research

Handwriting Movement Abnormalities in Older Adults with Silent Cerebral Small Vessel Disease—A Preliminary Study

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Abstract

Background: The features of cerebral small vessel disease (CSVD) range from occurrence of asymptomatic radiological markers to symptomatic characteristics that include cognitive deficits and gait decline. The aim of the present study was to examine whether handwriting movement is abnormal in older people with CSVD through handwriting and drawing tasks using digitized handwriting kinematic assessment technology. **Methods**: Older subjects (n = 60) were grouped according to Fazekas score, with 16 in the Severe CSVD group, 12 in the Non-severe group and 32 in the Healthy group. Kinematic data were recorded and analyzed during handwriting and drawing tasks: signature; writing of Chinese characters ("正" and "永"); and Archimedes' spiral drawing. **Results**: The Severe CSVD group showed lower velocity and higher tortuosity during signature writing, lower velocity of stroke #4 of "正" and vertical size of "永" than did the Non-severe and Healthy groups. Both Severe CSVD and Non-severe CSVD subjects displayed higher average normalized jerk than did the Healthy group. Partial correlation analysis adjusting for age, gender, education, and mini-mental state evaluation (MMSE) showed that CSVD burden was positively associated with tortuosity of signature and average normalized jerk of Archimedes' spiral, and was negatively associated with velocity of strokes #3 and #4 of "正", as well as vertical size of "永". **Conclusions**: Older adults with CSVD showed abnormal handwriting movement. And the handwriting abnormalities captured by digitized handwriting analysis were correlated with CSVD severity in users of simplified Chinese characters.

Keywords:
aging; cerebral small vessel disease; handwriting analysis; kinematics; magnetic resonance imaging (MRI); white matter hyperintensities

1. Introduction

Cerebral small vessel disease (CSVD) is a common condition that affects the small vessels in the brain and contributes to the development of leukoaraiosis, cerebral microbleeds, recent subcortical lacunar infarcts (clinically symptomatic), lacunes (clinically silent), prominent perivascular spaces, and atrophy lacunar infarcts, etc. [1,2]. CSVD can be quite "covert" in clinical manifestation [3]. Whereas most studies focused on dysfunction of the lower extremities in CSVD patients [4,5], only a few studies have examined whether silent CSVD patients showed abnormalities in upper extremities [6].

Handwriting and drawing are among the most common activities of daily living. They entail an intricate blend of cognitive, kinesthetic, visuospatial, and motor features [7]. With the development of new technologies in digital handwriting analysis, researchers managed to discover many tiny, but typical characteristics of handwriting and drawing, including size, velocity, fluency, pressure, etc. [8]. Digital handwriting analysis has been used in the early detection of many neurodegenerative diseases, such as Alzheimer's Disease [9], Parkinson Disease [10], and Huntington's Disease [11].

Using an anti-phase, horizontal-line-drawing task, our previous work confirmed that older adults with CSVD exhibit poor bimanual coordination [6]. The aim of the current study was to assess the characteristics of handwriting and drawing tasks in older individuals with silent CSVD using digitized handwriting kinematic analysis.

2. Materials and Methods

2.1 Participants

This is a cross-sectional observational study. From April 1st, 2020 to March 31st. 2021, a total of 16 aged adults (71.25 $\pm$ 5.77 years old) with high CSVD burden (i.e., Severe CSVD group), 12 aged patients (69.00 $\pm$ 8.60 years old) with moderate burden CSVD (Non-severe CSVD), and 32 mild burden CSVD or age-matched controls (aged 65.66 $\pm$ 4.75 years old) (Healthy group) were recruited and screened by 3.0 T magnetic resonance imaging (MRI) brain scan and grouped according to the Fazekas scale [12]. The subjects were grouped according to the severity of white matter hyperintensities: Grade 3 (confluent lesion) to the Severe CSVD group; Grade 2 (early confluent lesion) to the Non-severe CSVD group, Grade 1 (punctate lesions) and Grade 0 (no lesion) were assigned to the Healthy group. Exclusion criteria were: intracerebral hemorrhage; major psychiatric disorders; non-vascular dementia; psychotropic drugs use; multisystem diseases; MRI contraindication; overt neurologic findings that would impair handwriting, such as hemiplegic paralysis, numbness, unilateral neglect, etc.; and other causes of leukoencephalopathy (e.g., demyelination, genetic and immune factors). Basic demographic data, such as age, gender, identity, educational status and mini-mental state evaluation (MMSE) score, were collected from all participants.

2.2 Magnetic Resonance Imaging (MRI) Measurements

A 3.0 T MRI brain scan (Discovery MR750, GE Healthcare, Chicago, IL, USA) displayed white matter lesions reflecting the degree of CSVD. Brain MRI (slice and interslice thicknesses of 5 mm and 1.5 mm, respectively) was carried out as follows: T1 fluid-attenuated inversion recovery (repetition time (TR), 1750 milliseconds; echo time (TE), 23 milliseconds; T1, 780 milliseconds; field of view (FOV), 24 cm) and T2- weighted imaging (TR, 7498 milliseconds; TE, 105 milliseconds; FOV, 24 cm) sequences. The assessors were blinded to imaging findings.

2.3 Equipment

The subjects wrote and drew with a non-inking Wacom Pro Pen on Wacom Cintiq DTK1661KOF display digitizing tablets (100001967235, Heguan Technology Co., Ltd., Beijing, China). The tablet was connected via USB port to a notebook computer running MovAlyzeR6 handwriting movement software (NeuroScript LLC, Tempe, AZ, USA; www.neuroscript.net). The display tablets had an active area of 34.8 cm × 19.8 cm, a resolution of 0.001 cm, an accuracy of 0.01 cm, and a sampling rate of 100 Hz.

2.4 Handwriting and Drawing Tasks

Subjects completed the procedure for quantifying handwriting and drawing movements consisting of 4 patterns: signature (pattern 1); Chinese character "正" (pattern 2); Chinese character "永" (pattern 3); and Archimedes' spiral (pattern 4). All tasks were completed with the participant's dominant hand. The tasks were administered in random order with a fixed block of 3 trials for each.

2.5 Handwriting Analysis Variables

2.5.1 Pattern 1

The signature should be in cursive, and the variables included: average absolute velocity (AAV); average pen pressure (APP); and in-air length tortuosity between characters (TOR).

The signature has been commonly used as a handwriting task in numerous studies [8,11]. Because Chinese characters have their own shape, we decided to use TOR in segmentation between family name and given name during writing the full name, as a potential indicative parameter. TOR, defined by the ratio of the arc length to the Euclidean distance between end points, is a measure of curvature, and therefore indexes the smoothness of a specific writing output [13]. A highly tortuous curve has several bends or curves, whereas a low tortuous curve is one with relatively wide loops/curves and more straightness. Details were shown in Fig. 1A. The equation of TOR = 1 – Absolute Size / Road Length.

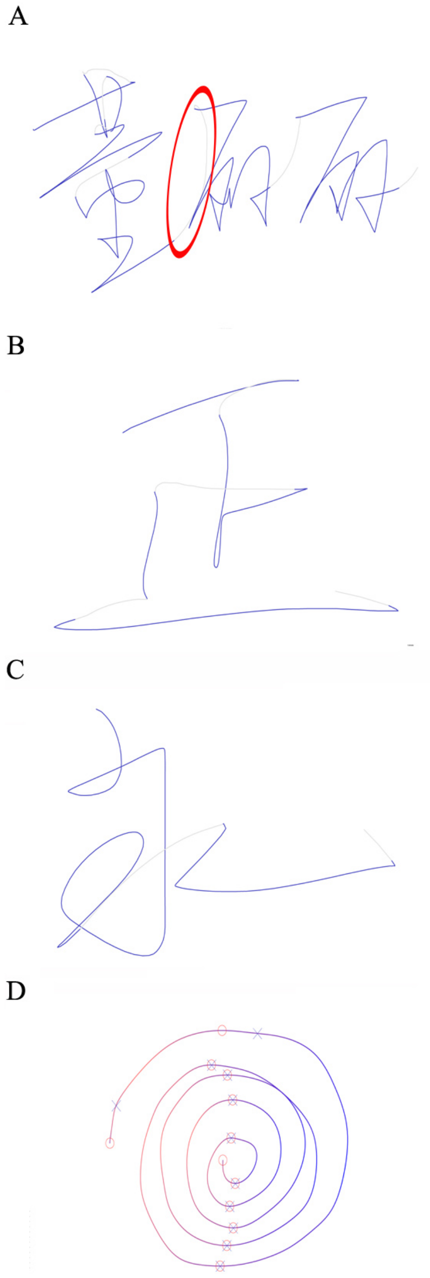

Fig. 1. Examples of the 4 handwriting and drawing tasks completed by a subject. (A) The figure shows performance on the signature. Tortuosity (TOR) is derived from the in-air part of between family name and given name (red loop area). (B) Chinese character "正". (C) Chinese character "永". (D) Archimedes' spiral.

2.5.2 Pattern 2

"正" was printed in simplified Chinese, and the variables included AAV of stroke #3 (AAV#3) and stroke #4 (AAV#4), APP of Stroke #3 (APP#3), and Stroke #4 (APP#4).

"正" (pronounced "Zheng") is a typical, simple, and commonly used Chinese character. It has been selected as a candidate in writing tasks in previous Chinese handwriting analysis studies [14,15]. Researchers decided to use "正" as a writing task because it is "square-like" and composed of five strokes, all of which are horizonal (stroke #1, #3, #5, from left to right) or vertical (stroke #2, #4, from up to down). As has shown in Fig. 1B, stroke #3 of "正" is a horizonal movement (from left to right) of the pen tip that is shorter than stroke #1 and stroke #5. Stroke #4 of "正" is a vertical movement (from up to down) of the pen tip and is shorter than stroke #2. In other words, strokes #3 and #4 need more control than other strokes of "正".

2.5.3 Pattern 3

"永" was printed in simplified cursive Chinese, and the variables included vertical size (VS) and horizontal size (HS) of "永". "永" was selected because the character contains eight basic forms of stroke [16]. Details are shown in Fig. 1C.

2.5.4 Pattern 4

Archimedes' spiral should be completed using than eight vertical strokes, and variables include average normalized jerk (ANJ). Details are shown in Fig. 1D. ANJ is unitless as it is normalized for stroke duration and length, and higher ANJ score was indicative of dysfluent writing movements [17].

ANJ is the average normalized jerk per stroke where normalized jerk per up- or down-stroke was calculated using the following equation [18]. Jerk, i.e., the time derivative of acceleration, is proportional with the force exerted to move the pen. As the time-varying *jerk(t)* is a vector ($jerk_x(t), jerk_y$(t)) can have any direction, we use the scalar ½ $jerk^2(t)$. This function was integrated across one up- or down stroke, hence ½ $\int dt\ jerk^2(t)$. As this value varies dramatically with stroke duration and stroke length, we normalized by multiplying with $duration^5$ / $length^2$. This will make normalized jerk unitless. The square root is taken to reduce the dynamic range. A perfectly fluent trial, e.g., a constant-velocity circle, should yield normalized jerk 10.96 (= π^3 / $2^{1.5}$). Any dysfluencies in the form of accelerations and decelerations will result in much higher values:

$$\sqrt{½ \int \mathrm{d}t\, jerk^2(t) \times duration^5 / length^2} \quad (1)$$

ANJ is then calculated by averaging normalized jerk across all strokes of a trial. Because variances were proportional to the mean scores for ANJ, ANJ scores were transformed using the natural logarithm to remove inequality of variance [17].

2.6 Statistical Analysis

Group differences in clinical and demographic data were analyzed by one-way analysis of variance (ANOVA). Further comparison of the adjusted means was carried out using a least-squares difference (LSD) test if necessary. Partial correlation was used to investigate the correlation between handwriting analysis variables and CSVD severity, adjusting for age, gender, education, and MMSE score. The significance threshold was set at $p \leq 0.05$ in group comparison and in correlation tests. Analysis was carried out using SPSS 25.0 software (IBM Corp., Armonk, NY, USA).

3. Results

3.1 Comparisons of Demographic Data

Severe CSVD, Non-severe CSVD, and Healthy groups did not show significant differences in gender composition and MMSE, whereas, Severe CSVD subjects were older and had a lower educational level, statistically, than the other two groups. Details were shown in Table 1.

3.2 Comparisons of Handwriting Features

The groups did not differ significantly in APP (507.65 ± 115.14 vs 516.18 ± 76.30 vs 507.57 ± 83.45) on signature. On the contrary, Severe CSVD group patients showed lower AAV (1.23 ± 0.34 vs 1.82 ± 1.04 vs 1.84 ± 0.72, *omnibus* p = 0.022) and higher Tortuosity (0.43 ± 0.22 vs 0.28 ± 0.18 vs 0.22 ± 0.17, *omnibus* p = 0.003) than did the Non-severe CSVD and Healthy groups. Details are shown in Table 2. For pattern 2, AAV#4 was significantly lower in the Severe CSVD group than in the Non-severe CSVD and Healthy groups (0.93 ± 0.30 vs 1.39 ± 0.72 vs 1.47 ± 0.59, *omnibus* p = 0.008). We did not find obvious differences in AAV#3 (0.83 ± 0.26 vs 0.92 ± 0.25 vs 1.09 ± 0.54), APP#3 (542.96 ± 120.74 vs 539.93 ± 75.79 vs 509.73 ± 98.83), and APP#4 (543.49 ± 109.22 vs 521.09 ± 79.77 vs 525.95 ± 96.78) among groups (Table 2). For pattern 3, Severe CSVD patients demonstrated statistically lower VS than did the Non-severe CSVD group patients and Healthy group (1233.25 ± 406.58 vs 1351.17 ± 383.91 vs 1566.15 ± 394.91, *omnibus* p = 0.022) during they wrote "永" character in cursive version. However, the significance disappeared in HS (1174.35 ± 450.89 vs 1345.53 ± 3424.27 vs 1392.40 ± 516.45, *omnibus* p = 0.341) (shown in Table 2). For pattern 4, we found remarkable higher Log (ANJ) in Severe CSVD group patients relative to Non-severe CSVD and healthy group individuals (1.54 ± 0.24 vs 1.74 ± 0.32 vs 1.72 ± 0.27, *omnibus* p = 0.027) during Archimedes' spiral drawing (Table 2).

Table 1. Clinical and demographic characteristics.

	Severe CSVD (n = 16)	Non-severe CSVD (n = 12)	Healthy (n = 32)	p value
Age in years, mean (SD)	71.25 (5.77)	69.00 (8.60)	65.66 (4.75)	0.006*#
Male/Female	9/7	4/8	18/14	0.364
Education in years, mean (SD)	9.69 (4.00)	12.67 (3.00)	11.88 (2.80)	0.034*#
MMSE score, mean (SD)	28.84 (1.05)	28.50 (1.50)	28.19 (1.60)	0.252

Notes: *$p < 0.05$ severe CSVD *vs.* non-severe CSVD, #$p < 0.05$ severe CSVD *vs.* healthy.

Abbreviations: MMSE, mini-mental state examination; CSVD, cerebral small vessel disease; SD, standard deviation.

Table 2. Handwriting analysis variables.

	Severe CSVD (n = 16)	Non-severe CSVD (n = 12)	Healthy (n = 32)	p value
Pattern 1				
AAV	1.23 (0.34)	1.82 (1.04)	1.84 (0.72)	0.022*#
APP	507.65 (115.14)	516.18 (76.30)	507.57 (83.45)	0.959
TOR	0.43 (0.22)	0.28 (0.18)	0.22 (0.17)	0.003*#
Pattern 2				
AAV#3	0.83 (0.26)	0.92 (0.25)	1.09 (0.54)	0.130
APP#3	542.96 (120.74)	539.93 (75.79)	509.73 (98.83)	0.479
AAV#4	0.93 (0.30)	1.39 (0.72)	1.47 (0.59)	0.008*#
APP#4	543.49 (109.22)	521.09 (79.77)	525.95 (96.78)	0.794
Pattern 3				
VS	1233.25 (406.58)	1351.17 (383.91)	1566.15 (394.91)	0.022*#
HS	1174.35 (450.89)	1345.53 (424.27)	1392.40 (516.45)	0.341
Pattern 4				
Log (ANJ)	1.54 (0.24)	1.74 (0.32)	1.72 (0.27)	0.027#△

Notes: Mean (SD), *$p < 0.05$ Severe CSVD *vs.* Non-severe CSVD, #$p < 0.05$ severe CSVD *vs.* healthy, △$p < 0.05$ Non-severe CSVD *vs.* healthy.

Abbreviations: CSVD, cerebral small vessel disease; AAV, average absolute velocity; APP, average pen pressure; TOR, tortuosity; AVV#3, average absolute velocity of stroke #3 of "正"; APP#3 average pen pressure of stroke #3 of "正"; AAV#4, average absolute velocity of stroke #4 of "正"; APP#4 average pen pressure of stroke #4 of "正"; VS, vertical size of "永"; HS, horizontal size of "永"; Log (ANJ), nature logarithm transformation of average normalized jerk.

3.3 Correlation between CSVD Severity and Handwriting Analysis Variables

Partial correlation, controlling for age, gender, education, and MMSE score, was used to analyze the relationship between CSVD severity and handwriting analysis variables. Fazekas score was positively associated with the TOR (r = 0.409, p = 0.002) and Log (ANJ) (r = 0.332, p = 0.012), and was negatively associated with AAV#3 (r = –0.314, p = 0.019), AAV#4 (r = –0.332, p = 0.012), and VS of "永" (r = –0.324, p = 0.015).

4. Discussion

In the current study, we managed to find out handwriting movement abnormalities in older adults with silent CSVD. First, the Severe CSVD group showed lower velocity and higher tortuosity during signature writing, lower velocity of stroke #4 of "正" and vertical size of "永" than did the Non-severe and Healthy groups. Second, both Severe CSVD and Non-severe CSVD subjects displayed higher average normalized jerk than did the Healthy group.

In general, a signature is considered to be an everyday life activity, and requires little thinking or in-air time [19]. Caligiuri *et al.* [20] reported that signature formation did not differ in handwriting kinematics in aged populations of English speakers younger than 79 years old. However, for those 80 or older, signatures featured lower velocity and pen pressure. In Hebrew speakers, Rosenblum *et al.* [21] found that Parkinson's patients showed lower velocity and pen pressure. In accordance with these findings, our results indicated that old patients with severe CSVD showed lower velocity than did our other two groups of subjects, but we did not find obvious differences in pen pressure. This can be explained by the fact that Chinese characters use a distinctly different writing style from that used for alphabetic letters.

Besides velocity and pen pressure, another variable, TOR, between the family name and the given name was collected. TOR was first reported by Grace *et al.* [13]; it is found in the lower handwriting quality of children diagnosed with autism spectrum disorder (ASD). Our previous study confirmed that air-time percentage during the digital Clock Drawing Test was associated with executive dysfunction in older adults with CSVD [1]. TOR of the signature was remarkably higher in the Severe CSVD group in the current study, and associated with CSVD severity.

"正" writing is a commonly used task to test for micrographia in Parkinson's patients in East-Asian countries, and a recent study revealed that "正" can be used as an indicative task for early detection of Alzheimer's disease or mild cognitive impairment [14]. The decrease in handwriting size in the horizontal direction, manifested by Parkinson's patients, was associated with wrist extension abnormalities. As has been reported and explained by Ma *et al.* [22], the fulfilling Strokes #3 and #4 of "正" require pure wrist and finger movements, respectively. It is interesting to note that in the current study, AAV#4, instead of AAV#3, was significantly lower in Severe CSVD subjects than in the Non-severe CSVD and Healthy groups. In addition, the Severe CSVD group demonstrated statistically lower VS than did the Healthy group. These findings about vertical directionality suggested that Severe CSVD patients might be suffered from finger-movement abnormalities. In fact, several studies in recent years have found that CSVD patients showed dysfunction in finger-tapping tasks [23,24].

ANJ is a well-accepted indicator of dysfluent writing movements [18]. Higher ANJ has been found in patients with Parkinson's disease, drug-induced parkinsonism, and tardive dyskinesia [10,17,25], reflecting an impairment of motor functions. In line with these findings, we found that ANJ was higher in both the Severe CSVD and Non-severe groups than in the Healthy group. This suggests that older CSVD patients exhibit fine-motor dysfunctions.

By using the Purdue pegboard and the grooved pegboard, previous investigators have shown that CSVD burden was associated with manual dexterity [26,27]. In agreement with these findings, the present study demonstrated that higher CSVD severity was associated with several handwriting analysis variables, including higher TOR of the signature, and dysfluency of Archimedes' spiral drawing, as well as lower velocity of "正" and vertical size of "永". These results indicate that digital handwriting features reflect CSVD burden.

Our results need to be considered in the context of study limitations. First, the sample size was not large. Second, common patterns used in existing handwriting analysis such as loops and circles, were not included in our handwriting and drawing tasks. In fact, we noticed that most subjects recruited in the present study were users of pure simplified Chinese, and were not familiar with loops and circles. Any unnecessary strangeness and hesitation may impact the accuracy of digital handwriting analysis, and we are still searching for the most suitable handwriting and drawing tasks for Chinese users, especially older persons.

5. Conclusions

Older adults with silent CSVD showed abnormal performance of handwriting movement during handwriting and drawing tasks, which could be captured by digitized kinematic technologies. CSVD severity was positive associated with tortuosity of signature and ANJ of Archimedes' spiral, and negatively associated with the velocity of strokes #3 and #4 of "正", and the vertical size of "永". These results suggest that deficits in digital handwriting analysis were associated with CSVD burden among users of simplified Chinese characters.

In future research, handwriting analysis might become an important movement test for those CSVD patients who cannot complete walking, or have high risk of falling. Because of the cross-cultural phenomenon of handwriting, the writing systems of different nations are not always the same. More detailed studies are still needed to find out a suitable task for the other language users [28]. In addition, a new emerging feature of cerebral small vessel disease, the progressive atrophy of grey matter [29], was reported to be associated with bimanual coordination [30], thus, investigators should try to discover the potential handwriting movement abnormalities in silent CSVD patients with the progressive atrophy of grey matter.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to that the signature has subject's private information. But are available from the corresponding author on reasonable request.

Author Contributions

YH designed the research study. CX performed the research. HT provided help and advice on analyzed the data. HZ conducted a literature review. LC analyzed data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All participants provided written informed consent while the study protocol was approved by the ethics committee of the Seventh Medical Center of People's Liberation Army (PLA) General Hospital, Beijing, China (the ethical approval code is 2020-104).

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Conflict of Interest

The co-author Hans-Leo Teulings is the owner of the company NeuroScript that developed and markets the MovAlyzeR handwriting movement software. All authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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