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Title: Digital Handwriting Analysis of Characters in Chinese Patients with Mild Cognitive Impairment

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Author Questionnaire

1. Microscopy: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or similar? **N**

2. Software: Does the part of your protocol being filmed demonstrate software usage? **Y**

3. Interview statements: Considering the Covid-19-imposed mask-wearing and social distancing recommendations, which interview statement filming option is the most appropriate for your group? **Please select one**.

☒ Interviewees self-record interview statements outside of the filming date. JoVE can provide support for this option.

4. Filming location: Will the filming need to take place in multiple locations (greater than walking distance)? **N**

Protocol Length
Number of Shots: **24**

Introduction

1. Introductory Interview Statements

REQUIRED:

1.1. **Yonghua Huang**: Handwriting analysis has been used to detect cognitive and motor dysfunctions. Some aspects of handwriting difficulties can be an indicator for MCI and related to disease progression **[1]**.

1.1.1. LAB MEDIA: To be provided by Authors: Named talent says the statement above in an interview-style shot, looking slightly off-camera

REQUIRED:

1.2. **Hóngyi Zhào**: The main advantage of this study is that it uses a digital handwriting analysis system for simplified Chinese character users **[1]**.

1.2.1. LAB MEDIA: To be provided by Authors: Named talent says the statement above in an interview-style shot, looking slightly off-camera

OPTIONAL:

1.3. **Hóngyi Zhào**: This method can be also applied to the detection of psychomotor retardation in patients with depression, schizophrenia, or other psychiatric disorders who are simplified Chinese users **[1]**.

1.3.1. LAB MEDIA: To be provided by Authors: Named talent says the statement above in an interview-style shot, looking slightly off-camera

Introduction of Demonstrator on Camera

1.4. Demonstrating the procedure will be Cuiqiao Xia, a doctor from my laboratory **[1][2]**.

1.4.1. LAB MEDIA: To be provided by Authors: Author saying the above
1.4.2. The named demonstrator(s) looks up from workbench or desk or microscope and acknowledges the camera

Ethics Title Card

1.5. Procedures involving human subjects have been approved by the Academic Ethics Committee of the Biological Sciences Division of Seventh Medical Center of PLA General Hospital in Beijing, China.

Protocol

2. Method Development

2.1. Before beginning an analysis, select a 410- x 265- x 17.5-millimeter USB digitizer with a 3840- x 2160-dot spatial resolution, a 0.9- x 0.9-millimeter pixel size, a 30-millisecond temporal resolution, and an 8192-pressure level **[1]** and a handheld stylus pen for the handwriting movements **[2]**.

2.1.1. WIDE: Talent picking up/checking out digitizer

2.1.2. Talent picking up/checking out stylus OR Shot of digitizer, then stylus being placed next to digitizer

2.2. Connect a laptop PC to the digitizer to collect and exhibit the handwriting traces **[1]** and install an appropriate data recording, processing, and analyzing software program **[2]**.

2.2.1. Talent connecting laptop to digitizer
2.2.2. Talent opening software, with monitor visible in frame

2.3. Recruit mild cognitive impairment Participants who present with a memory complaint, an objectively impaired memory function, intact activities of daily living, and the absence of dementia **[1-TXT]**.

2.3.1. Talent shaking nodding/ waving/similar introductory gesture with Participant **TEXT: See text for full participant inclusion/exclusion criteria**

3. Handwriting Task

3.1. To perform a handwriting task, use the stylus to create sample Chinese characters in the writing area of the digitizer **[1]**.

3.1.1. WIDE: Talent writing character *Videographer: Important step*

3.2. Give the digitizer and stylus to the Participant **[1]** and instruct the Participant to use the stylus to write their name in Chinese with the dominant hand while holding the digitizer in a comfortable position **[2]**.

3.2.1. Talent giving digitizer to Participant *Videographer: Important step*
3.2.2. Participant writing name *Videographer: Important step*

3.3. Next, instruct the Participant to use the dominant hand to write the printed version of the Chinese character "Zheng" **[1]**.

3.3.1. Talent instructing, Participant writing *Videographer: Important step*

3.4. If the character is being written in the wrong stroke order, stop the trial and trace **[1]** and show the subject how to write the character in the correct stroke order **[2]**.

3.4.1. Character being written in wrong stroke order, then trace being stopped *Videographer: Important step*
3.4.2. Talent demonstrating how to write character *Videographer: Important step*

3.5. If any hesitation is derived from a lack of knowledge, stop the trial **[1]** and show the Participant how to write the character correctly **[2-TXT]**.

3.5.1. Participant hesitating/Talent stopping trial *Videographer: Important step*
3.5.2. Character being written correctly *Videographer: Important step* **TEXT: Repeat task x3**

3.6. Then instruct the Participant to use the dominant hand to sign their name in Chinese three times **[1]**.

3.6.1. Talent instructing/Participant signing name *Videographer: Important step*

4. Data Analysis

4.1. To analyze the handwriting task data, in the software analysis program **[1]**, right click on **Experiment** to select **Properties**, **Processing**, and **Segmentation**. In **Segmentation Flags**, click **Add first segmentation at any rate**, **Add last segmentation at any rate**, and **Move segmentation point to nearest pendown if on a penlift [2]**.

4.1.1. WIDE: Talent at computer, opening program, with monitor visible in frame
4.1.2. SCREEN: 4.1.2: 00:03-00:20

4.2. In **Segmentation Methods**, click on **At pendown trajectories** and reset the previously selected **Segmentation Flags** parameters **[1]**.

4.2.1. SCREEN: 4.2.1: 00:02-00:008

4.3. For parameter calculation, in "Zheng", select the Participant and click **Handwriting Trials [1]**.

4.3.1. SCREEN: 4.3.1: 00:01-00:05

4.4. Use the tracing system to trace the handwriting process and stroke order of "Zheng" step by step and locate the segmentation of stroke number 3 of "Zheng" **[1]**. The **Average Absolute Velocity** will be automatically calculated within the **Extracted data [2]**.

4.4.1. SCREEN: 4.3.1: 00:35-00:45
4.4.2. SCREEN: 4.4.1: 00:03-00:11

4.5. Locate the segmentation of stroke number 4 of "Zheng". The software will automatically calculate the **Average Absolute Velocity** for strong number 4 **[1]**.

4.5.1. SCREEN: 4.5.1: 00:04-00:14

4.6. The **Pen Pressure** of each segmentation and **Average Pen Pressure** will also be calculated by the software **[1]**.

4.6.1. SCREEN: 4.6.1: 00:03-00:18 *Video Editor: please speed up*

4.7. Next, select the Participant in "Zheng", click **Handwriting Trials [1]**, and use the tracing system to trace the handwriting process and stroke order of the Participant's signature step by step **[2]**.

4.7.1. SCREEN: 4.7.1: 00:05-00:08
4.7.2. SCREEN: 4.7.1: 00:39-01:01

4.8. Locate the segmentation of the stroke between the characters. The **Absolute Size** and **Road Length** will be calculated **[1]**.

4.8.1. SCREEN: 4.8.1: 00:06-00:34 *Video Editor: please speed up*

4.9. Then use the formula to calculate the in-air length tortuosity in the segmentation between characters **[1-TXT]**.

4.9.1. BLACK TEXT WHITE BACKGROUND: In-air length tortuosity = 1-Absolute Size/Road Length %

Protocol Script Questions

A. Which steps from the protocol are the most important for viewers to see? Please list 4 to 6 individual steps.

3.1.-3.6.

B. What is the single most difficult aspect of this procedure and what do you do to ensure success? Please list 1 or 2 individual steps from the script above.

4.8., 4.9.

Results

5. Results: Representative Subject Demographic and Handwriting Analysis

5.1. As shown in the Table **[1]**, during the writing of the Chinese character "Zheng", elderly subjects with mild cognitive impairment exhibited a lower average absolute velocity of the number 3 **[2]** and number 4 strokes **[3]** and a higher average pen pressure **[4]** compared to healthy elderly subjects **[5]**.

5.1.1. LAB MEDIA: Table 1
5.1.2. LAB MEDIA: Table 1 *Video Editor: please emphasize 1.82 +/- 0.55 data cell*
5.1.3. LAB MEDIA: Table 1 *Video Editor: please emphasize 1.93 +/- 0.50 data cell*
5.1.4. LAB MEDIA: Table 1 *Video Editor: please emphasize 281.99 +/- 37.90 data cell*
5.1.5. LAB MEDIA: Table 1 *Video Editor: please emphasize 2.46 +/- 0.40, 2.61 +/- 0.46, 237.43 +/- 39.77 data cells*

5.2. Additionally, during the signing of Chinese names, the elderly subjects with mild cognitive impairment exhibited a higher in-air length tortuosity in segmentations between the characters **[1]** compared to healthy elderly subjects **[2]**.

5.2.1. LAB MEDIA: Table 1 *Video Editor: please emphasize 31.66 +/- 7.53 data cell*
5.2.2. LAB MEDIA: Table 1 *Video Editor: please emphasize 12.57 +/- 6.96 data cell*

Conclusion

6. Conclusion Interview Statements

6.1. **Hóngyi Zhào**: The most important step is confirming the character legibility. Using "Zheng" as an example, the 3rd stroke should be shorter than the other horizonal strokes **[1]**.

6.1.1. LAB MEDIA: To be provided by Authors: Named talent says the statement above in an interview-style shot, looking slightly off-camera (3.3.)

6.2. **Cuiqiao Xia**: An inappropriate stroke length may give rise to a bias in the detection of the velocity **[1]**.

6.2.1. LAB MEDIA: To be provided by Authors: Named talent says the statement above in an interview-style shot, looking slightly off-camera

6.3. **Yonghua Huang**: This method may be useful for diagnosing motor cognitive risk syndrome and cerebral small vessel disease **[1]**.

6.3.1. LAB MEDIA: To be provided by Authors: Named talent says the statement above in an interview-style shot, looking slightly off-camera