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Title: Evaluation of the Cognitive Performance of Hypertensive Patients with Silent Cerebrovascular Lesions

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Author Questionnaire

1. Microscopy: Does your protocol involve video microscopy, such as filming a complex dissection or microinjection technique? **N**

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

Videographer: All screen capture files provided, do not film

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

Script Length

Number of steps: **31**

Introduction

1. Introductory Interview Statements

REQUIRED:

1.1. **Raymond Tak Fai Cheung**: Silent cerebrovascular lesions can cause various functional impairments and cognitive deficits. However, the distinct effects of each type of lesions on cognitive performance remain unclear **[1]**.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

REQUIRED:

1.2. **Raymond Tak Fai Cheung**: Using both neuropsychological tests and multi-sequence MRI scans, we can assess whether various types of silent cerebrovascular lesions are differentially associated with deficits in specific cognitive domains **[1]**.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

Introduction of Demonstrator on Camera

1.3. **Raymond Tak Fai Cheung**: Demonstrating the study procedures will be done by Junling Gao, my research officer, and Tracy Lam, my technical officer **[1]**~~**[2]**~~. NOTE: (sic)

1.3.1. INTERVIEW: Author saying the above

~~1.3.2. Named demonstrator(s) looks up from workbench or desk or microscope and acknowledges camera~~

Ethics Title Card

1.4. Procedures involving human subjects have been approved by the Institutional Review Board (IRB) at the University of Hong Kong/Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) for human research.

Protocol

2. Neuropsychological Assessments

2.1. To set up a symbol digit modalities test, pair 1-9 digits in numeric order with nine unassociated symbols **[1]** and show a list of the symbols in a random order without the corresponding digits **[2]**.

2.1.1. WIDE: Talent preparing test, with monitor visible in frame
2.1.2. LAB MEDIA: Figure 1C

2.2. Before starting the test, instruct the Participant to fill in the blank with the correctly paired digit below each symbol **[1-TXT]**.

2.2.1. Participant filling in blank(s) **TEXT: Allow participant to check pair legend for reference as necessary**

2.3. Allow the Participant fill in the first 10 blanks as practice **[1]**, pointing out any errors during the practice stage and encouraging the Participant to be correct **[2]**.

2.3.1. Shot of filled in blanks
2.3.2. Talent pointing out error to/encouraging Participant

2.4. When the Participant is ready, start the test, encouraging the Participant to fill in the blanks as quickly and accurately as possible in 90 seconds **[1]**.

2.4.1. Talent timing Participant while Participant fills in blanks

2.5. When the Participant has finished or the time has run out, record the number of correct responses **[1]** and re-start the test, this time having the Participant provide the correctly paired digits verbally **[2-TXT]**.

2.5.1. Talent recording correct responses
2.5.2. Participant reading correct digits **TEXT: Record number of correct oral-SDMT responses**

2.6. To assess verbal fluency, ask the Participant to verbally provide a list of names **[1]** belonging to each of two categories for one minute per category **[2]**.

2.6.1. Participant providing names
2.6.2. Shot of lists

2.7. Then record the total number of names listed for each category **[1]**.

2.7.1. Shot of lists with totals being written for list(s)

3. Visual Silent Cerebrovascular Lesion (SCL) Rating: Silent Lacunes

3.1. To perform visual ratings of the lesions, first import the data into an appropriate medical imaging software program **[1-TXT]** and use the anonymize button to anonymize the participant's information **[2]**.

3.1.1. WIDE: Talent importing data, with keyboard visible in frame **TEXT: Here Osirix DICOM Viewer Lite is used (https://www.osirix-viewer.com)**

3.1.2. SCREEN: 1_silentlacune: 00:10-00:19

3.2. To rate visual silent cerebrovascular lesions, first locate the silent lacunes in T1-weighted horizontal images, in which the lesions appear as hypointense, 2-15-millimeter-diameter foci **[1]**.

3.2.1. SCREEN: 1_silentlacune: 02:31-02:41

3.3. Search all of the brain regions in a pre-specified order from one side to the other to avoid any omission. For example, search from the frontal lobe **[1]**, insula and basal ganglion **[2]**, temporal lobe, parietal lobe and occipital lobe **[3]**, cerebellum **[4]**, and brain stem **[5]**.

3.3.1. SCREEN: 1_silentlacune: 00:56-01:00
3.3.2. SCREEN: 1_silentlacune: 01:00-01:04
3.3.3. SCREEN: 1_silentlacune: 01:05-01:12
3.3.4. SCREEN: 1_silentlacune: 01:13-01:15
3.3.5. SCREEN: 1_silentlacune: 01:15-01:20

3.4. To confirm the presence of the silent lacunes, view the FLAIR (flair) and T1-weighted images, in which the lacunes can be observed as hypointense foci of 2-15-millimeter diameters, often with a hyperintense rim, and the T2-weighted images, in which the lacunes are hyperintense **[1-TXT]**.

3.4.1. SCREEN: 1_silentlacune: 03:31-03:38 *Video Editor: with FLAIR and T1-weighted, please emphasize right image, with T2-weighted, please emphasize left image* **TEXT: FLAIR: fluid-attenuated inversion recovery**

4. Visual SCL Lesion Rating: Cerebral Microbleeds and White Matter Hyperintensities

4.1. To identify cerebral microbleeds as punctuate or 2-10-millimeter-diameter, round-oval, hypointense foci and their locations, load susceptibility-weighted images into the software **[1]** and use the Brain Observer MicroBleed Scale to divide the entire brain region into seven anatomical locations **[2]**.

~~4.1.1. WIDE: Talent loading images, with monitor keyboard visible in frame~~

4.1.2. ADDED: SCREEN: 2_microbleeds: 00:08-00:26 NOTE: Replace WIDE (4.1.1.) with SCREEN (4.1.2.)

4.1.3. LAB MEDIA: Figure 3 *Video Editor: please emphasize or sequentially emphasize 7 labeled regions in images*

4.2. A participant is considered to have strictly lobar cerebral microbleeds when all of the lesions are confined to the cortex **[1]** and the subcortical white matter **[2]**.

4.2.1. SCREEN: 2_microbleeds: 00:19-00:25

4.2.2. SCREEN: 2_microbleeds: 04:38-04:43

4.3. To identify white matter hyperintensities as bilateral, almost symmetrical hyperintense areas, view the T2-weighted and FLAIR images **[1-TXT]**.

4.3.1. SCREEN: 3_WMH: 03:06-03:11 **TEXT: Confirm white matter hyperintensities on T1-weighted images as isointense or hypointense areas at same locations**

4.4. Use the Fazekas scale to score periventricular hyperintensities appearing as “caps” or pencil-thin lining as grade 1 foci **[1]**, smooth “halos” as grade 2 **[2]**, and irregular signals extending into the deep white matter as grade 3 **[3]**.

4.4.1. SCREEN: 3_WMH: 00:28-00:36

4.4.2. SCREEN: 3_WMH: 01:18-01:28

4.4.3. SCREEN: 3_WMH: 02:00-02:06

4.5. Rate deep white matter hyperintensities appearing as punctate foci as grade 1 **[1]**, small confluent areas as grade 2 **[2]**, and large confluent areas as grade 3 **[3]**.

4.5.1. SCREEN: 3_WMH: 00:37-00:43

4.5.2. SCREEN: 3_WMH: 01:30-01:37

4.5.3. SCREEN: 3_WMH: 02:09-02:13

Results

5. Results: Representative SCL Distribution and Associations Between Neurovascular Architecture and Cognitive Function

5.1. In this representative analysis, the mean age of the 398 participants was 72 years **[1]** and 213 of the participants were men **[2]**.

5.1.1. LAB MEDIA: Table 3 *Video Editor: please emphasize Mean age row*
5.1.2. LAB MEDIA: Table 3 *Video Editor: please emphasize Male row*

5.2. Here the neuropsychological assessment results for the participants are shown **[1]**.

5.2.1. LAB MEDIA: Table 4

~~5.3. Only five participants had all four types of silent cerebrovascular lesions **[1]**.~~

~~5.3.1. LAB MEDIA: Table 5 *Video Editor: please emphasize All four types row*~~

5.4. One or more types of silent cerebrovascular lesions were found in 169 participants **[1]**, with 35 participants exhibiting two types **[3]** and 17 exhibiting three types **[3]**.

5.4.1. LAB MEDIA: Table 5 *Video Editor: please emphasize One, Two, and Three types rows*
5.4.2. LAB MEDIA: Table 5 *Video Editor: please emphasize 35 (8.8) text*
5.4.3. LAB MEDIA: Table 5 *Video Editor: please emphasize 17 (4.3) text*

5.5. Only five participants had all four types of silent cerebrovascular lesions **[1]**.

5.5.1. LAB MEDIA: Table 5 *Video Editor: please emphasize All four types row* NOTE: Step moved from before 5.4. to after

5.6. The data confirmed an independent association between the burden of periventricular white matter hyperintensities and a poorer performance in executive function and information processing speed **[1]**.

5.6.1. LAB MEDIA: Table 6 *Video Editor: please emphasize PVHs severity data rows*

5.7. An increasing load of cerebral microbleeds was associated with impaired language-related performance and additional adjustment for vascular risk factors and other types

of silent cerebrovascular lesions did not affect the independent impact of cerebral microbleeds on language function **[1]**.

5.7.1. LAB MEDIA: Table 6 *Video Editor: please emphasize Strictly lobar CMBs*

5.8. Although there was a significant association between the presence of silent lacunes and a poorer performance on executive function, this association was lost following additional correction for other types of silent cerebrovascular lesions **[1]**.

5.8.1. LAB MEDIA: Table 6 *Video Editor: please emphasize Deep SLs*

Conclusion

6. Conclusion Interview Statements

6.1. **Junling Gao**: While it is not difficult to learn how to administer the neuropsychological assessments, it can be challenging to follow the standardized procedures on hundreds of patients over three years **[1]**.

6.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

6.2. **Raymond Tak Fai Cheung**: A unified standard should be adopted for both the neuropsychological assessments and ratings of MRI lesion for participants. These procedures should be reviewed periodically to ensure their uniformity **[1]**.

6.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

6.3. **Junling Gao**: Some of the neuropsychological tests have overlaps in their evaluated domains. In future, computer-based tests can be more precise, and additional functional neuroimaging studies can be developed for specific cognitive domains **[1]**.

6.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera NOTE: (sic)