Submission ID #: 67871
Scriptwriter Name: Pallavi Sharma
Project Page Link: https://review.jove.com/files_upload.php?src=20700703

Title: Evaluating Tests of Cognition Using a Computerized Touch-Sensitive Tablet, Eye Tracking, and Functional Magnetic Resonance Imaging

Authors and Affiliations:
Alexandra Pavel[1]*, Francis A. Fernandes[1]*, Sean Rose[1], C. Fung[1], Serenna Gerhard[1], Fred Tam[1], Corinne E. Fischer[2,3], Nathan W. Churchill[2], Tom. A. Schweizer[2,4], Simon J. Graham[1,5]

[1]Physical Sciences Platform, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre
[2]Keenan Research Centre for Biomedical Science, the Li Ka Shing Knowledge Institute, St. Michael's Hospital
[3]Department of Psychiatry, Faculty of Medicine, University of Toronto
[4]Division of Neurosurgery, Faculty of Medicine, University of Toronto
[5]Department of Medical Biophysics, Temerty Faculty of Medicine, University of Toronto

*These authors contributed equally

Corresponding Authors:

Simon J. Graham	Simon.Graham@utoronto.ca

Email Addresses for All Authors:

Alexandra Pavel	alexandrapavel863@gmail.com
Francis A. Fernandes	F.Fernandes@mail.utoronto.ca
Sean Rose	sean11kr@hotmail.com
C. Fung	c29fung@uwaterloo.ca
Serenna Gerhard	Serenna.Gerhard@sri.utoronto.ca
Fred Tam	Fred.Tam@sri.utoronto.ca

Corinne E. Fischer Corinne.Fischer@unityhealth.to
Nathan W. Churchill Nathan.Churchill@unityhealth.to
Tom A. Schweizer Tom.Schweizer@unityhealth.to
Simon J. Graham Simon.Graham@utoronto.ca

Author Questionnaire

1. Microscopy: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? No

2. Software: Does the part of your protocol being filmed include step-by-step descriptions of software usage? Yes, all done

3. Filming location: Will the filming need to take place in multiple locations? **Yes. MRI control panel/MRI suite and interview room.**

~5 minute walk.

Current Protocol Length
Number of Steps: 22
Number of Shots: 52

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

1.1. **Simon Graham:** We develop MRI technology to study brain structure and function. We aim to improve understanding of neurological diseases and support improved use of MRI for clinical applications, including image-guided treatments.

1.1.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B roll: 2.3*

What technologies are currently used to advance research in your field?

1.2. **Serenna Gerhard:** A touch-sensitive digitizing tablet enables naturalistic writing and drawing during functional MRI of brain activity. This technology provides new opportunities for evaluating brain-behaviour relationships.

1.2.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B roll: 2.8.2*

What are the current experimental challenges?

1.3. **Fred Tam:** FMRI must be done very carefully. The participant must lie supine and keep their head still. The tablet technology must not produce magnetic forces, radiofrequency heating, or radiofrequency interference.

1.3.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B roll: 2.5.2*

What research gap are you addressing with your protocol?

1.4. **Simon Graham:** The neural circuits engaged during standardized cognitive tests that involve writing and drawing remain poorly understood. Our fMRI results help researchers and clinicians to interpret cognitive test results better.

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

What new scientific questions have your results paved the way for?

1.5. **Sean Rose:** Investigation of how visual, proprioceptive, oculomotor, and hand motor processes integrate at the levels of brain activity and behavior, alongside the development of broad-ranging fMRI studies with improved ecological validity.

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

Videographer: Obtain headshots for all authors available at the filming location.

Ethics Title Card

This research has been approved by the Research Ethics Board (REB) at the Sunnybrook Health Sciences Centre

Protocol

2. Experimental Setup for Recording Visuomotor Behavior and Brain Activity

Demonstrators: Serenna Gerhard, Fred Tam, Maryam Akhshi

2.1. To begin, secure the tablet to its frame and attach the MRI-compatible video camera **[1]**. Apply fresh blue tape across the tablet surface, ensuring the entire touch area is covered without major creases **[2]**. Remove any excess tape from the tablet edges **[3]**.

2.1.1. WIDE: Talent attaching the tablet firmly to its supporting frame and connecting the MRI-compatible video camera.
Videographer's Note: Take 1 wide, takes 2 and 2 are close up

2.1.2. Talent applying fresh blue tape smoothly across the tablet's surface, carefully pressing down to avoid creases.
Videographer's Note: 2.1.2 and 2.1.3 are combined

2.1.3. Talent trimming the tape around the tablet edges.

2.2. Bring the tablet, stylus, tablet link cable, and tablet video camera link cables into the magnet room **[1]**. Connect the tablet link and video camera link cables to the magnet-room side of the RF penetration panel **[2]**. Then, slide the MRI-compatible tablet clips into the patient table rails, securing two clips on each side to fasten the tablet system in place **[3]**.

2.2.1. Talent carrying the tablet, stylus, and cables into the magnet room.

2.2.2. Talent connecting the tablet link and camera cables to the RF penetration panel.

2.2.3. Talent inserting tablet clips into both rails of the patient table and securing them.
Videographer's Note: Take 1 is a WIDE shot, take 2 is CU

2.3. Next, place the MRI-compatible projector behind the back end of the magnet, approximately 1 meter away from the magnet bore **[1]**. Mount the MRI-compatible rear projection screen inside the magnet bore, approximately 2 meters from the projector **[2]**.

2.3.1. Talent placing the projector on a stable surface 1 meter behind the magnet bore.
Videographer's Note: shot in 4K, combined with 2.3.2, take 2 is backup shot of MRI camera monitor for 2.3.1 until 2.4.2

2.3.2. Talent positioning and securing the projection screen inside the magnet bore at the correct distance from the projector.

2.4. Place the MRI-compatible eye-tracking camera between the projector screen and the outer edge of the magnet bore, ensuring the camera mount is flush with the bore edge **[1]**. Tighten the plastic screws on the mount to secure the eye-tracking system in place **[2]**.

2.4.1. Talent positioning the eye-tracking camera inside the magnet bore between the screen and the bore edge. Videographer's Note: shot in 4K, combined with 2.4.2

2.4.2. Talent adjusting and tightening plastic screws on the camera mount to secure it firmly to the bore.

2.5. Now, prepare the patient table by installing the 64-channel head coil **[1]**. Instruct the participant to lie supine on the table and position their head fully into the coil **[2]**. Place padding around the participant's head to restrict movement and ensure a secure fit **[3]**. Secure the head coil and use the landmark laser to confirm that the participant's head is centered within the coil **[4]**.

2.5.1. Talent placing the 64-channel head coil onto the MRI patient table. Videographer's Note: take 1 and 2 wide shots, take 3 close up

2.5.2. Talent guiding the participant to lie supine and adjusting their head into the head coil.

2.5.3. Talent placing padding on both sides of the participant's head.

2.5.4. Talent securing the head coil and using the laser tool to verify head alignment within the coil. Videographer's Note: take 1 and 2 are placing head coil, take 3 is the laser shot in 4K

2.6. Adjust the position of the head coil mirror until the participant can see the rear projection screen clearly and without obstruction **[1]**.

2.6.1. Talent adjusting the mirror attached to the head coil while communicating with the participant to confirm visibility of the screen.

2.7. Then, place the tablet mount across the participant's waist so that the touch-sensitive surface rests comfortably to support writing and drawing movements **[1]**.

2.7.1. Talent positions the tablet mount across the participant's waist and adjusts its angle for ergonomic access.

2.8. Now, place the tablet stylus in the participant's dominant hand and instruct them to hold it like a pen **[1]**. Ask the participant to touch all four corners of the tablet surface with the stylus to assess range and comfort **[2]**. Adjust the mount position and add padding under the elbow if needed to improve comfort or access **[3]**.

2.8.1. Talent placing the stylus into the participant's hand and demonstrating how to hold it.

2.8.2. Talent observing as the participant touches all corners of the tablet. Videographer's Note: Taken at the end of the shoot

2.8.3. Talent adjusting tablet mount and adding padding under the elbow to optimize comfort.
Videographer's Note: take 1 wide shot, take 2 close up

2.9. Using Velcro straps, fasten the tablet system to the patient bed **[1]**. Slowly slide both the participant and tablet system into the magnet bore, ensuring the tablet does not contact the bore edge and the cables remain untangled **[2]**.

2.9.1. Talent tightly securing the tablet system to the patient table using Velcro straps.

2.9.2. Talent carefully slides the participant into the magnet bore while monitoring tablet alignment and cable management.

2.10. On the video camera computer, launch the Video camera.exe *(Camera-E-X-E)* program **[1]**. Then, create a new screen capture session for the participant [**2**].

2.10.1. SCREEN: 67871_2.10.1cam.mp4: 00:06-00:07, 00:33-00:37

2.10.2. SCREEN: 67871_2.10.2cam.mp4: 00:14-00:18, 00:23-00:25

2.11. Following the EyeLink *(Eye-Link)* 100 Plus User Manual recommendations, configure pupil and corneal reflection thresholds, and calibrate and validate the eye-tracking camera **[1].**

2.11.1. SCREEN: 67871_2.11.1cam.mp4: 00:04-00:16

2.12. To adjust the eye-tracking camera to focus on the participant's right eye, switch between camera views, fine-tune the lens, and modify the illuminator until the view is optimized **[1]**. Once the pupil threshold and corneal reflection values are acceptable, document the values and initiate the 9-point calibration **[2]**.

2.12.1. SCREEN: 67871_2.12.1cam.mp4: 00:05-00:15

2.12.2. SCREEN: 67871_2.12.2cam.mp4: 00:06-00:23

2.13. Then, validate the calibration **[1]**. Record both the average and maximum validation angle values before proceeding to the fMRI experiment **[2-TXT]**.

2.13.1. SCREEN: 67871_2.13.1cam.mp4: 00:12-00:15

2.13.2. SCREEN: 67871_2.13.2eyetracker.mp4: 00:05-00:13, 00:25-00:29. **TXT: Repeat calibration until avg. error ≤ 0.5° & max error ≤ 1.0**

2.14. Following the EyeLink *(Eye-Link)* 1000 Plus User Manual recommendations, configure pupil and corneal reflection thresholds, and calibrate and validate the eye-tracking camera **[1]**. Instruct the participant to use the stylus to consecutively touch and release the three targets that appear on the screen within the allotted time limits **[2]**.

2.14.1. SCREEN: 67871_2.14.1stim.mp4: 00:05-00:23

2.14.2. SCREEN: 67871_2.14.2cam.mp4: 00:03-00:23

2.15. Once calibration is complete, launch the referenced graphics editing application **[1]**. Instruct the participant to draw freely to confirm accurate stylus tracking **[2]**.

2.15.1. SCREEN: 67871_2.15.1stim.mp4: 00:00-00:05

2.15.2. SCREEN: 67871_2.15.2cam.mp4: 00:06-00:14

2.16. Now, familiarize the participant with tablet-based writing by asking them to complete a self-paced training task used in essential tremor studies **[1]**.

2.16.1. SCREEN: 67871_2.16.1cam.mp4: 00:05-00:08, 00:34-00:37, 00:50-01:07

2.17. To familiarize the participant with the TMT *(T-M-T),* guide them through a simplified training version of TMT-A and TMT-B, each with 12 items **[1]**. Then, proceed to alternate full-sized versions of TMT-A and TMT-B with rearranged items, using experimental task timing **[2]**. Monitor the participant's performance throughout to ensure the tablet remains properly calibrated and the task is followed accurately **[3]**.

2.17.1. SCREEN: 67871_2.17.1-2stim: 00:58-01:19

2.17.2. SCREEN: 67871_2.17.1-2cam.mp4; 02:20-02:40

2.17.3. Talent monitoring the participant's performance.

2.18. Now, begin the eye-tracking session by selecting **Start Recording** in the **Screen Recorder** program on the video camera computer **[1]**. Then, on the stimulus or response computer, open the **TMT-Run1_slow.ebs2** *(T-M-T-Run-One-Slow-E-B-S-two)* E-Prime script file using E-Run **[2]**. Input the **participant ID** and the **session number** when prompted by the E-Run script **[3].**

2.18.1. SCREEN: 67871_2.18.1cam.mp4: 00:04-00:08

2.18.2. SCREEN: 67871_2.18.2-3stim.mp4: 00:01-00:19

2.18.3. SCREEN: 67871_2.18.2-3stim.mp4: 00:21-00:29

2.19. During the run, assign one lab member to monitor the eye-tracking data to ensure a stable signal **[1]**. Simultaneously, have a second lab member observe the participant's performance on the TMT task, ensuring that instructions are being followed and that no technical issues are present, such as unreliable projection or stylus tracking **[2]**. Ask the second lab member to also document any errors in TMT-A or TMT-B performance, along with the associated trial number **[3]**.

2.19.1. Show a lab member reviewing the real-time eye-tracking data graph for signal stability on the recording computer.

2.19.2. Show another lab member watching the participant's stylus trace as it appears on-screen, noting any delays or mismatches. Videographer's Note: combined with 2.19.3

2.19.3. Show a log being filled in with any detected TMT-A or TMT-B performance errors, along with trial numbers.

2.20. After the run is complete, stop the eye-tracker recording **[1]**. In the SR Research Screen Recorder software, perform a single-point drift check by selecting **Drift Correct [2-TXT]**.

2.20.1. SCREEN: 67871_2.20.1cam.mp4: 00:06-00:13

2.20.2. SCREEN:67871_2.20.2cam.mp4: 00:05-00:16

TXT: If error ≥ 2.0°, repeat 9-pt calibration until avg. < 1.0° & max < 2.0°

2.21. For Run 2, restart the eye-tracking recording session on the video camera computer **[1]**. On the stimulus or response computer, open the **TMT-Run2_slow.ebs2** E-Run script file **[2]**. Enter the same participant ID and session number used in Run 1. Repeat the task instructions **[3].**

2.21.1. SCREEN: 67871_2.21.1cam.mp4: 00:10-00:15

2.21.2. SCREEN: 67871_2.21.2-3stim.mp4: 00:02-00:17

2.21.3. SCREEN: 67871_2.21.2-3stim.mp4: 00:19-00:26

2.22. Once the experiment concludes, perform one final eye-tracking validation to confirm calibration accuracy **[1]**. Then, click **File** followed by **Close** on the eye-tracking software to finalize and export the data **[2]**. Remove the participant from the magnet bore and begin equipment take-down **[3]**. At last, shut off all computers and equipment **[4].**

2.22.1. SCREEN: 67871_2.22.1eyetracker: 00:16-00:35

2.22.2. SCREEN: 67871_2.22.2cam.mp4

2.22.3. WIDE: Talent carefully guiding the participant out of the magnet

Added shot: Talent removing the tablet system and related equipment.

2.22.4. Talent shutting off the computer and equipment

Results

3. Results

3.1. During the initial seconds of both TMT-A and TMT-B, the participant's gaze searched for targets before initiating stylus movement **[1].** Across all time intervals shown, gaze consistently preceded the stylus linking motion in both TMT-A and TMT-B **[2].**

3.1.1. LAB MEDIA: Figure 7C and D. *Video editor: Highlight the red gaze path in the first panel (0s - 2.5s) before any blue lines appear*.

3.1.2. LAB MEDIA: Figure 7C and D. *Video editor: In each of the four time segments, highlight the red path leading slightly ahead of the blue line.*

3.2. Completion time trended longer for TMT-B than for TMT-A **[1].** Stylus pause latency showed a trend of being higher for TMT-B than for TMT-A **[2].**

3.2.1. LAB MEDIA: Table 1. *Video editor: Highlight the row "Completion time" and compare the values for TMT-A and TMT-B.*

3.2.2. LAB MEDIA: Table 1**.** *Video editor: Highlight the row "SPL" and show the higher average value for TMT-B compared to TMT-A.*

3.3. No significant differences were found between TMT-A and TMT-B in linking period durations**,** non-linking period durations, total distance, extra distance travelled, or distance per link **[1].**

3.3.1. LAB MEDIA: Table 1**.** *Video editor: Highlight the rows "Linking period", "Non-linking period", "D", "EDT", and "DPL", showing similar values for both TMT-A and TMT-B.*

3.4. Stylus force trended slightly higher during TMT-B compared to TMT-A **[1],** and blink count per trial was significantly greater during TMT-B **[2].**

3.4.1. LAB MEDIA: Table 1. *Video editor: Highlight the row "Stylus Force" and show the higher value for TMT-B compared to TMT-A.*

3.4.2. LAB MEDIA: Table 1. *Video editor: Highlight the row "Blink Count" and emphasize the difference between TMT-B and TMT-A.*

3.5. Blink rate remained significantly higher in TMT-B even after accounting for completion time differences **[1].** The percentage of time spent in fixation was significantly lower during TMT-B than during TMT-A **[2].**

3.5.1. LAB MEDIA: Table 1. *Video editor: Highlight the row "Blink Rate" and show the value for TMT-B compared to TMT-A.*

3.5.2. LAB MEDIA: Table 1. *Video editor: Highlight the row "Fixation %" and compare* *the lower value for TMT-B with TMT-A.*

3.6. Functional MRI revealed widespread positive brain activation during both TMT-A and TMT-B compared to visual fixation **[1].** Brain activation included regions such as the cerebellum, parietal lobules, occipital gyri, and frontal areas **[2].**

3.6.1. LAB MEDIA: Figure 8.

3.6.2. LAB MEDIA: Figure 8. *Video editor: Highlight the yellow and orange activation clusters across the different brain slices*.

3.7. No significant brain activation differences were observed when contrasting TMT-B directly against TMT-A **[1].**

3.7.1. LAB MEDIA: Figure 8.

Pronunciation Guide:

- functional
  Pronunciation link: https://www.merriam-webster.com/dictionary/functional
  IPA: /ˈfʌŋkʃənəl/
  Phonetic Spelling: FUNK-shuh-nul
- magnetic
  Pronunciation link: https://www.merriam-webster.com/dictionary/magnetic
  IPA: /mægˈnɛtɪk/
  Phonetic Spelling: mag-NET-ik
- supine
  Pronunciation link: https://www.merriam-webster.com/dictionary/supine
  IPA: /suːˈpaɪn/
  Phonetic Spelling: soo-PINE
- visuo-motor (visual + motor)
  Pronunciation link: No confirmed link found
  IPA: /ˌvɪʒuˈmoʊtər/
  Phonetic Spelling: viz-yoo-MOH-ter
- stylus
  Pronunciation link: https://www.merriam-webster.com/dictionary/stylus
  IPA: /ˈstaɪləs/
  Phonetic Spelling: STY-lus
- calibration
  Pronunciation link: https://www.merriam-webster.com/dictionary/calibration
  IPA: /ˌkælɪˈbreɪʃən/
  Phonetic Spelling: kal-ih-BRAY-shun
- fixation
  Pronunciation link: https://www.merriam-webster.com/dictionary/fixation
  IPA: /fɪkˈseɪʃən/
  Phonetic Spelling: fik-SAY-shun
- latency
  Pronunciation link: https://www.merriam-webster.com/dictionary/latency
  IPA: /ˈleɪtənsi/
  Phonetic Spelling: LAY-tuhn-see
- cohort
  Pronunciation link: https://www.merriam-webster.com/dictionary/cohort
  IPA: /ˈkoʊhɔːrt/
  Phonetic Spelling: KOH-hort

- ecologically (as in "ecological validity")
  Pronunciation link: https://www.merriam-webster.com/dictionary/ecologically
  IPA: /ˌiːkəˈlɒdʒɪkli/ (US: /ˌiːkəˈlɑːdʒɪkli/)
  Phonetic Spelling: ee-kuh-LAA-ji-klee