An Examination of Associative Memory using Functional Near Infrared Spectroscopy

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Abstract

Functional Near-Infrared Spectroscopy (fNIRS) is a neuroimaging technology that overcomes many of functional MRI's technical limitations (including lower cost, motion tolerance, and higher temporal resolution). While some tasks have been validated in fNIRS, many areas of study, such as associative memory, have not been thoroughly examined. Functional MRI studies have shown that associative memory engages multiple brain regions, including the ventral and dorsal visual streams, medial temporal lobe, and frontal cortical areas. However, few studies have examined whether similar patterns of cortical activation are detected in older adults using fNIRS. To investigate this issue, we recorded fNIRS from 30 cognitively intact older adults encoding object-location associations of common household objects within a virtual room. Results showed greater activation for novel compared to repeated object-location pairs in the occipital and posterior parietal cortices, as well as regions in dorsolateral and ventrolateral frontal cortices. Our overall results are consistent with prior fMRI evidence from associative memory studies, while also suggesting some differences between fNIRS and fMRI methodologies. A key future direction includes comparing fNIRS and fMRI results within the same participants to further understand the differences between the two neuroimaging techniques.

Keywords: fNIRS, associative memory, object-location association, older adults

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Overview of Functional Neuroimaging Methods

Functional neuroimaging has transformed the field of human neuroscience with its potential for detailed characterization of neural networks and their role in cognition. Specific areas of the brain are activated when a subject performs a particular task, and functional neuroimaging allows for analyses of the relationship between task-relevant brain regions and associated mental functions. One traditional and widely used functional neuroimaging method is functional magnetic resonance imaging (fMRI). Recently, a newer form of neuroimaging called functional near infrared spectroscopy (fNIRS) has been gaining popularity (Lloyd-Fox, 2017).

Functional MRI, a common method for studying brain activity for over 20 years, has many strengths but also has significant limitations. This method uses magnetic field gradients to detect changes in oxygenated blood across the brain, which are linked to neural activity. Functional MRI has better spatial resolution than most other neuroimaging methods, allowing researchers to compare levels of activation in distinct brain areas. Additionally, fMRI is noninvasive, making it safe for general use (Bandettini, 2020). Nonetheless, fMRI has several significant limitations that may preclude important experiments from study. It has little tolerance for movement, requiring participants to lay still for extended periods of time to acquire high quality data. In addition, each scan is costly, which may constrain the number of participants that can be recruited for a given study. It also excludes individuals with claustrophobia and those with larger bodies due to the tightly enclosed bore of the MRI machine. Individuals with metal implants must also be excluded due to machine's use of a magnetic field (Scarapicchia et al., 2017). These exclusions affect the generalizability of experiments using fMRI, necessitating alternative techniques for assessing brain function.

Some of the limitations of fMRI are overcome by functional near infrared spectroscopy (fNIRS). This newer method of functional neuroimaging uses near-infrared light to measure changes in concentrations of oxygenated and deoxygenated hemoglobin resulting from neural activity. Sources send near infrared (NIR) light into the brain that travel through brain matter, and the refraction of light is then captured and measured by detectors. As NIR light shines through layers of the brain, it is absorbed by oxygenated hemoglobin (HbO) and deoxygenated hemoglobin at differing levels, allowing researchers to determine levels of brain activation (Bigio & Fantini, 2016). While fNIRS only measures approximately 1.5 cm below surface and has slightly lower spatial resolution than fMRI (Pinti et al., 2020), it has better movement tolerability than fMRI due to its more flexible and mobile cap (Balardin et al., 2017; McKendrick et al., 2017; Pinti et al., 2020). The more natural environment permitted by fNIRS' portability (e.g. sitting upright in a chair or walking around) rather than laying still in a scanner more closely reflects real-life scenarios and therefore produces more generalizable results. fNIRS is also more cost-effective than fMRI. In addition, fNIRS has better temporal resolution than fMRI (Pinti et al., 2020). fNIRS studies can also include individuals with implants, claustrophobia, or large body sizes, diversifying the study populations collected.

Validation of fNIRS Results Using fMRI

Multiple experimental paradigms have been validated with fNIRS, including N-Back, go/no-go, and line orientation tasks (Cui et al., 2011). The N-Back task measures working memory capacity, or the ability to store and process small amounts of information over short periods of time (Gajewski et al., 2018). N-Back studies with fMRI have found significant cortical activation in the bilateral dorsolateral prefrontal cortex and bilateral medial posterior parietal cortex (Owen et al., 2005). This is similar to fNIRS studies which showed significant

activation in frontoparietal cortical regions including inferior frontal gyrus, left superior frontal gyrus, and right inferior parietal cortex (Meidenbauer et al., 2021). The go/no-go task measures response inhibition, or the ability to withhold an expected response to a stimulus (Cui et al., 2011). Go/no-go studies using fMRI have identified activation in the right prefrontal cortex, similar to fNIRS studies which show activation in the right inferior and middle prefrontal gyri (Monden et al., 2015). The line orientation task measures visuospatial perception in which subjects are asked to estimate the orientation of a given line. Bilateral dorsolateral and superior parietal cortices were the primary areas of activation identified in line orientation studies using both fMRI and fNIRS (Baker et al., 2018; Herrmann et al., 2005). While there is clear consistency between fMRI and fNIRS results in many commonly used tasks, our goal was to explore the validity of fNIRS in associative memory.

Neuroimaging Investigations of Associative Memory

Associative memory refers to binding together separate features of an object or figure for subsequent recall or recognition, such as pairing a face with a name or an object with a location in space (Wang & Cui, 2017). These tasks have strong ecological validity, or the extent to which an experimental task reflects day-to-day occurrences, as they are direct translations of memory challenges in everyday situations. Therefore, they are relevant to how the brain controls behavior in everyday situations.

One associative memory task that mirrors everyday occurrences that has not been investigated using fNIRS is the object location association (OLA) task. The OLA memory paradigm requires participants to recall the location of an object within a virtual room (Hampstead et al., 2011). This task was designed to have high ecological validity, as losing objects is a common problem for both older adults and individuals with dementia. Postma et al.

(2008) postulated that the OLA task elicits three specific cognitive processes: object processing, spatial-location processing, and object-to-location binding. Object processing refers to the visual recognition of an object that a visual stimulus is referencing. This process is associated with activation in the left posterior inferior temporal cortex. Spatial location processing is the means of remembering the position of an object in space, irrespective of object information. This coordinate positional memory typically activates the right posterior parietal cortex, right dorsolateral prefrontal cortex, and the right hippocampal formation. Finally, object-to-location binding combines the memory of an object's identity with memory of an object's location in space. This process mainly activates the bilateral hippocampal formations and bilateral posterior parietal cortices (Postma et al., 2008).

Hampstead and colleagues (2011) investigated brain activity during an OLA task using fMRI. They found activation in the ventral visual stream (projecting from occipital to temporal cortices), the dorsal visual stream (projecting from occipital to superior parietal cortices), the medial temporal lobe region, and frontal cortical areas (Hampstead et al., 2011), during encoding of object-location pairs. This result replicated across subsequent fMRI studies (Graumann et al., 2022; Thoma & Henson, 2011), but the OLA paradigm has not been employed while measuring brain activity using fNIRS.

The Present Study

The goal of my thesis project was to measure brain activation in older adults during an OLA task using fNIRS to identify the brain regions recruited during task performance. Given past findings from fMRI studies (Graumann et al., 2022; Hampstead et al., 2011; Thoma & Henson, 2011), we hypothesized that fNIRS would detect significant activation in areas of the prefrontal cortex and the bilateral dorsal visual stream, including the superior parietal lobule and

posterior parietal cortex. Due to fNIRS' inability to detect activity beyond the cortical layers of the brain and limited optode coverage, activation will not be measured in certain regions of the cortex, such as the medial temporal lobe, or areas behind the ear, such as the ventral visual stream.

Methods

Participants

The Institutional Review Boards of the University of Michigan Medical School approved this study. Previously published results (Yeung, Lee, & Chan, 2021; Yeung, Lee, Han, et al., 2021) of fNIRS studies suggest mean cognitive effect sizes (in Cohen's d) of 0.51 for sessions of N-Back testing to measure working memory activation. Given this effect size of 0.5, an alpha error probability set at 0.05, and a power of 0.80, we estimate an ideal sample size to be 34 (via G*Power). Due to this project's time constraints, our sample size of 30 was just short of achieving a power of 0.80.

Participants over the age of 50 were recruited from the University of Michigan Health Research list-serve and the Michigan Alzheimer's Disease Center. Exclusion criteria included presence of objective cognitive impairment, epilepsy, severe mental illness, current alcohol or substance abuse/dependence, active cancer treatment, sensory impairments that limit participation such as extremely limited vision/hearing, and other medical factors that may limit completion of study activities. Cognitive status was measured using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph et al., 1998) and the Trail Making Test (Tombaugh, 2004). Unimpaired cognitive status was confirmed through consensus between two licensed neuropsychologists (Drs. Ben Hampstead and Annalise Rahman-Filipiak).

All participants were stable on prescribed medications for approximately 4 weeks prior to study enrollment via self-report. See Table 1 for demographic information and standardized test scores.

Table 1

Demographic Information of Participant Sample

Variable	Value (Mean ± standard deviation)
Age	65.4 ± 7.1
Education (years)	16.5 ± 1.8
RBANS	110.5[a] ± 15.2
Trail Making Test A	101.9[ab] ± 8.4[b]
Trail Making Test B	105.2[a] ± 6.8
Gender (Male:Female)	7:23
Race (White:Black)	25:5

[a] Mean scores are reported in standard scores

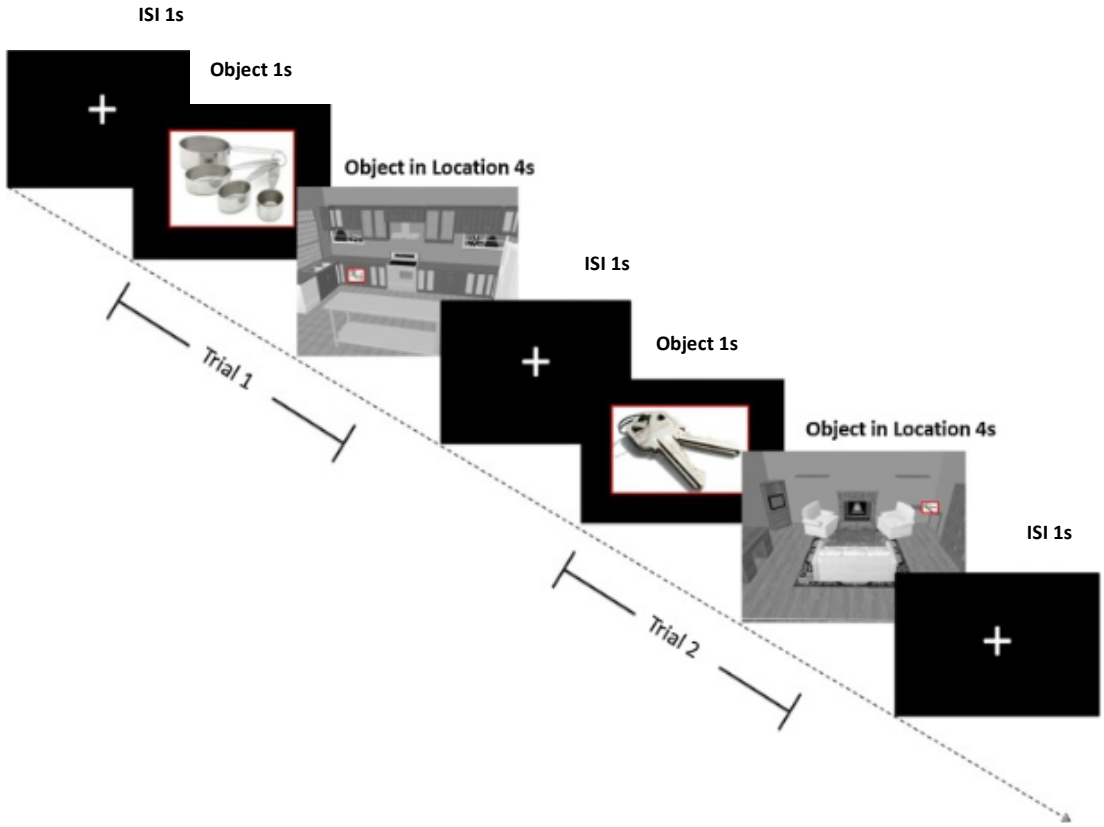
[b] One participant score removed from Trail Making Test A due to outlier and not reflecting cognitive ability of individual.

Experimental Design

We adapted a version of the object location association paradigm from Hampstead and colleagues (2011) for use with fNIRS. While both encoding and retrieval stages of this paradigm were completed for each participant, only the encoding stages were examined for this study. During each block of the encoding stage, participants were shown a virtual room and presented with five objects in specific locations within the room. Each object was presented alone for one second and then presented in a specific location in a virtual room for four seconds. The participants were instructed to remember where each object belonged in the room. Each object

Figure 1

Diagram Displaying Encoding Stage of Task



Adapted from Hampstead et al., 2011.

presentation (i.e., "trial") was separated by a one-second interstimulus interval (ISI) (see Figure 1). A 20-second rest block, in which only a fixation cross was shown, followed each five-trial block. Each of two runs of the task consisted of six blocks, half of which were novel and half repeated (see Figure 2). During novel blocks, participants were presented with object-location pairs that they had not yet viewed. During repeated blocks, participants were repeatedly shown two alternating object-location pairs to control for basic perceptual processes. Using EPrime (pstnet.com), objects were placed in random but plausible locations to establish the greatest ecological validity in the task's design. The timing of the task was slightly altered from

Figure 2

Run Design

Note. This figure shows a representation of each of two runs of the OLA task. Run begins with 30 seconds (s) of rest followed by six periods alternating between 30 seconds of a trial (either repeated (R) or novel (N)) and 20 seconds of rest.

Hampstead et al., 2011 to maintain a consistent interval between trials while ensuring the block lengths stayed the same to compare between active and rest blocks. Notably, approximately half of the participants (14/30) had seen the stimuli once before during an fMRI session as part of a larger, paired study. Following setup, participants carried out a practice run in which the repeated object-location stimuli were presented to ensure these stimuli were familiar to the participant prior to data collection.

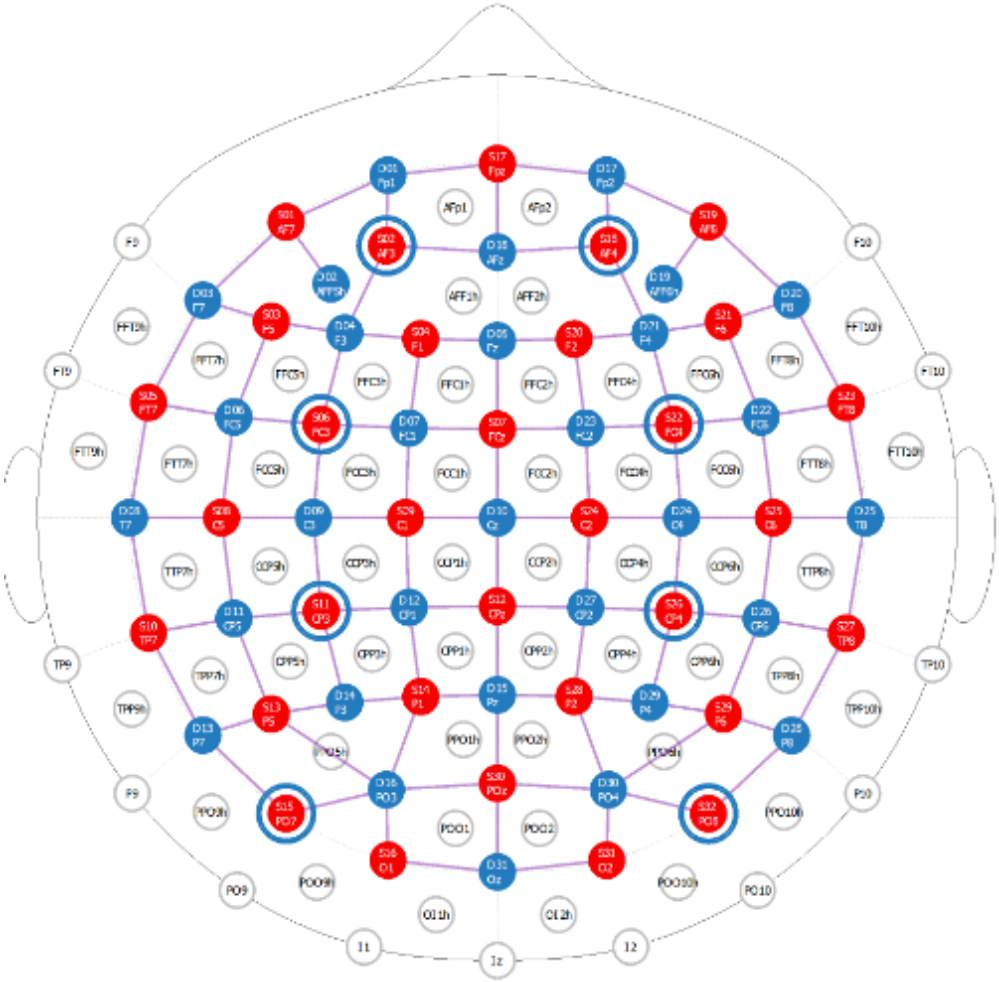
fNIRS Data Collection

We collected brain activity data using a NIRSport2 fNIRS system (NIRx.com) with wavelengths of 760 and 850 nanometers and a sampling rate of 3.8 Hz. Our fNIRS cap was set up using a full head montage with 32 sources and 31 detectors concentrated over frontoparietal areas to target regions essential to associative memory (see Figure 3). The distance between each source and detector was fixed at 3cm, allowing a penetration depth of about 1.5cm. The montage

also included 8 short channel detectors spaced 6-8mm apart from the sources throughout the montage to account for physiological noise.

Figure 3

Montage Used for fNIRS Cap



Note. This figure shows the layout of the fNIRS montage: Montage is in EEG-128 space (top is anterior). Red circle = source; Blue circle = detector; blue circle around source = short-channel detector.

Preprocessing and Data Analysis

We processed fNIRS data using the NIRS Toolbox (Santosa et al., 2018). Raw fNIRS data were visually inspected to remove any data with overtly poor signal. We then converted the raw signal into optical density data and converted this into concentrations of oxygenated hemoglobin and deoxygenated hemoglobin via the modified Beer-Lambert Law (Kocsis et al., 2006). Physiological noise and motion artifacts were accounted for using a modified General Linear Model (Barker et al., 2013) consisting of an autoregressive iteratively reweighted least square algorithm (Huppert, 2016; Karim et al., 2014). Using this method, we derived beta weights for each source-detector pair in each condition by fitting the measured activity to a canonical hemodynamic response function convolved with a boxcar function representing the onset and duration of each task block. We compared beta weights between the novel and repeated conditions using a two-tailed t-test. Our results represent the significant differences in activation between novel and repeated conditions. The areas of brain activation to be analyzed are regions between each source-detector pair as they appear on the montage. Specific regions of activation were determined by Atlas Viewer's "Project to Cortex" function which draws a vector perpendicular to the surface of the brain at the midpoint of each source-detector pair in template (MNI) space (Aasted et al., 2015).

Results

Encoding of Novel Versus Repeated Object-Location Pairs (Table 2, Figure 4)

There was significantly higher HbO concentration during Novel compared to Repeated objects in bilateral posterior prefrontal cortices and left temporal-occipital areas (Table 2-A). Significantly lower HbO concentration was detected in the bilateral anterior prefrontal cortex, bilateral temporal cortices, and right parietal-occipital areas (Table 2-B).

Table 2

Regions of Significantly Different HbO Concentration in Novel vs. Repeated Condition.

Channel (S – D)	Location	T-statistic
	Novel > Repeated	
AF8-Fp2	R. middle frontal gyrus	**3.600*** **
F1-F3	L. superior frontal gyrus	**2.401***
F2-FC2	R. superior frontal gyrus	**5.868*** **
FC3-FC5	L. inferior frontal gyrus	**4.004*** **
FC4-F4	R. inferior frontal gyrus	**3.449*** **
FT7-FC5	L. rolandic operculum	**4.389*** **
FC3-FC2	R. supplementary motor area	**2.788***
CP3-P3	L. inferior parietal lobule	2.227*
P5-CP5	L. angular gyrus	**2.748****
P5-P3	L. angular gyrus	**2.864*** **
P5-P7	L. middle temporal gyrus	**2.343***
P6-P8	R. middle temporal gyrus	**3.135****
P5-PO3	L. middle occipital gyrus	**5.315*** **
PO7-PO3	L. middle occipital gyrus	**5.466*** **
O1-PO3	L. cuneus	**6.657*** **
Poz-Oz	Medial cuneus	**3.284****
O1-Oz	L. superior occipital gyrus	**3.513*** **
	Repeated > Novel	
Channel (S - D)	Location	T-statistic
Fpz-AFz	Medial superior frontal gyrus	**-3.660*** **
AF7-Fp1	L. superior frontal gyrus	**-5.346*** **
AF4-AFz	R. superior frontal gyrus	-2.061*
AF7-F7	L. middle frontal gyrus	**-2.626****
AF4-F4	R. middle frontal gyrus	-2.27*
F2-F4	R. middle frontal gyrus	**-3.662*** **
AF8-F8	R. inferior frontal gyrus	**-4.572*** **
F5-F3	L. inferior frontal gyrus	**-6.147*** **
F6-F4	R. middle frontal gyrus	-2.231*
F2-Fz	R. superior frontal gyrus	**-2.728****
F6-F8	R. inferior frontal gyrus	**-4.171*** **
FT7-T7	L. middle temporal gyrus	**-3.136*** **

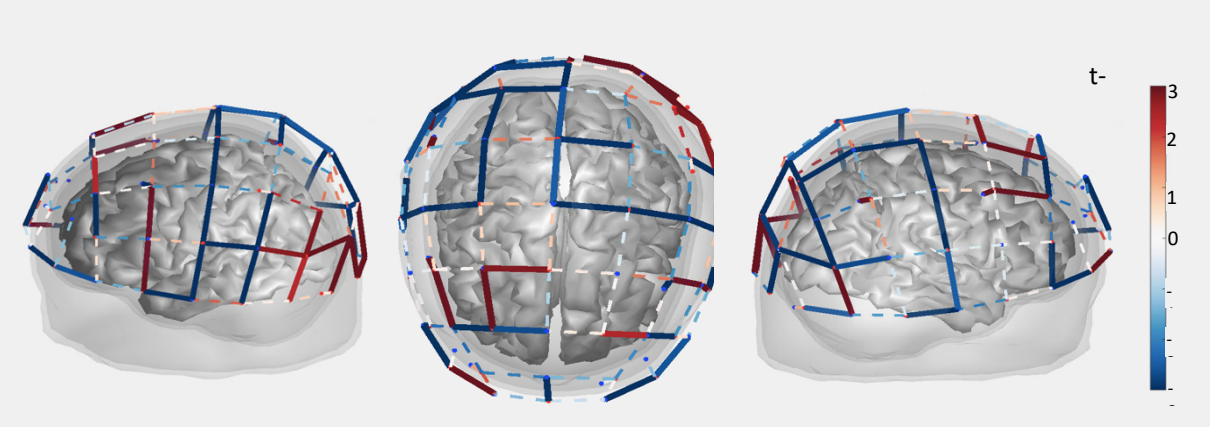
Table 2 (cont'd)

Repeated > Novel		
Channel (S - D)	Location	T-statistic
C5-T7	L. superior temporal gyrus	**-4.897*** **
FT8-T8	R. superior temporal gyrus	-2.172*
C6-C8	R. superior temporal gyrus	**-2.495***
P6-CP6	R. superior temporal gyrus	**-2.700****
C5-CP5	L. rolandic operculum	**-3.875*** **
C5-C3	L. superior parietal gyrus	**-4.168*** **
C1-C3	L. postcentral gyrus	**-2.961*** **
C6-C4	R. postcentral gyrus	**-3.671*** **
C2-C4	R. postcentral gyrus	**-3.467*** **
CPz-CP1	L. precentral gyrus	**-3.531*** **
C4-CP2	R. precentral gyrus	**-6.971*** **
C1-Cz	L. paracentral lobule	**-3.485*** **
CPz-Cz	L. paracentral lobule	**-2.575***
TP7-CP5	L. middle temporal gyrus	**-4.963*** **
TP8-T8	R. middle temporal gyrus	**-2.980****
PO8-P8	R. inferior temporal gyrus	**-2.634****
CP3-CP5	L. supramarginal gyrus	**-8.164*** **
CPz-Pz	Medial precuneus	**-2.576***
POz-Pz	Medial precuneus	**-3.221*** **
CP4-P4	R. angular gyrus	-2.203*
P6-P4	R. angular gyrus	**-5.194*** **
P2-Pz	R. superior parietal gyrus	**-6.253*** **
P2-P4	R. superior parietal gyrus	**-4.195*** **
P2-CP2	R. superior parietal gyrus	**-5.008*** **
P4-POz	R. middle occipital gyrus	**-3.565*** **
POz-PO4	R. superior occipital gyrus	**-2.835****
O2-Oz	R. superior occipital gyrus	-2.111*
O2-PO4	R. superior occipital gyrus	**-5.377*** **

*=p<0.05, **p <0.01,*** = p < 0.005. Values displayed in bold survived FDR correction. S = source; D = detector.

Figure 4

Significant Channels for Novel vs. Repeated



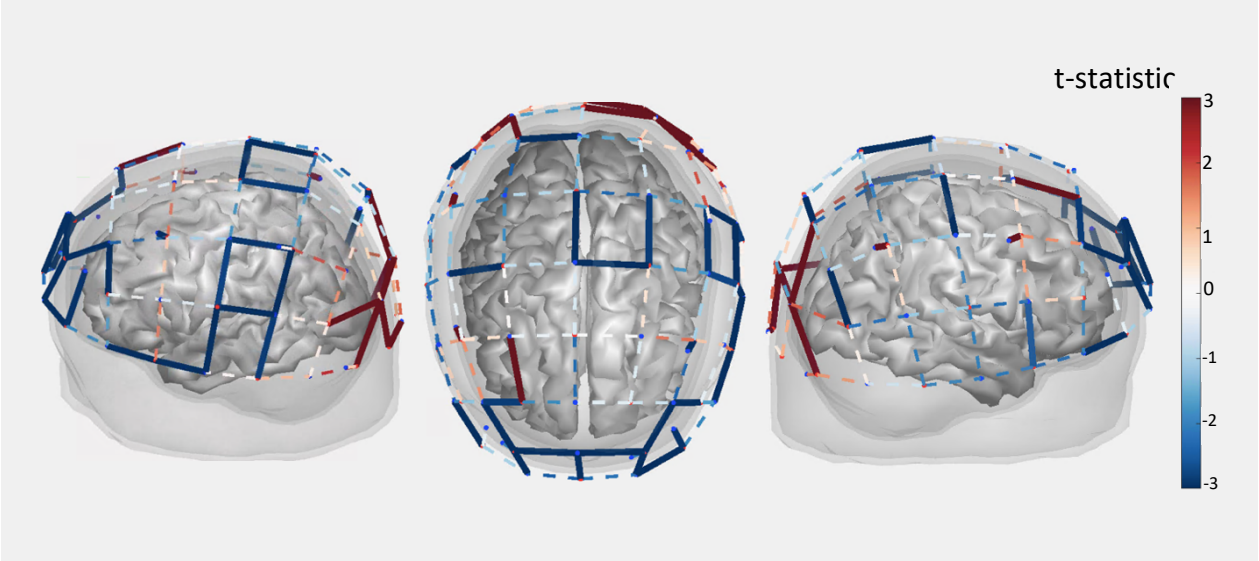
Note. Lateral Left (Left), Dorsal (Middle), and Lateral Right (Right) views of the Novel versus Repeated conditions based on an FDR corrected p-value < 0.05. Solid red lines show activation (Novel > Repeated) and solid blue lines show deactivation (Repeated > Novel). Adapted from NIRS Toolbox (Santosa et al., 2018).

Encoding of Novel Object-Location Pairs Relative to Baseline (Figure 5)

During Novel object-location pair encoding, the HbO concentration was significantly higher in bilateral occipital cortices and the right frontal eye fields compared to Baseline. HbO concentration was significantly lower in the left paracentral lobule and bilateral prefrontal cortices.

Figure 5

Significant Channels for Novel vs. Baseline



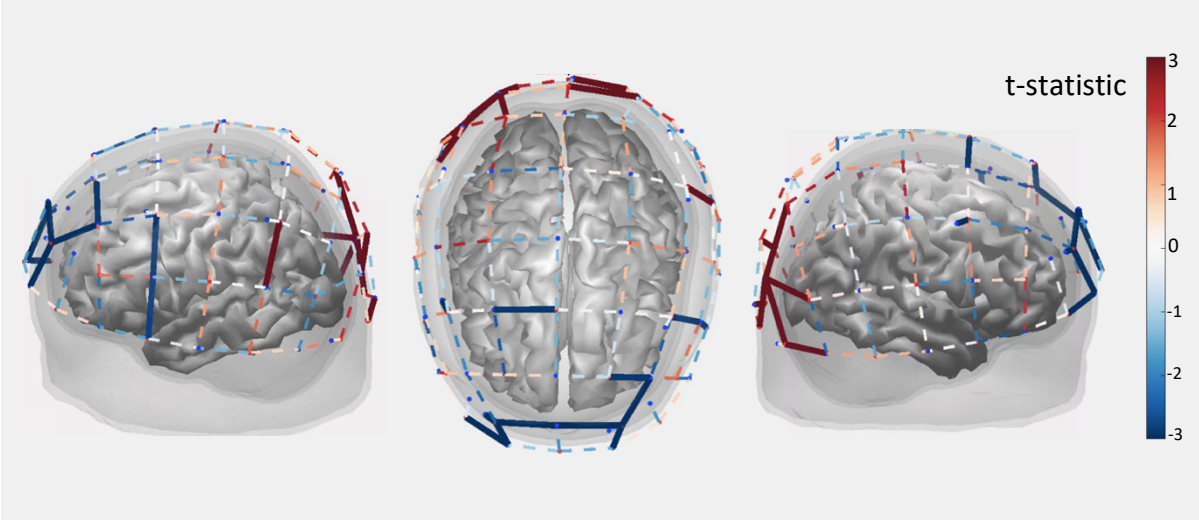
Note. Lateral Left (Left), Dorsal (Middle), and Lateral Right (Right) views of the Novel versus Baseline conditions based on an FDR corrected p-value < 0.05. Solid red lines show activation and solid blue lines show deactivation. Adapted from NIRS Toolbox (Santosa et al., 2018).

Encoding of Repeated Object-Location Pairs Relative to Baseline (Figure 6)

During the Repeated condition, HbO increased significantly from Baseline in bilateral occipital cortices and a portion of the left parietal cortex. It decreased significantly from Baseline in bilateral prefrontal cortices and the right primary motor cortex.

Figure 6

Significant channels for Repeated vs. Baseline



Note. Lateral Left (Left), Dorsal (Middle), and Lateral Right (Right) views of the novel versus repeated conditions based on an FDR corrected p-value < 0.05. Solid red lines show activation and solid blue lines show deactivation. Adapted from NIRS Toolbox (Santosa et al., 2018).

Discussion

To our knowledge, this project is the first to examine neuronal activity during object-location associations using fNIRS. We found fNIRS detected differences between Novel and Repeated conditions of the OLA task in bilateral areas of the prefrontal cortex and left dorsal visual stream, with emphasis on the left posterior parietal cortices. These results demonstrated patterns of activity that were generally similar to OLA studies using fMRI (Hampstead et al., 2011; Sommer et al., 2005a; Sommer et al., 2005b). Notable differences were also evident, including lack of visibility for subcortical and temporal medial activation and deactivation in the right dorsal visual stream in Novel versus Repeated conditions.

The activity detected in the left posterior parietal and temporal-occipital cortices is consistent with prior studies of the OLA paradigm using fMRI. These regions are portions of the left dorsal visual stream, which is involved in processing object and categorical position information (Postma et al., 2008). Categorical position is the location of an object according to its relative position to another object (Postma et al., 2008). Processing information by thinking about its categorical position is crucial for object-location associations and is concentrated in the left hemisphere (Binder & Fernandino, 2015). Activity demonstrated in several frontal regions (inferior, middle, and superior frontal gyri) is also consistent with past studies. These areas are generally activated in working memory, executive function, and critical processing, all of which are important aspects of the OLA task (Hampstead et al., 2011).

Some differences from prior investigations are primarily due to the technical differences between fMRI and fNIRS. We could not detect activation in subcortical brain areas due to fNIRS' limited penetration depth of approximately 1.5cm (Pinti et al., 2020). If we had used an imaging technology with greater penetrative depth, we likely would have also seen engagement of the medial temporal lobe, including the hippocampus, perirhinal cortex, entorhinal cortex, and parahippocampal gyrus as well as the ventral visual stream (Hampstead et al., 2011; Sommer et al., 2005a; Sommer et al., 2005b). Additionally, the limited spatial resolution of fNIRS makes direct comparison with fMRI difficult. While we used the NIRS Toolbox (Santosa et al., 2018) to ensure the greatest accuracy of the reported regions of activation, this was a projected estimation due to the limited spatial resolution of fNIRS as compared to fMRI. For example, channels of activation in the prefrontal cortex may not follow the cortical topography exactly in that a channel may span across multiple regions.

Differences in environment between fNIRS and fMRI also likely contributed to discrepancies between results. The loud, enclosed environment of the MRI scanner reduces the potential for auditory and visual distractions. By contrast, fNIRS is administered in a quiet room, and it is possible that participants may lose focus more easily in this environment. In addition, muffled noise from the neighboring rooms may be distracting. Although this may contribute to inconsistency between fNIRS and fMRI results, it is also more consistent with daily life than the fMRI environment, increasing the ecological validity of the task. These environmental differences might also have caused changes in participants' performance of the task. While we did not analyze the behavioral data in the current study, it would be interesting for future investigations to do a comparison between these performance results in fNIRS and fMRI.

Differences in age between the current study's sample and Hampstead et al., 2011's sample may help explain the differences in neuronal activity. The average age of participants in Hampstead et al., 2011 was 7 years older than the average age of the current study. This may have affected our findings because older adults require more neuronal resources than younger adults. The compensation-related utilization of neural circuits hypothesis (CRUNCH) states that older adults show greater and more widespread activation on fMRI because of the increased recruitment of neuronal resources required to execute tasks (Reuter-Lorenz & Cappell, 2008). The hemispheric asymmetry reduction in older adults (HAROLD) model suggests that older adults show a more bilateral activation pattern in areas of the prefrontal cortex as compared to younger adults' unilateral activation (Cabeza, 2002). Whereas in previous fMRI studies (Hampstead et al., 2011) there was bilateral activation of the posterior parietal regions, here we observed significant activation only in the left parietal lobe and instead saw significant

deactivation in the right posterior parietal region for the Novel vs. Repeated contrast. The CRUNCH and HAROLD models might explain these differences.

Another explanation for differences in lateralized activation in the parietal lobe is that our participants may have relied more on categorical position and semantic information than exact coordinate position in space to encode objects and their associated locations. Processing of categorical position is primarily associated with the left parietal-temporal lobe, whereas coordinate position (i.e. location in space) engages similar regions in the right hemisphere (Kessels et al., 2002; van Asselen et al., 2008). Specifically, Kessels et al., 2002 found that individuals with lesions in their left posterior parietal cortex could not bind categorical position (e.g. relative location) and object information in memory. Given our finding of significant activation in the left posterior parietal cortex, our participants may have prioritized categorical position over coordinate position. For example, participants may have processed object-location information as “keys on shelf” or “keys to left of plate” rather than “keys in top right corner”. One speculation is that participants may have also used semantic information in conjunction with categorical position to remember where objects are located. Therefore, it is reasonable to presume that participants may be relying on preexisting semantically related constructs to aid recall (e.g., keys go on table, not on floor). Enriching semantic encoding through mnemonic strategy training, whereby techniques like semantic organization, semantic elaboration, and mental imagery are used to connect new learning to prior knowledge, has been found successful in improving memory performance of OLA tasks (Hampstead et al., 2012). Participants may subconsciously recall that they often place their keys on the shelf in their own home, or they may consider that they may have left the keys on the dining table after coming home from work. Future studies should investigate whether manipulating the number of similar objects in the room

results in different types of processing, and therefore different regions of activation. For example, an object could theoretically be placed on one of six chairs rather than on the one table in the room to weaken the reliability of semantic associations and promote the use of spatial processing. Rather than just remembering “book on table”, participants would have to encode “book on left center chair”.

Our use of a block design in conjunction with the OLA task, when previous studies used event-related design, may have impacted the results of the study. Block design yields the highest signal-to-noise ratio (Dale & Buckner, 1997), statistical power (Friston et al., 1999), and time efficiency (Donaldson, 2004) within an experiment. The separate blocks of this experimental construct allowed for more accurate comparison of significant channels of brain activity between specific conditions. However, block design can prompt habituation (Klingner et al., 2011) that does not occur in the event-related design. In the object location association task, this may occur during repeated conditions due to the predictability of the repeatedly alternating objects.

Limitations

The current study has limitations that may have impacted its outcome. The predominantly white and female population of our sample is not representative of the general population, and the average years of education among our participants was higher than both the national and global average. Additionally, a higher number of years of education may potentially result in neuropsychological scores that are above the impaired threshold even after a large decline from baseline. Because the neuropsychological scores we collected are baseline data, we are unable to confirm that they have not undergone undiagnosed cognitive decline. While we did try to account for this by asking about subjective memory decline, it is difficult for many individuals to accurately differentiate normal cognitive decline due to aging from decline due to dementia.

Conclusion

In summary, the results of the current study aligned fairly well with fMRI studies investigating OLA while also having notable differences. We saw significant activation in the bilateral posterior prefrontal cortex and areas of the left dorsal visual stream including areas of the parietal cortex and neighboring regions. The left parietal activation suggests that semantic processing was likely employed to encode object-location associations. However, we also observed deactivation in the right parietal and temporal cortices, which is dissimilar to past OLA studies, likely due to a variety of factors possibly including neuroimaging technique, study environment, age, block design, and processing strategies. Future studies should use an object location paradigm that specifically engages both spatial and semantic processing to assess whether the lack of right parietal activation in the current study is due to participants' emphasis on using semantic and categorical processing to encode information to memory. Additionally, comparing fNIRS and fMRI imaging and behavioral results within the same participants would lead to a deeper understanding of the differences between the two neuroimaging techniques.

References

Aasted, C. M., Yücel, M. A., Cooper, R. J., Dubb, J., Tsuzuki, D., Becerra, L., Petkov, M. P., Borsook, D., Dan, I., & Boas, D. A. (2015). Anatomical guidance for functional near-infrared spectroscopy: AtlasViewer tutorial. *Neurophotonics*, *2*(2), 1-16. https://doi.org/10.1117/1.NPh.2.2.020801

Baker, J. M., Bruno, J. L., Gundran, A., Hosseini, S. M. H., & Reiss, A. L. (2018). FNIRS measurement of cortical activation and functional connectivity during a visuospatial working memory task. *PLOS ONE*, *13*(8), e0201486. https://doi.org/10.1371/journal.pone.0201486

Balardin, J. B., Zimeo Morais, G. A., Furucho, R. A., Trambaiolli, L., Vanzella, P., Biazoli, C., & Sato, J. R. (2017). Imaging brain function with functional near-infrared spectroscopy in unconstrained environments. *Frontiers in Human Neuroscience*, *11*, 258. https://doi.org/10.3389/fnhum.2017.00258

Bandettini, P. A. (2020). *FMRI*. MIT Press.

Barker, J. W., Aarabi, A., & Huppert, T. J. (2013). Autoregressive model based algorithm for correcting motion and serially correlated errors in fNIRS. *Biomedical Optics Express*, *4*(8), 1366-1369. https://doi.org/10.1364/BOE.4.001366

Bigio, I. J., & Fantini, S. (2016). *Quantitative biomedical optics: Theory, methods, and applications*. Cambridge University Press.

Binder, J. R., & Fernandino, L. (2015). Semantic processing. In *Brain Mapping* (pp. 445–454). Elsevier. https://doi.org/10.1016/B978-0-12-397025-1.00266-9

Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. *Psychology and Aging*, *17*(1), 85–100. https://doi.org/10.1037/0882-7974.17.1.85

Cui, X., Bray, S., Bryant, D. M., Glover, G. H., & Reiss, A. L. (2011). A quantitative comparison of NIRS and fMRI across multiple cognitive tasks. *NeuroImage*, *54*(4), 2808–2821. https://doi.org/10.1016/j.neuroimage.2010.10.069

Dale, A., & Buckner, R. (1997). Selective averaging of rapidly presented individual trials using fMRI. *Human Brain Mapping*, *5*(5), 329–340. https://doi.org/10.1002/(SICI)1097-0193(1997)5:5<329::AID-HBM1>3.0.CO;2-5

Donaldson, D. I. (2004). Parsing brain activity with fMRI and mixed designs: What kind of a state is neuroimaging in? *Trends in Neurosciences*, *27*(8), 442–444. https://doi.org/10.1016/j.tins.2004.06.001

Friston, K. J., Holmes, A. P., Price, C. J., Büchel, C., & Worsley, K. J. (1999). Multisubject fMRI studies and conjunction analyses. *NeuroImage*, *10*(4), 385–396. https://doi.org/10.1006/nimg.1999.0484

Gajewski, P. D., Hanisch, E., Falkenstein, M., Thönes, S., & Wascher, E. (2018). What Does the N-Back task measure as we get older? Relations between working-memory measures and other cognitive functions across the lifespan. *Frontiers in Psychology*, *9*, 2208. https://doi.org/10.3389/fpsyg.2018.02208

Graumann, M., Ciuffi, C., Dwivedi, K., Roig, G., & Cichy, R. M. (2022). The spatiotemporal neural dynamics of object location representations in the human brain. *Nature Human Behaviour*, *6*(6), 796–811. https://doi.org/10.1038/s41562-022-01302-0

Hampstead, B. M., Sathian, K., Phillips, P. A., Amaraneni, A., Delaune, W. R., & Stringer, A. Y. (2012). Mnemonic strategy training improves memory for object location associations in both healthy elderly and patients with amnestic mild cognitive impairment: A

randomized, single-blind study. *Neuropsychology*, *26*(3), 385–399. https://doi.org/10.1037/a0027545

Hampstead, B. M., Stringer, A. Y., Stilla, R. F., Amaraneni, A., & Sathian, K. (2011). Where did I put that? Patients with amnestic mild cognitive impairment demonstrate widespread reductions in activity during the encoding of ecologically relevant object-location associations. *Neuropsychologia*, *49*(9), 2349–2361. https://doi.org/10.1016/j.neuropsychologia.2011.04.008

Hampstead, B. M., Stringer, A. Y., Stilla, R. F., Deshpande, G., Hu, X., Moore, A. B., & Sathian, K. (2011). Activation and effective connectivity changes following explicit-memory training for face–name pairs in patients with mild cognitive impairment: A pilot study. *Neurorehabilitation and Neural Repair*, *25*(3), 210–222. https://doi.org/10.1177/1545968310382424

Herrmann, M. J., Ehlis, A.C., Wagener, A., Jacob, C. P., & Fallgatter, A. J. (2005). Near-infrared optical topography to assess activation of the parietal cortex during a visuo-spatial task. *Neuropsychologia*, *43*(12), 1713–1720. https://doi.org/10.1016/j.neuropsychologia.2005.02.011

Huppert, T. J. (2016). Commentary on the statistical properties of noise and its implication on general linear models in functional near-infrared spectroscopy. *Neurophotonics*, *3*(1), 1 - 10. https://doi.org/10.1117/1.NPh.3.1.010401

Karim, H. T., Sparto, P. J., Aizenstein, H. J., Furman, J. M., Huppert, T. J., Erickson, K. I., & Loughlin, P. J. (2014). Functional MR imaging of a simulated balance task. *Brain Research*, *1555*, 20–27. https://doi.org/10.1016/j.brainres.2014.01.033

Kessels, R. P. C., de Haan, E. H. F., Kappelle, L. J., & Postma, A. (2002). Selective impairments in spatial memory after ischaemic stroke. *Journal of Clinical and Experimental Neuropsychology*, *24*(1), 115–129. https://doi.org/10.1076/jcen.24.1.115.967

Klingner, C. M., Nenadic, I., Hasler, C., Brodoehl, S., & Witte, O. W. (2011). Habituation within the somatosensory processing hierarchy. *Behavioural Brain Research*, *225*(2), 432–436. https://doi.org/10.1016/j.bbr.2011.07.053

Kocsis, L., Herman, P., & Eke, A. (2006). The modified Beer–Lambert law revisited. *Physics in Medicine and Biology*, *51*(5), N91–N98. https://doi.org/10.1088/0031-9155/51/5/N02

Lloyd-Fox, S. (2017). Functional near-infrared spectroscopy. In B. Hopkins, E. Geangu, & S. Linkenauger (Eds.), *The Cambridge Encyclopedia of Child Development* (2nd ed., pp. 129–136). Cambridge University Press. https://doi.org/10.1017/9781316216491.022

McKendrick, R., Mehta, R., Ayaz, H., Scheldrup, M., & Parasuraman, R. (2017). Prefrontal hemodynamics of physical activity and environmental complexity during cognitive work. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, *59*(1), 147–162. https://doi.org/10.1177/0018720816675053

Meidenbauer, K. L., Choe, K. W., Cardenas-Iniguez, C., Huppert, T. J., & Berman, M. G. (2021). Load-dependent relationships between frontal fNIRS activity and performance: A data-driven PLS approach. *NeuroImage*, *230*, 117795. https://doi.org/10.1016/j.neuroimage.2021.117795

Monden, Y., Dan, I., Nagashima, M., Dan, H., Uga, M., Ikeda, T., Tsuzuki, D., Kyutoku, Y., Gunji, Y., Hirano, D., Taniguchi, T., Shimoizumi, H., Watanabe, E., & Yamagata, T. (2015). Individual classification of ADHD children by right prefrontal hemodynamic

responses during a go/no-go task as assessed by fNIRS. *NeuroImage: Clinical*, *9*, 1–12. https://doi.org/10.1016/j.nicl.2015.06.011

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*(1), 46–59. https://doi.org/10.1002/hbm.20131

Pinti, P., Tachtsidis, I., Hamilton, A., Hirsch, J., Aichelburg, C., Gilbert, S., & Burgess, P. W. (2020). The present and future use of functional near-infrared spectroscopy (fNIRS) for cognitive neuroscience. *Annals of the New York Academy of Sciences*, *1464*(1), 5–29. https://doi.org/10.1111/nyas.13948

Postma, A., Kessels, R., & Vanasselen, M. (2008). How the brain remembers and forgets where things are: The neurocognition of object–location memory. *Neuroscience & Biobehavioral Reviews*, *32*(8), 1339–1345. https://doi.org/10.1016/j.neubiorev.2008.05.001

Randolph, C., Tierney, M. C., Mohr, E., & Chase, T. N. (1998). The repeatable battery for the assessment of neuropsychological status (RBANS): Preliminary clinical validity. *Journal of Clinical and Experimental Neuropsychology*, *20*(3), 310–319. https://doi.org/10.1076/jcen.20.3.310.823

Reuter-Lorenz, P. A., & Cappell, K. A. (2008). Neurocognitive aging and the compensation hypothesis. *Current Directions in Psychological Science*, *17*(3), 177–182. https://doi.org/10.1111/j.1467-8721.2008.00570.x

Santosa, H., Zhai, X., Fishburn, F., & Huppert, T. (2018). The NIRS brain analyzIR toolbox. *Algorithms*, *11*(5), 73. https://doi.org/10.3390/a11050073

Scarapicchia, V., Brown, C., Mayo, C., & Gawryluk, J. R. (2017). Functional magnetic resonance imaging and functional near-infrared spectroscopy: Insights from combined recording studies. *Frontiers in Human Neuroscience*, *11*, 1-12. https://doi.org/10.3389/fnhum.2017.00419

Sommer, T., Rose, M., Gläscher, J., Wolbers, T., & Büchel, C. (2005). Dissociable contributions within the medial temporal lobe to encoding of object-location associations. *Learning & Memory*, *12*(3), 343–351. https://doi.org/10.1101/lm.90405

Sommer, T., Rose, M., Weiller, C., & Büchel, C. (2005). Contributions of occipital, parietal and parahippocampal cortex to encoding of object-location associations. *Neuropsychologia*, *43*(5), 732–743. https://doi.org/10.1016/j.neuropsychologia.2004.08.002

Thoma, V., & Henson, R. N. (2011). Object representations in ventral and dorsal visual streams: FMRI repetition effects depend on attention and part–whole configuration. *NeuroImage*, *57*(2), 513–525. https://doi.org/10.1016/j.neuroimage.2011.04.035

Tombaugh, T. (2004). Trail Making Test A and B: Normative data stratified by age and education. *Archives of Clinical Neuropsychology*, *19*(2), 203–214. https://doi.org/10.1016/S0887-6177(03)00039-8

Tomczak, M., Tomczak, E., Kleka, P., & Lew, R. (2014). Using power analysis to estimate appropriate sample size. *Trends in Sports Sciences*, *4*, 195–206. https://doi.org/10.1007/978-3-8349-3752-0_5

Van Asselen, M., Kessels, R. P. C., Kappelle, L. J., & Postma, A. (2008). Categorical and coordinate spatial representations within object-location memory. *Cortex*, *44*(3), 249–256. https://doi.org/10.1016/j.cortex.2006.05.005

Wang, J.-H., & Cui, S. (2017). Associative memory cells: Formation, function and perspective. *F1000Research*, *6*, 283. https://doi.org/10.12688/f1000research.11096.2

Yeung, M. K., Lee, T. L., & Chan, A. S. (2021). Negative mood is associated with decreased prefrontal cortex functioning during working memory in young adults. *Psychophysiology*, *58*(6), 1-12. https://doi.org/10.1111/psyp.13802

Yeung, M. K., Lee, T. L., Han, Y. M. Y., & Chan, A. S. (2021). Prefrontal activation and pupil dilation during n-back task performance: A combined fNIRS and pupillometry study. *Neuropsychologia*, *159*, 107954. https://doi.org/10.1016/j.neuropsychologia.2021.107954