**UREAP – Final Report**

Using fNIRS to identify age-related neurocognitive changes in working memory

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## 1. Abstract

The process of aging causes changes in the brain, which may have effects on working memory; this is an important aspect of brain functioning necessary to complete everyday tasks (Peters, 2006, Scahill et al., 2003, Svennerholm et al., 1997). Researchers have shown that older adults (OAs) demonstrate more brain activity when compared to younger adults; that is, they show bilateral activation (both hemispheres) rather than lateralized (one hemisphere) activation, as young adults show for working memory tasks. This bilateral activation also correlates with better performance in OAs; thus, it is thought to be compensatory and used to counteract deficits caused by aging and cognitive decline (Niu et al., 2013, Talamonti et al., 2020, Vermeij et al., 2012). However, some researchers do not find that additional bilateral activity is compensatory and indicates neural inefficiency (Knights et al., 2021, Morcom & Henson, 2018). Thus, more research is needed to further investigate the role of bilateral activity and better define its compensatory effects.

This study, during the April-September UREAP term, will use functional near-infrared spectroscopy (fNIRS) to examine younger adults' (18-25) brain activity while completing cognitive tasks examining working memory function (computer-based, visuospatial N-back tasks). The study will then further continue past September to examine older adults' (>65) brain activity while completing the same working memory tasks, which will then be compared to the results from the young adult group in multiple domains (reaction time, accuracy, and brain activity patterns). The goal of this research is to further understand the role of widespread brain activity, which may lead to further research in cognitive decline and the characterization of healthy cognitive aging.

## 2.1. Background

As advances in medicine and public health measures, among other factors, have lengthened the average lifespan of humans, the proportion of older adults (aged >65 years) is rapidly increasing (Cabeza et al., 2018). The aging process continues to be closely associated with cognitive decline in many individuals, therefore the number of older adults diagnosed with a memory-related illness such as Alzheimer's disease is predicted to rapidly increase within the population (Cabeza et al., 2018). This prompts the urgent need for research that can help us understand the underlying neural mechanisms behind optimal aging, where cognitive abilities remain intact, as opposed to cognitive decline, which may progress into conditions such as Alzheimer's disease (McDonough et al., 2022; Cabeza et al., 2018).

Studies have indicated that age-related differences in brain activity are linked to changes in behavior, such as cognitive decline, and are reflected in task-specific cognitive performance. However, there remains a significant gap in research examining the correlation between changes in brain activity and performance, and the underlying neural mechanisms behind these changes (Cabeza et al., 2018). These mechanisms span various levels, from cellular and molecular processes to factors such as brain atrophy and white matter degradation (McDonough et al., 2022; Cabeza et al., 2018).

One of the most pressing questions in cognitive neuroscience is why some individuals experience more rapid cognitive decline than others (McDonough et al., 2022). This also highlights the critical importance of employing effective brain imaging techniques, like functional near-infrared spectroscopy (fNIRS), to investigate age-related differences in brain

activity. Such research may aid in uncovering early indicators of brain diseases that impact cognitive functions, particularly memory.

Cognitive aging is a multifaceted process marked by both physiological and behavioral changes that can influence daily life. Specifically, changes in brain function have been correlated with deficits in working memory (Peters, 2006; Scahill et al., 2003; Svennerholm et al., 1997). For some individuals, these changes can escalate into neurodegenerative diseases, such as mild cognitive impairment, which is often a precursor to Alzheimer's disease. Therefore, understanding the characteristics of healthy aging is crucial for identifying those at risk of progressing into disease.

Researchers have observed that older adults often exhibit bilateral brain activity, meaning both hemispheres are active, during cognitive tasks. In contrast, younger adults tend to show lateralization, where one side of the brain is predominantly engaged (Cabeza, 2002). The Hemispheric Asymmetry Reduction in Older Adults (HAROLD) model suggests that this bilateral activation serves as a compensatory mechanism to counteract age-related cognitive decline, particularly in tasks involving the prefrontal cortex (Cabeza, 2002). Compensation, in this context, refers to the enhancement of cognitive performance through the recruitment of additional brain networks (Cabeza et al., 2018). This bilateral brain activity appears to enhance older adults' task performance, as exemplified by studies indicating that low-performing older adults activate similar networks to younger adults but achieve lower performance, whereas high-performing older adults employ bilateral activation (Cabeza et al., 2002). Nevertheless, some studies challenge the HAROLD model's claims, suggesting that bilateral activity might not necessarily be compensatory but rather indicative of an inability to use neural resources efficiently (Knights et al., 2021; Morcom & Henson, 2018). Consequently, there's a pressing

need for further research to better understand the role of bilateral brain activity in older adults and its impact on performance.

Studies using fNIRS have demonstrated enhanced working memory performance in older adults when accompanied by increased bilateral activity in the prefrontal cortex (Niu et al., 2013; Talamonti et al., 2020; Vermeij et al., 2012). Therefore, utilizing fNIRS to compare the brain activity of older adults with that of younger adults during cognitive tasks can be used to examine the significance of bilateral activation in older adults' performance. This study therefore aims to provide deeper insight into the changes occurring in brain function and cognition as we age. With a more comprehensive understanding of these neurological processes, researchers may be better equipped to target changes in brain activity before they evolve into more severe forms of cognitive impairment.

### 2.2. Cognitive Performance, Cognitive Load, and Task Complexity

Understanding how cognitive load influences brain activation patterns can offer valuable insights into the mechanisms of brain activity in older adults relative to younger counterparts. By manipulating the complexity of working memory tasks, we can explore the intricate relationship between cognitive load, task complexity, and brain activity across age groups. This exploration may aid in understanding the limitations of brain activity changes at specific levels of task complexity.

The Compensation-Related Utilization of Neural Circuits Hypothesis (CRUNCH) model of brain aging (Reuter-Lorenz & Cappell, 2008) highlights the significance of manipulating task complexity as well as differences in cognitive load. According to CRUNCH, age-related

compensatory mechanisms involve the recruitment of additional brain regions, often observed in the prefrontal cortex (PFC), to maintain cognitive performance at levels comparable to young adults (Reuter-Lorenz & Cappell, 2008). Furthermore, the CRUNCH model states that when task complexity surpasses a certain threshold, cognitive load exceeds capacity, leading older adults to exhibit reduced activity compared to younger adults (Reuter-Lorenz & Cappell, 2008). Despite these findings, only a limited number of studies have tested the CRUNCH model's predictions (Bauer et al., 2015; Toepper et al., 2014; Mattay et al., 2006), and some have produced results contradictory to its claims (Schneider-Garces, 2010; Jamadar, 2020). This highlights the need for further experimental research that manipulates cognitive load to determine whether the increased brain activity seen in older adults is limited to a certain level of task difficulty, or whether these neural recruitment strategies are employed regardless of cognitive load.

### 2.3. Exploring Age-Related Frontoparietal Activation with fNIRS

Functional Near-Infrared Spectroscopy (fNIRS) is a non-invasive method of studying brain activity across various age groups. Unlike other imaging techniques such as fMRI, fNIRS offers better temporal resolution and lower sensitivity to body movements (Pinti et al., 2020). It functions by emitting near-infrared light at various wavelengths (ranging from 650-950nm) from a transmitting optode. This light penetrates through the layers of the head (skin, skull, cerebrospinal fluid) and reaches cortical brain tissue. Subsequently, the light undergoes attenuation, absorption, and scattering, which is detected by receiving optodes (Pinti et al., 2020). By measuring the concentrations of oxygenated hemoglobin (HbO2) and deoxygenated hemoglobin (HbR), fNIRS serves as a proxy for cortical activity. This technology enables

researchers to investigate changes in brain activity within different regions as individuals age, making it an ideal tool for examining age-related changes in targeted brain areas.

While many studies have traditionally focused on brain activity within the prefrontal cortex (Yeung et al., 2016; Vermeij et al., 2017; Nguyen et al., 2019), more recent research using brain imaging technologies, such as fMRI and fNIRS, examines multiple brain regions at once (Heinzel et al., 2015; Kato et al., 2017; Kito et al., 2014). This approach allows researchers to investigate functional connectivity within the brain. Studying functional connectivity, rather than isolating individual brain regions, is critical for understanding age-related changes in the brain. It enables researchers to explore the coordinated activity and communication patterns between different brain regions, offering a more holistic view of the brain's functional organization (Ferras-Permayner, 2019). Recent findings using fNIRS have demonstrated changes in brain activity not only in the frontal lobe but also in the parietal lobe, shedding light on the importance of exploring frontoparietal connectivity through neural pathways (Meidenbauer et al., 2021; Yuk et al., 2020; Fishburn et al., 2014). These outcomes emphasize the value of using fNIRS to investigate functional connectivity within the frontoparietal lobe and its potential influence on performance.

Our study aims to use fNIRS to investigate prefrontal cortex and parietal lobe activity, as well as frontoparietal connectivity using fNIRS. We will employ a visuospatial N-back task that manipulates task complexity, leading to an increase in cognitive load among participants. This research seeks to examine how differences in brain activity translate into distinct behavioral patterns, as well as how task complexity affects these brain activity patterns and how this relates to performance. Additionally, we will administer cognitive assessments to our older adult participants, such as the RBANS and MoCA, to explore potential associations between brain

activity patterns (e.g., compensation) and cognitive function. The results from our study could potentially begin to help us better understand the underlying neural mechanisms associated with aging.

Furthermore, we plan to examine cognitive function in participants who previously engaged in an N-back study 12 months prior by implementing the MoCA and RBANS tests. This longitudinal approach will allow us to compare performance across sessions and potentially identify cognitive decline associated with previously measured brain activity.

## 3. Methods

### 3.1 Participants

This study involved a sample of twenty young adults ranging from 18 to 25 years old. Recruitment efforts were made in various ways, including the posting of informational flyers in establishments like TCC and Golds Gym (with permission) and word-of-mouth referrals. Before any experimental procedures began, participants were provided with a consent form, which they were required to read and sign. Eligibility criteria for participation included various factors, such as: age within the aforementioned range, normal or corrected vision, English fluency (90-100%), a minimum of six years of formal education, absence of known neurological or psychological disorders (such as stroke, brain injury, Parkinson's disease, bipolar disorder, or depression), non-smoking status, no use of Aricept (attention-enhancing medication) or psychoactive drugs, and right-handedness. These criteria were communicated in the recruitment posters, and potential participants were screened for compliance via phone or email before visiting TRU to partake in

the study. The study received prior approval from TRU's research ethics committee before the experimental testing began.

### 3.2 Procedure

Upon signing the consent form and addressing any questions or concerns about the experiment, participants were fitted with the fNIRS Brite head cap (Artinis, Medical Systems, The Netherlands). The cap's placement, centered at Cz according to the 10-20 system, was standardized for all participants to ensure accurate cap placement. The fNIRS cap array features ten light-emitting optodes transmitting NIR light within the 650-950 nm range and eight receivers designed to detect changes in light absorption, capturing data at a rate of 25 Hz. These optodes were positioned 3 cm apart, and consisted of 21 recording channels across the right prefrontal cortex (PFC), left PFC, and right parietal cortex (see Figure 1.). Continuous monitoring of changes in oxygenated and deoxygenated hemoglobin concentrations from each channel allowed the assessment of brain activity, with greater oxygenated hemoglobin delivery indicating increased brain activity. To reduce "noise" factors such as movement artifacts and physiological noise, a short separation channel (SSC, 1.5 cm) was positioned on the left PFC. Subsequently, this SSC data was filtered during analysis to enhance the isolation of the hemodynamic response concerning brain activity during the working memory task and to reduce the risk of false positives.

fNIRS data acquisition was performed using Oxysoft (Artinis, Medical Systems, The Netherlands, version 3.2.51.4) through a Bluetooth connection to a laptop. After ensuring a reliable signal, including adjusting hair that might obstruct the optodes’ access to the scalp,

participants were asked to participate in three N-back tasks, each increasing in difficulty (1-back, 2-back, and 3-back tasks, respectively). These tasks involved continuous observation of visual stimuli, requiring participants to determine if the current visual stimulus (indicated by a blue box) matched the previous box presented either 1 box ago (1-back), 2 boxes ago (2-back), or 3 boxes ago (3-back), denoted by pressing 'S' for similar or 'D' for different. The task design utilized E-prime 3.0 (Psychology Software Tools, PA, USA) and was presented on a laptop (Dell Latitude 3410, 14" HD, 1920 x 1080 resolution) positioned in front of the participants. Each session lasted 45 to 60 minutes, with rest breaks provided between the three N-back tasks and as requested.

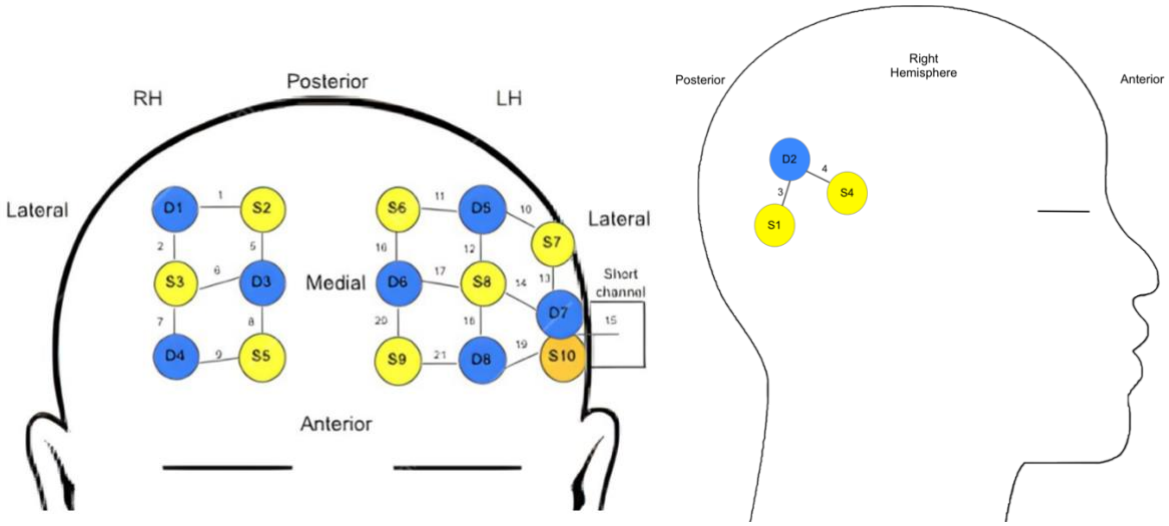



**Figure 1.** Frontal and profile view of the placement of fNIRS optodes on the prefrontal and parietal cortex, where D (blue) represents detecting optodes and S (yellow) represents transmitting optodes. The source-detector pairings make up 21 channels across the right and left hemispheres, with channels covering right prefrontal cortex (PFC), left PFC, and right parietal cortex (PC). A short-separation channel in the left hemisphere can also be indicated (S10 and D7, channel 15).

### 3.3 N-Back Tasks

In each N-back task, participants encountered rest blocks lasting 20 seconds, serving as a baseline measurement for the hemodynamic response. During these intervals, participants relaxed while viewing a blank screen with the word "rest" displayed in the middle. Following each rest block, a 40-second trial block ensued, during which participants performed the designated N-back task (1-back, 2-back, or 3-back). Each participant performed the 1-back task first, then either the 2-back or 3-back next (the order to which the tasks were performed were randomly assigned to each participant prior to testing).

In these tasks, a blue box appeared at one of six possible positions relative to a central cross on the screen. The box's position changed during the 40-second trial block, appearing for 0.5 seconds and then disappearing. Participants had the remaining 1.5 seconds before the next box appeared to indicate whether the current stimulus position matched that of 1, 2, or 3 boxes ago, using the 'S' key for a match and the 'D' key for a difference, all performed with their right hand. Each trial block was comprised of twenty boxes, with 20% (4 trials) designated as targets (matching the position from 2 trials ago and indicated by the “S” key) and 80% (16 trials) as non-targets (position different from 2 trials ago and indicated by the “D” key). This cycle of 20-second rest and 40-second task periods was repeated four times in total, amounting to approximately 4 minutes for each condition, followed by a 5-minute rest period between conditions.

### 3.4 Analysis

Data from each of the three N-back tasks for each participant were extracted from E-prime and compiled into an Excel database. Trials with no observed responses and those with reaction times less than 80 milliseconds (which is indicative of a guess rather than a calculated response) were excluded from further analysis. Calculations included error rates (total incorrect responses divided by total possible responses), Pr values were calculated as a measure of accuracy (calculated by subtracting incorrect non-target responses from correct target responses), and reaction times (obtained from correct responses) for each participant across the three N-back tasks and for target and non-target categories (see Figures 2-4). These measures were then averaged across all participants to identify behavioral differences in accuracy and reaction times.

To determine the distance traveled by light emitted from the optodes, an age-dependent differential path-length factor (DPF) was applied. Data exported from Oxysoft were converted to .snirf format for further analysis using the AnalyzIR toolbox (MATLAB, 2021). The modified Beer-Lambert Law (Sassaroli & Fantini, 2004) was employed to convert changes in optical density to changes in HbO concentration (μM). Only HbO values from this conversion were considered for subsequent analysis (Blum et al., 2021). A preprocessing technique combining autoregressive pre-whitening methods and short-channel regression was utilized to extract movement artifacts and physiological noise (Huppert, 2016).

A subject-level general linear model (GLM) was applied to identify significantly active channels during the N-back trial blocks for each condition. Task event onsets and durations were used as model parameters. The GLM, a well-established method for analyzing event-related activity, minimizes the likelihood of false positive events often encountered with peak values or

areas under the curve methods. It assumes a canonical hemodynamic response function (HRF) and calculates beta coefficients as indicators of changes in HbO signal intensity and direction across all channels during task epochs. T-test contrasts, corrected for multiple comparisons, were employed to identify significant differences in brain activity across all 21 channels between task load conditions, with significance set at $p < .05$.

Future analyses will encompass between-group correlational analyses, comparing young adults to older adults, to examine differences in reaction times, accuracy, and brain activity patterns during each of the three N-back tasks.

## 4. Results

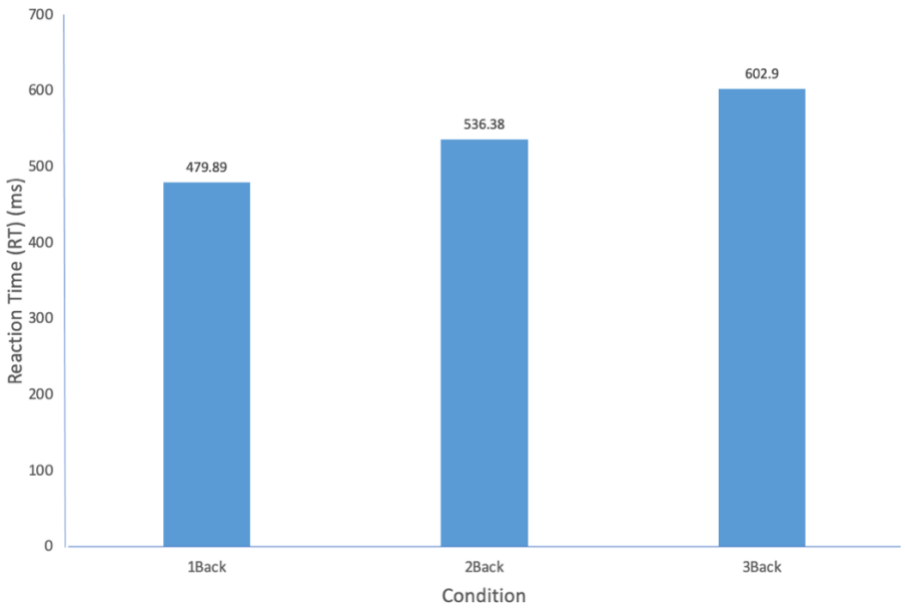



**Figure 2.** Average reaction time (RT) between presentation of stimulus and participant response to stimulus (ms) over 1-Back, 2-Back, and 3-Back task conditions (n=20)

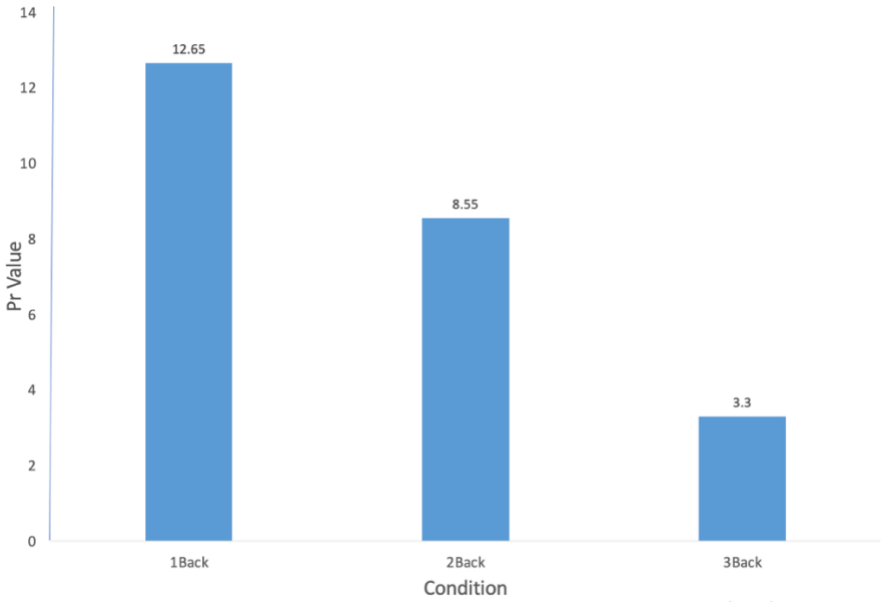



**Figure 3.** Average Pr Values over 1-Back, 2-Back, and 3-Back task conditions (n=20)

(Pr= [correct target responses - incorrect non-target responses])

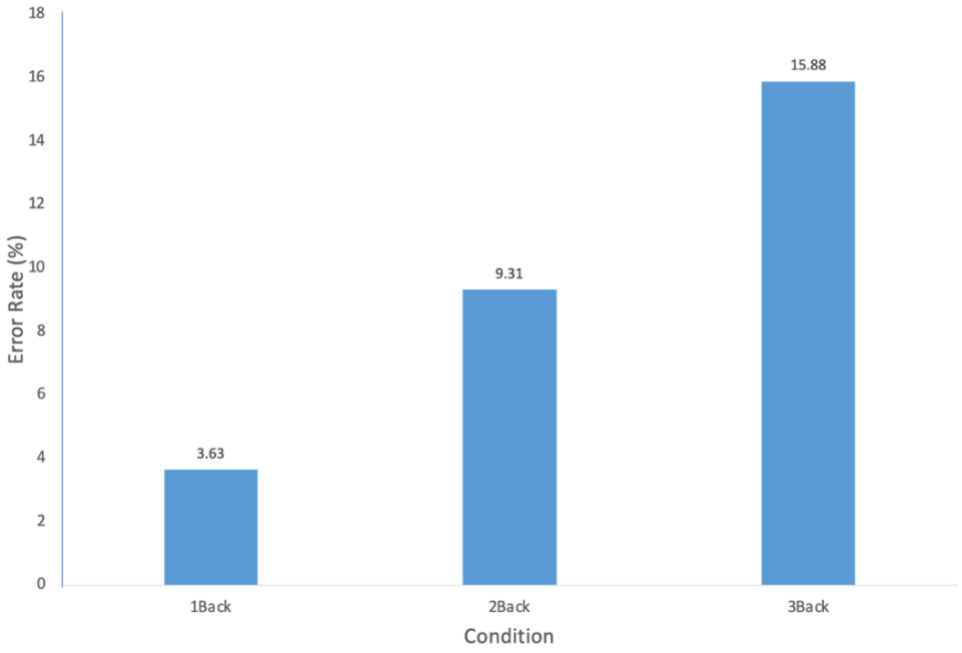



**Figure 4.** Average error rate percentages over 1-Back, 2-Back, and 3-Back task conditions (n=20)

(error rate % = number of incorrect responses/total number of possible responses x 100)

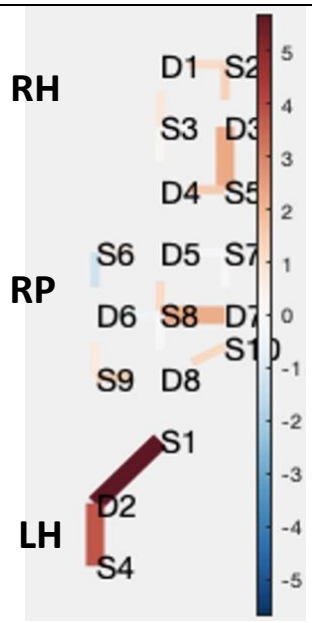
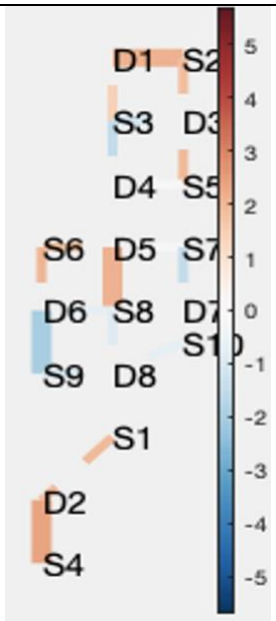
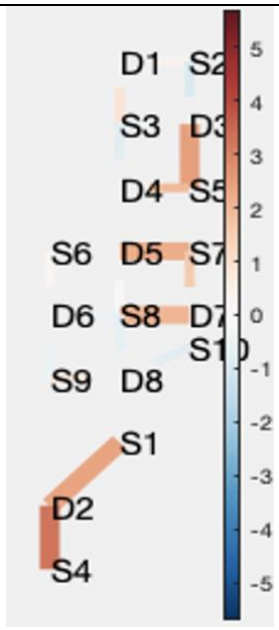
| 1-Back | 2-Back | 3-Back |
|---|---|---|
|  |  |  |



**Figure 5.** Visualization of active channels for each load condition in young adults (n=20), where red lines indicate more brain activity and blue lines indicate less brain activity.

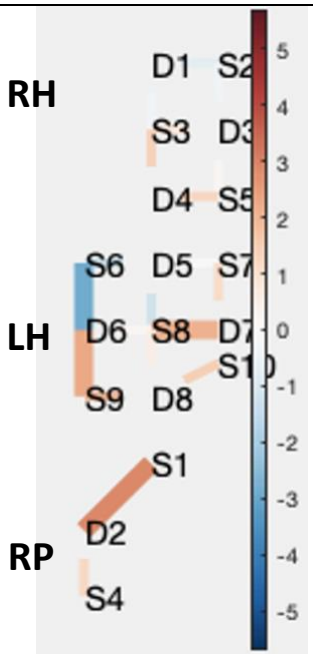
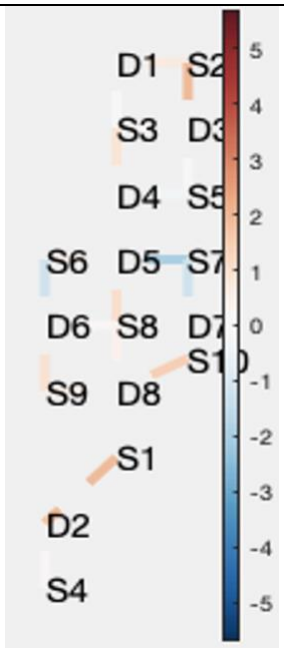
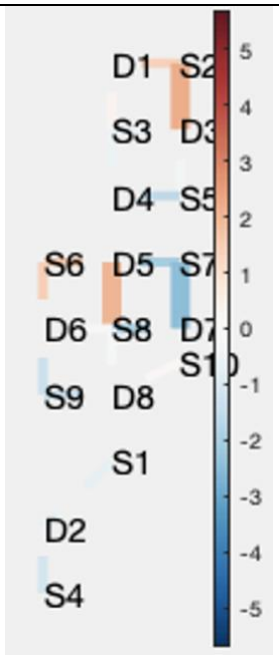
| 1-Back – 2-Back | 1-Back – 3B-Back | 2-Back – 3-Back |
|---|---|---|
|  |  |  |



**Figure 6.** Visualization of active channels for group-level contrasts between task load conditions in young adults (n=20), where red lines indicate more brain activity and blue lines indicate less brain activity.

**Table 1.** Active channels relative to baseline for each load condition for young adults (n=20).

| Relative to baseline | Source | Detector | CH | Hemisphere | beta | T-stat | p-value |
|---|---|---|---|---|---|---|---|
| **1-Back** | 1 | 2 | 3 | RH | 1.235 | 5.689 | >0.001 |
| | 4 | 2 | 4 | RH | 0.987 | 3.836 | >0.001 |
| | 5 | 3 | 8 | RH | 0.296 | 2.290 | .025 |
| | 8 | 7 | 14 | LH | 0.271 | 2.165 | .035 |
| **2-Back** | 2 | 1 | 1 | RH | 0.232 | 2.087 | .041 |
| | 4 | 2 | 4 | RH | 0.566 | 2.354 | .022 |
| | 8 | 5 | 12 | LH | 0.216 | 2.140 | .037 |
| | 9 | 6 | 20 | LH | -0.267 | -2.044 | .046 |
| **3-Back** | 1 | 2 | 3 | RH | 0.609 | 2.392 | .020 |
| | 4 | 2 | 4 | RH | 0.965 | 3.306 | .002 |
| | 5 | 3 | 8 | RH | 0.314 | 2.494 | .016 |
| | 7 | 5 | 10 | LH | 0.361 | 2.185 | .033 |
| | 8 | 7 | 14 | LH | 0.241 | 2.019 | .048 |

**Table 2.** Group-level contrast results with significantly active channels between task load conditions for young adults (n=20).

| Relative to baseline | Source | Detector | CH | Hemisphere | beta | T-stat | p-value |
|---|---|---|---|---|---|---|---|
| **1-Back-2-Back** | 1 | 2 | 3 | RH | 0.831 | 2.883 | .006 |
| | 6 | 6 | 16 | LH | -0.391 | -2.889 | .005 |
| | 8 | 7 | 14 | LH | 0.301 | 2.066 | .043 |
| | 9 | 6 | 20 | LH | 0.351 | 2.240 | .029 |
| **2Back-3Back** | 2 | 3 | 5 | RH | 0.413 | 2.229 | .030 |
| | 7 | 7 | 13 | LH | -0.374 | -2.508 | .015 |
| | 8 | 5 | 12 | LH | 0.226 | 2.020 | .048 |

### 5.1.Discussion

After calculating reaction times (ms), error rates (%), and Pr values for each task load condition in young adults, some behavioural differences between 1-Back, 2-Back, and 3-Back tasks can be observed. Average reaction time, which was calculated as the difference in time between presentation of the stimulus and participant response to the stimulus, indicated by pressing the “S” or “D” key (in ms), was shown to increase with an increase in task load complexity (1-Back<2-Back<3-Back); an increase in reaction time is indicative of a slower participant response. The average reaction times over the twenty young adult participants were calculated as: 479.89 ms (±89.28) for the 1-Back task, 536.38 ms (±143.53) for the 2-Back task, and 602.9 ms (±191.24) for the 3-Back task, respectively.

Pr values were calculated as a measure accuracy of responses, which was done by subtracting the incorrect non-target responses or "false alarms" from the correct target responses. The results demonstrated a decrease in Pr values or accuracy with an increase in task load complexity (1-Back<2-Back<3-Back) . The average Pr values for the twenty young adult participants were calculated as: 12.65 (±3.32) for the 1-Back task, 8.55 (±2.48) for the 2-Back task, and 3.3 (±3.60) for the 3-Back task, respectively.

Error rate percentage was calculated by dividing the total number of incorrect responses by the total number of possible responses within a given task and multiplied by 100; the results demonstrated an increase in error rate percentage with an increase in task load complexity (1-Back<2-Back<3-Back). The average error rate percentage over twenty young adult participants were calculated as: 3.63% (±3.71) for the 1-Back task, 9.31% (±3.10) for the 2-Back task, and 15.88% (±4.50) for the 3-Back task, respectively.

Brain activity was measured using fNIRS and analyzed using MATLAB software (see Figures 5- 6). The results showed differences in brain activity between 1-Back, 2-Back, and 3-Back task conditions, as well as for group-level contrasts (1-Back – 2-Back, 1-Back – 3-Back, 2-Back – 3-Back). While there seem to be differences in brain activity in the younger adult participants for each of the three task conditions, further analysis is needed to examine the extent of these differences and their significance.

An analysis of significantly active channels for the three task load conditions as well as the group-level contrasts can be seen in Table 1. And Table 2. above, which are based on a significance value of $p < .05$ and averaged over the twenty young adult participants. It can be observed that there are 4 active channels in the 1-Back task condition, 4 active channels in the 2-Back task condition, and 5 active channels in the 3-Back condition. For group-level contrasts,

there are 4 active channels for the 1-Back – 2-Back contrast, 3 active channels for the 2-Back – 3-Back contrasts, and no significantly active channels for the 1-Back – 3-Back contrasts. These results, along with the visualizations in Figures 5 and 6, will be used for future analysis to compare with the results from the older adult (>65+) participant group for the same three task load conditions.

### 5.2. Future Considerations

While there are observable differences in behavioral and brain activity differences between the three task load conditions in young adult participants, further analysis will need to be conducted after the experimental testing of the older adult participant group to perform both between-group and within-group correlational analyses. The results shown in this report have demonstrated that task complexity seems to have an effect on reaction time, error rate percentage, and accuracy, however the significance of these reactions cannot yet be reported.

Future work for the Fall 2023 and Winter 2024 semesters will aim to examine behavioral and brain activity differences in older adult participants using fNIRS, as well as run between-group correlational analyses to further examine whether there are distinctive brain activity differences between young and old adults. We hypothesize that these results will align with the predictions of the HAROLD model, which states that older adults will have bilateral brain activity as means of compensation, while young adults will have lateralized or unilateral brain activity. Additionally, the manipulation of task complexity will allow us to compare our results to the predictions of the CRUNCH model, which proposes that older adults will show less brain activity when and if task complexity exceeds cognitive abilities. Finally, MoCA and RBANS

cognitive assessments will be conducted on older adult participants to examine the potential relationships between brain activity patterns and cognitive load.

## 6. References

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## 7. Appendix

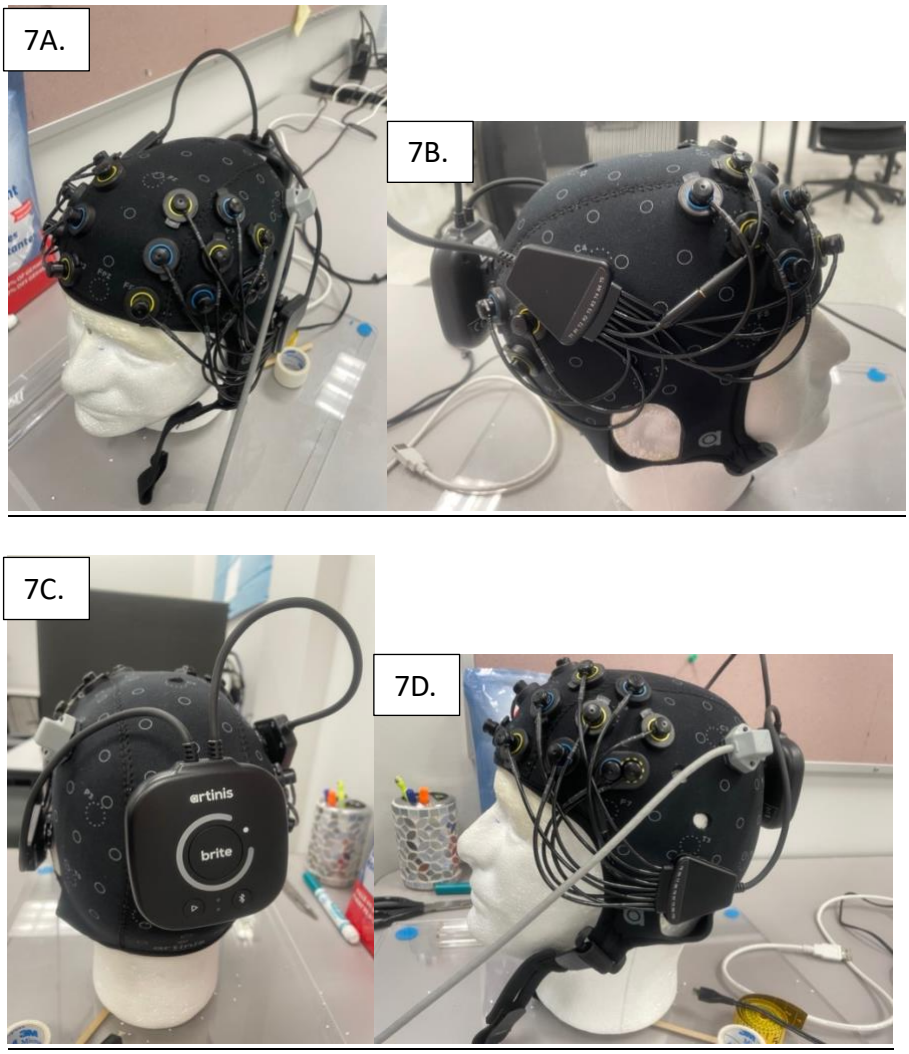


**Figure 7A-7D.** Experimental set-up of fNIRS cap for study, performed in Vision & Cognition Lab at TRU (where 7A is anterior view, 7B is right-hemisphere view, 7C is posterior view, and 7D is left-hemisphere view).