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

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Introduction

Cognitive aging is a process that is associated with both physiological and behavioural changes that may affect everyday life. Specifically, changes in brain function are correlated with deficits in working memory (7,8,9). In some individuals, these changes may progress into neurodegenerative diseases (e.g., mild cognitive impairment); thus, it is important to be able to better understand the changes that occur in healthy aging to be able to identify those that progress into disease.

Researchers have observed that older adults have bilateral (i.e., both hemispheres) brain activity when performing cognitive tasks. In contrast, younger adults show lateralization for the same tasks, which is when one side of the brain is being used (1). The Hemispheric Asymmetry Reduction in Older adults (HAROLD) model proposes that this bilateral activation is used as a compensatory mechanism to counteract age-related cognitive decline, particularly in tasks requiring prefrontal cortex activation (1). Compensation can then be defined as the enhancement of cognitive performance by the recruitment of additional brain networks (3). In terms of behaviour, these compensatory mechanisms allow older adults to perform at a comparable level to younger adults during cognitive tasks. Thus, bilateral brain activity seems to benefit older adults' performance. For example, previous research findings show that low-performing older adults recruit similar networks to younger adults but do not perform as well, whereas high-

performing older adults use bilateral activation (2). Other studies, however, have not found support for the HAROLD model and suggest that bilateral activity is not compensatory but simply reflects inability to use neural resources effectively (4,5). Thus, more research is needed to better characterise the role of bilateral brain activity in older adults and how it may influence performance.

Studies using fNIRS have shown improved performance in working memory with increased bilateral activity in the prefrontal cortex (6,10,11). Using fNIRS to compare the brain activity of older adults with younger adults during cognitive tasks is thus a feasible way to better understand the role of bilateral activation in older adults' performance. This study will provide more insight into the changes that occur in brain function and cognition as we age. With a greater understanding of these neurological processes, researchers can begin to target changes in brain activity before they manifest into more severe forms of cognitive impairment.

Objectives

The purpose of this study is to examine brain activity in (20) younger (18-25 years) and (20) older adults (> 65 years) using fNIRS technology. The main objective of this project is to determine if bilateral activation is occurring in older adults and if this activation correlates with better performance and is thus, compensatory. Specifically, we hope to measure the fronto-parietal network to concurrently measure functional connectivity between the frontal and parietal lobes, which will give us a better understanding of where this bilateral activity is occurring. To measure this objective, we will be using three different N-back tasks, each with increasing complexity, while the participant is wearing the fNIRS cap. We will also use standardized tests

(e.g., MoCA, RBANS) to examine the relationship between bilateral activity and cognitive function in older adults. 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.

Materials & Methods

Participants

20 younger adults (18-25 years) and 20 older adults (>65 years) will be recruited to participate in this project. The younger adults will be recruited by word of mouth as well as advertisement across campus and through psychology courses at TRU. Advertisement in various community spaces that have given consent to advertisement (e.g., TCC, Golds Gym) as well as email advertisement will be used to recruit older adults for this project. Posters will be printed and placed on bulletin boards in these community spaces. Additionally, recruitment will also be advertised in online recruitment sites such as social media (e.g., Facebook), with permission of site administrators, and/or on the local Castanet news media.

Testing will be done in the Psychology Lab (AE136), located in the Arts & Education building at TRU. Participants will be asked to park in a nearby lot and use a funded parking pass, they will be given directions to the lab prior to testing.. Prior to the experiment, participants will be given a consent form with details on the project which they will have to sign.

Participants will be screened to ensure they meet the inclusion criteria of the study prior to testing, which will be done via phone or email. This is measured by various factors:

participants must be within the selected age range, have normal or corrected vision, be fluent in English (90-100%), have at least 6 years of formal education, have no known neurological or psychological disorders (e.g., stroke, brain injury, Parkinson's disease, bipolar disorder, depression), are non-smokers, are not taking Aricept (attention enhancing medication) or psychoactive drugs, and are right-handed.

Procedure

When participants arrive, they will be debriefed on the experimental procedure as well as any potential risks or benefits associated. They will then be asked to sign the consent form. After this, older adult participants will complete multiple cognitive assessments to determine their overall cognitive function (such as working memory, verbal fluency, and visual spatial attention); this will be done on paper and administered by the researcher. These include: the Montreal Cognitive Assessment (MoCA), the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

All participants will then be fitted with the fNIRS Brite head cap (Artinis Medical Systems) to ensure the right size is being used (either medium or large). The center of the participant's head will be measured and marked using a measuring tape to ensure the centre of the fNIRS cap aligns with the centre of the head, and to ensure the cap is in the same location for every participant. The cap is equipped with light-emitting optodes that transmit NIR light (650-950 nm) as well as receivers that detect changes in light absorption (25 Hz). The optodes are all 3 cm apart from each other; the connection between optodes (transmitters and receivers) is considered a recording channel. While previous studies have used various numbers of recording channels to measure various brain networks, 21 recording channels will be used (which consists

of 10 transmitters and 8 receivers, respectively). Brain activity from both the left and right hemispheres of the fronto-parietal cortex will be measured, and fNIRS will be continuously recording changes in oxygenated and deoxygenated hemoglobin concentrations from each recording channel. A greater level of oxygenated hemoglobin will indicate a higher level of hemoglobin delivery to the particular brain area, which is directly indicative of greater brain activity. One short separation channel will be placed on the fNIRS cap, located on the left hemisphere; these are used as a regressor for long separation channels and essentially eliminate physiological "noise" or activity not relevant to the task.

Once a good signal has been established (making sure to move any hair that may interfere with the ability for the optode to access the scalp), the participant will be asked to complete three different N-back tasks, each with increasing complexity. More specifically, participants will complete a visuospatial 1-back, 2-back, and 3-back task, with each condition increasing in cognitive load, respectively. For these tasks, participants will view stimuli continuously and will need to indicate if a current presented stimulus (simple or dual) is similar (S) or different (D) from either 1 trial back (1-back), 2 trials back (2-back) or 3 trials back (3-back). The task will be designed with E-prime 3.0 (Psychology Software tools, PA, USA) and presented on a laptop, which is positioned in front of the seated participant. The participant will have to quickly react to the stimulus and press either the "S" key for similar or the "D" key for different on the laptop. There will be rest blocks of 20 seconds to measure baseline data of the participant's hemodynamic response, during which participants will relax while observing a blank screen (the word "rest" will appear in the middle of the screen during this period). Following each 20-second rest block, there will be a 40 second block during which the participants will perform the task. The participants will receive practice until they feel comfortable performing the recorded task.

The testing session will take about 45-60 minutes to complete for young adults, and 90 minutes to complete for older adults (including an extra 30 minutes of cognitive assessment administration). Brain activity from bilateral fronto-parietal cortices will be recorded while participants complete the task using the Artinis Medical Systems fNIRS device; the data will be collected using Oxysoft via Bluetooth to a laptop.

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. 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 for further analysis using the AnalyzIR toolbox (MATLAB, 2021). The modified Beer-Lambert Law 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. A preprocessing technique combining autoregressive pre-whitening methods and short-channel regression was utilized to extract movement artifacts and physiological noise.

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 $p < .05$.

Further 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.

Note: This project has been approved by the ethics committee at TRU; the research student (Jaida Lewis) has completed the Course on Research Ethics based on the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2: CORE 2022)

Expected Results

The outcomes of this study can provide insight into the process of aging and how it impacts working memory. Using fNIRS during cognitive tasks may provide further understanding of widespread activity in older adults and whether this compensatory process is advantageous in counteracting decline. Since cognitive decline is often a precursor to the development of neurodegenerative diseases such as dementia, a greater understanding of this

process will potentially allow better identification of age-related changes as part of healthy aging or disease and therefore early interventions. Early interventions could be the key to the prevention of neurodegenerative diseases.

Timeline

August/September	Experimental design, training in fNIRS technology; begin the process of recruiting participants and piloting
September/October	Data collection
October 1	Final, revised thesis proposal submitted to Honours coordinator; any major revisions will be finalized by Oct.3
November/December	Data collection will be completed and begin analyzing data
December/January	Honours Update presentation: oral presentation will be prepared with progress on project
January/February	Complete analysis of data
March	Poster conference: poster will be prepared with summary of results from analysis. First draft of completed thesis submitted.
April	Oral defense of thesis.
May	Finalized version of thesis submitted to Honours coordinator.

Budget

Amount	**Expense**
$250.00	Participant parking pass
$665.00	Participant recruitment & advertising expense
$915.00	**TOTAL COST**

All of the above expenses will be covered by a UREAP award which the research student (Jaida Lewis) has been awarded for the May to August semester.

Literature Sources

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