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Functional transcranial Doppler ultrasound (fTCD) is a non-invasive sensing modality that measures blood flow velocities in cerebral arteries (CBFV) with high temporal resolution. Few studies have examined the relationship of CBFV change during visual search and visual memory cognitive tasks. Here a protocol to compare lateralization between these two similar tasks using fTCD is demonstrated. Thirteen healthy volunteers were shown visual scenes on a computer and performed visual search and visual memory tasks while CBFV in the bilateral middle cerebral arteries was monitored with fTCD. Each subject completed 40 trials, consisting of baseline, calibration, instruction, and task periods. Lateralization was computed for each trial by subtracting the percent increase in CBFV on the right side from that on the left side. Results showed significant lateralization of both tasks, with memory reaching left lateralization of 1.3 percent, and search reaching right lateralization of 0.5 percent, agreeing with the hypothesis that memory is more left lateralized and search is more right lateralized. The protocol is straightforward and the equipment inexpensive, introducing a low-cost, high temporal resolution technique to further study lateralization of the brain.

Keywords—Biomedical imaging; Ultrasonography; Transcranial Doppler; Lateralization; Functional imaging

I. INTRODUCTION

The close relationship between neural activity and cerebral blood flow is well established [1-4]. Cerebral blood flow (CBF) is measured in units of volume per time and is regulated by the vasodilation and vasoconstriction of small cerebral arteries [5] and cerebral precapillaries and arterioles [6]. Current techniques used to measure hemodynamic changes related to neural activation include functional magnetic resonance imaging (fMRI) (for example, see [7-9]), but this technique has the disadvantages of high cost and having limited time resolution for imaging transient changes in hemodynamics. Functional transcranial Doppler ultrasound (fTCD) is a non-invasive sensing modality that measures blood flow velocities in cerebral arteries (CBFV) with high temporal resolution. CBFV change is linearly related to CBF change, as long as vessel diameter remains constant [5,10]. CBF change is correlated to changes in cerebral oxygen uptake, enabling fTCD to measure brain activity and lateralization with high accuracy.

Few fTCD studies have examined visual search [11] and visual memory [12, 13] cognitive tasks, and no studies have compared the two tasks to the authors' knowledge. The purpose of this paper is to develop a standard procedure to compare two related cognitive tasks: visual search, and visual memory, using fTCD.

II. METHODS AND MATERIALS

A. Subjects

The subjects for this experiment consisted of 13 volunteers (5 male, 8 female), with an average age of 21.4 ± 1.7 years. Ten subjects were found to be right-handed and three were left-handed using the Edinburgh Inventory [14].

B. Transcranial Doppler

TCD ultrasound (DWL DopplerBoxX, Compumedics Germany Gmbh) was used to collect bilateral blood flow velocity data. A fixation device was used to hold the transducers to the left and right transtemporal windows (i.e., the points on the skull where the bone is thinnest) of the subjects [15]. The middle cerebral arteries (MCAs) were insonated at depths between 43 and 55 mm, with Doppler gate size between 8 and 10 mm. The transducers were 2 MHz pulsed-wave transducers (Compumedics Germany Gmbh). The depth was initially set to expected depths for the MCA, based on published values [16], and the strongest signal was found by manual adjustment of the depth and transducer position. Once the signal was optimized, the transducers were locked in place.

C. Experimental Setup and Procedures

Visual stimuli were displayed on a 19-inch flatscreen VGA monitor (85 Hz) at a viewing distance of 90 cm. Testing took place in a dimly lit, sound attenuated testing room. The subject rested their head in a frame that kept their head steady and was asked to view various visual scenes (for example, Fig. 1). The

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Fig. 1. Example of a visual scene used in the experiment.

subject was given specific instructions about how to view the scene according to a previously published procedure [17].

The subject viewed a total of 40 visual scenes, corresponding to 40 trials. Each trial had four parts: a baseline period (25 seconds), a calibration period of variable length (for eye tracking equipment, not described here), a cue period where instructions were given to the subject visually (2.5 seconds), and a task period where the subject viewed the scene according to the instructions (20 seconds).

The task periods consisted of a total of 20 search tasks and 20 memory tasks, which were given in random order. In the search task the subject was asked to search for a small letter hidden in the scene, and in the memory task the subject was asked to memorize the scene in preparation for a quiz to be given later. The same set of scenes was used for both trials; the small letters for the search task were hidden very well so that they would not affect the memory task.

D. Data Recording

Blood flow velocity data were recorded and then exported for further analysis in MATLAB (R2014b v. 8.4.0, Mathworks, Natick, MA, USA). The data were recorded simultaneously on both sides of the brain; specific parameters that were recorded included the envelope waveform (the maximum velocities present in the Doppler spectrum at each point in time), systolic velocity (V_s, the maximum velocity present in the envelope waveform over one heartbeat cycle), diastolic velocity (V_d, the minimum velocity present in the envelope waveform over one heartbeat cycle), mean velocity (V_m, the average of the envelope waveform over one heartbeat cycle), Gosling's pulsatility index (PI = $(V_s-V_d)/V_m$) [18], and Pourcelot's resistivity index (RI = $(V_s-V_d)/V_s$ [19, 20]). All parameters were recorded for blood flow in both directions (towards and away from the transducer). The PI and RI both capture information about resistance distal to the point being insonated [20]. The sampling frequency of the recorded data (i.e. the envelope waveform, V_s, V_d, V_m, PI and RI values vs. time) was 100 Hz.

E. Data Processing

1) Filtering: The positive envelope waveforms (denoting flow towards the transducer) were first filtered with a median filter with a length of 5 samples, in order to remove spurious noise in the envelope waveform. Next, following [21], any samples were omitted from the envelope if the sample values were either greater than 2 times the truncated average (i.e., the average of all data except for the top and bottom 2.5% of values) of the entire filtered envelope for the experiment or less than 0.3 times the truncated average of the entire filtered envelope. All omitted samples were then replaced with the truncated average of the entire filtered envelope, to avoid discarding data. No subject had more than 5% of samples in the left or right envelope replaced, and most had less than 1% replaced. The waveforms were then filtered with a lowpass filter (189th order equiripple finite impulse response filter, 1 dB attenuation at 0.25 Hz and 40 dB attenuation at 1 Hz, filtered data corrected for time lag) using the function *filter* in MATLAB.

The start times of the cue periods were obtained from the software used to present the visual scenes and were used to break the TCD envelope data into the four periods mentioned above (the software used to present the visual scenes and the TCD recording were started simultaneously to allow synchronization).

2) Averaging: For each subject, an average was taken across all 20 task periods plus the immediately preceding cue periods for (a) search and (b) memory tasks. An average was taken across all 40 baseline periods for search and memory tasks, as no difference was expected in baselines for the two tasks.

3) Calculating Percent Change: The percent change from baseline, $dV_L(t)$ or $dV_R(t)$, for the left or right sides was then found as follows for the averaged search and memory cognitive tasks [21-24]:

$$dV_{L(R)}(t)\ (\%)=100\%*(V_{L(R)}(t) - V_{base,L(R)})/V_{base,L(R)} \quad (1)$$

where $V_{L(R)}(t)$ is the envelope waveform vs. time for the left or right side after averaging, and $V_{base,L(R)}$ is the time average of the last 10 seconds of the average baseline waveform for the left or right side. The last 10 seconds of the average baseline waveform were used to find $V_{base,L(R)}$ because it was the portion of the baseline period with the smallest standard deviation, and because it allowed subjects at least 15 seconds to recover from the previous task, similar to the recovery time observed in other TCD studies [25, 26]. The time during which the cue word was displayed was not included in calculating $V_{base,L(R)}$ because of possible effects of anticipation of the upcoming tasks on blood flow patterns [27].

4) Calculating Lateralization: The lateralization $\Delta V_{Search}(t)$ or $\Delta V_{Memory}(t)$ for the left and right sides was found as follows:

$$\Delta V_{Search(Memory)}(t)\ (\%) = dV_L(t)\ (\%) - dV_R(t)\ (\%) \quad (2)$$

A plot of $\Delta V_{Search}(t)$ and $\Delta V_{Memory}(t)$ vs. time for one subject is shown in Fig. 2.

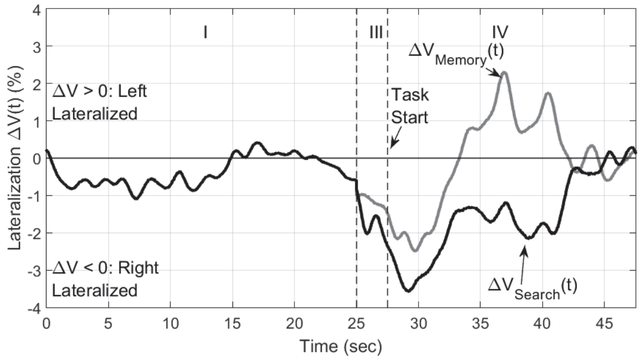

Fig. 2. Example plot of $\Delta V_{Search}(t)$ and $\Delta V_{Memory}(t)$ vs. time for one subject. I, III, and IV indicate baseline, cue, and task time periods (the calibration period is not shown due to variable length). The baseline period is the same for both tasks as baseline waveforms from both tasks were pooled when averaging.

Two equivalent methods were used to find the average lateralization vs. time for all 13 subjects. In **method 1**, all subjects' values of the lateralization $\Delta V_{Memory}(t)$ or $\Delta V_{Search}(t)$ were averaged together sample-by-sample, giving the ensemble average $\Delta V_{Memory}(t)$ and $\Delta V_{Search}(t)$ vs. time (Fig. 3). In **method 2**, the percent changes for the left and right sides $dV_L(t)$ and $dV_R(t)$ were averaged across all subjects sample-by-sample for search and memory tasks. These ensemble averages were then used along with (2) to calculate $\Delta V_{Search}(t)$ and $\Delta V_{Memory}(t)$.

5) Statistical Analysis: For statistical analysis, at 5 second intervals during the task period, a two-tailed two-sample Student's t-test with equal variances was performed on two sets of 50 consecutive points from the ensemble averaged $\Delta V_{Memory}(t)$ and $\Delta V_{Search}(t)$.

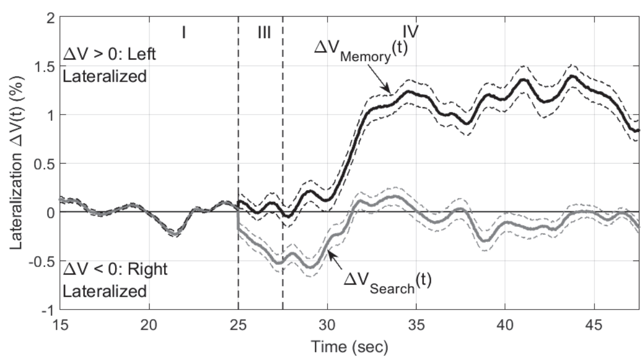

Fig. 3. Ensemble average lateralization $\Delta V_{Search}(t)$ and $\Delta V_{Memory}(t)$ vs. time for search and memory tasks for all subjects (solid lines), calculated using **method 1**. Dashed lines above and below solid lines represent +/- 1 standard error of the mean. I, II, and III indicate the baseline period, cue period, and task period.

III. Results

Fig. 3 shows the plots of ensemble average lateralization $\Delta V_{Search}(t)$ and $\Delta V_{Memory}(t)$ vs. time, for comparison between the search and memory tasks. On average, the memory task tended to have more positive values of lateralization than the search task, indicating that the memory task was more left lateralized, and the search task was more right lateralized. In Fig. 3, the ensemble average memory task lateralization $\Delta V_{Memory}(t)$ begins at about 0% before the cue word presentation period and remains constant until the beginning of the task period, when it begins to increase, and reaches a first maximum left lateralization of 1.2% about 7 seconds after the start of the task period. The value of $\Delta V_{Memory}(t)$ then decreases to about 1% at about 10 seconds after start of the task period, and rises up to a second maximum of about 1.3% at about 14-16 seconds after the start of the task period before falling to 0.8% at the end of the task period.

In Fig. 3, the ensemble average search task lateralization $\Delta V_{Search}(t)$ begins at 0% before the cue period and becomes more right lateralized during the cue period, reaching a maximum right lateralization of about -0.5% at approximately the start of the task period. The value of $\Delta V_{Search}(t)$ then returns to 0% by about 4 seconds after the start of the task period and has a slight decrease to -0.25% at 12 seconds after the start of the task period before returning to close to 0% for the rest of the task period, indicating less hemispheric dominance overall during the search task than during the memory task.

For statistical analysis, at all times chosen except task period start (i.e., 5, 10, 15, and 20 seconds after task period start), the p-value was much less than 0.001, suggesting a significant difference between the two tasks.

IV. Discussion

This research demonstrated two novel features: 1) the application of fTCD to study the cognitive tasks of visual search and memory in the same study, and 2) the use of identical stimuli for both tasks. In the first novel feature, lateralization over time was examined for visual search and visual memory cognitive tasks. The memory task tended to be more left-lateralized overall, and the search task tended to be more right-lateralized than memory. A possible explanation for this is that in the memory task, subjects may have tried to focus on details in a scene when memorizing it in preparation for a quiz to be given later (the left hemisphere is thought to play a role in local processing [28]); in the search task, subjects may have employed a strategy involving looking at the "big picture" in order to search as much of the picture as possible (the right hemisphere is thought to be involved in "global" or "holistic" processing [28, 29] and is known to play a role in visual search tasks [30]). The second novel feature of the research was that the same set of visual scenes were used as stimuli for both cognitive tasks, allowing a direct comparison to be made between visual search and visual memory tasks without confounding variables between the two tasks.

A possible confounding factor in the experimental procedure described is that subjects may not have all employed the same strategies during the tasks. For example, during the memory task, the subjects may have verbalized object names and locations, activating the left cerebral hemisphere [13].

The procedure outlined above, e.g. comparing two similar cognitive tasks by finding the lateralization vs. time for each task, provides a way to compare lateralization time courses between any two similar cognitive tasks which may be performed using the same set of visual stimuli. Some possible

applications include comparing cognitive tasks such as viewing a visual scene with no specific instructions vs. viewing a scene with instructions to assign a pleasantness rating to the scene, among others [17].

V. CONCLUSIONS AND FUTURE WORK

An application of fTCD was presented for comparison of the lateralization of two related cognitive tasks. This modality is unique in its ability to display changes in lateralization with high temporal resolution. The transcranial Doppler ultrasound data suggest that during visual search and visual memory tasks there may be different patterns of lateralization vs. time for cerebral blood flow, suggesting different patterns of cerebral activation between the two tasks. Specifically, a difference in average lateralization over all participants between search and memory tasks was found to be significant by plotting the standard errors of the mean of the lateralization data vs. time and by performing t-tests. Significantly, the same visual scenes were used as stimuli in both search and memory tasks, allowing a comparison to be made between average lateralization during search and memory cognitive tasks without the presence of confounding variables due to different experimental procedures for each task. Future work will involve studying lateralization vs. time during visual search and visual memory cognitive tasks for left and right-handed subjects separately, as well as during other cognitive processes.

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