INVESTIGATION OF FRONTAL CORTEX, MOTOR CORTEX AND SYSTEMIC HAEMODYNAMIC CHANGES DURING ANAGRAM SOLVING

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Abstract: We have previously reported changes in the concentrations of oxy- ($\Delta[HbO_2]$) deoxy- ($\Delta[HHb]$) and total haemoglobin ($\Delta[HbT] = \Delta[HbO_2] + \Delta[HHb]$) measured using near infrared spectroscopy (NIRS) over the frontal cortex (FC) during an anagram solving task. These changes were associated with a significant increase in both mean blood pressure (MBP) and heart rate (HR). The aim of this study was to investigate whether the changes in MBP previously recorded during an anagram solving task produces associated changes in scalp blood flow (flux) measured by laser Doppler and whether any changes are seen in NIRS haemodynamic measurements over a control region of the brain (motor cortex: MC). During the 4-Letter anagram task significant changes were observed in the $\Delta[HbO_2]$, $\Delta[HHb]$ and $\Delta[HbT]$ in both the frontal and motor cortex (n=11, FC $p<0.01$, MC $p<0.01$). These changes were accompanied by significant changes in both MBP (n=11, $p<0.01$) and scalp flux (n=9, $p=0.01$). During the 7-Letter anagram task significant changes were observed in the $\Delta[HbO_2]$ and $\Delta[HbT]$ (n=11, FC $p<0.01$, MC $p<0.01$), which were accompanied by significant changes in both MBP (n=11, $p=0.05$) and flux (n=9, $p=0.05$). The task-related changes seen in MBP and flux in this study appear to contribute to the changes in the NIRS signals over both the activated and control regions of the cortex.

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1. INTRODUCTION

A major aim of functional mapping studies of the human brain is to monitor the magnitude and spatial distribution of activity associated with brain function. To that extent cranial functional near-infrared spectroscopy (NIRS) has been widely used to investigate the haemodynamic changes which occur in response to functional activation of specific regions of the cerebral cortex. Based on the tight coupling of neuronal activity and oxygen delivery, changes in the concentration of oxygenated ($\Delta[HbO_2]$) and deoxygenated ($\Delta[HHb]$) haemoglobin as measured by NIRS are quantified and taken as indicators of cortical activation.

NIRS is increasingly being used to monitor the haemodynamic response over the frontal and prefrontal regions during cognitive tasks such as colour Stroop,[1] working memory,[2] Wisconsin card sorting test,[3] calculations,[4] mathematical problems,[5] playing video games,[6] and anagram solving tasks.[7] It is possible that some mental tasks used in these studies may elicit a systemic response which may affect the measured NIRS signals. We have previously reported that significant changes in mean blood pressure (MBP) and heart rate (HR) occur during anagram activation tasks and observed that NIRS haemodynamic changes were in some volunteers significantly correlated with these systemic changes.[8]

The aim of this study is to investigate whether the changes in MBP during anagram solving tasks produce associated changes in scalp blood flow and whether any changes are seen in NIRS haemodynamic measurements over a control region of the brain.

2. MATERIALS AND METHODS

2.1 Subjects

11 healthy volunteers (6 males and 5 females) all right handed with English as their first language (age 20 to 36 years; mean 25 years) took part in this study.

2.2 Instrumentation

A continuous wave near-infrared spectrometer with a sampling rate of 6Hz (NIRO 300, Hamamatsu Photonics KK) was used to measure changes in tissue $[HbO_2]$ and $[HHb]$ using the modified Beer-Lambert law. The optodes from the dual channel system were placed on the head based on the 10/20 EEG electrode placement system. Channel 1 was placed on the left motor cortex (MC) responsible for finger and hand movement identified as the C3 position. Channel 2 was placed on the left frontal cortex (FC) identified as the Fp1 position. Both channels were shielded from ambient light by using an elastic bandage and a black cloth. An optode spacing of 4 or 5cm was used in order to optimise the detected light intensity. For the conversion of the optical attenuation changes to concentration changes a differential pathlength factor (DPF) of 6.26 was applied.[9] A Portapres® system (TNO

Institute of Applied Physics) was used to continuously and non-invasively measure MBP and HR from the finger. Finally a laser Doppler probe (FloLab, Moore Instruments) was placed over the forehead to monitor the changes in scalp blood flow (flux) in nine of the eleven subjects.

2.3 Procedure

All the volunteers were positioned in a comfortable sitting position. Data were recorded during two minutes of the subject at rest (baseline), followed with one minute period of the subject solving 4-Letter anagrams (15 anagrams, 4 seconds per anagram) and then with one minute period of the subject solving 7-Letter anagrams (6 anagrams, 10 seconds per anagram). Each anagram-solving period was repeated a total of three times, with the study ending after a 2-minute rest period (total study time 10 minutes). In this study solving an anagram was defined as producing one coherent word using only the letters from another word (e.g. icon – coin; reserve – reverse).

The subjects were encouraged to solve as many anagrams as possible and were instructed to say possible solutions out loud (without moving); however, the subjects were not scored on their performance.

2.4 Analysis

The NIRS haemoglobin signals were first detrended to remove any slow drift, then all the signals including MBP, HR and flux, were low pass filtered at 0.08Hz to minimise the effects of other signal components. The filtering was carried out by a 5th order low pass Butterworth digital filter in forward backward directions to avoid introducing a phase delay (MatLab Mathworks Inc). The filtered signals from each volunteer were ensemble averaged over the repetition cycles (per volunteer two rest periods, three 4-Letter periods and three 7-Letter periods). Changes in total haemoglobin concentration (Δ[HbT]) were calculated from the sum of $\Delta[HbO_2]$ and Δ[HHb].

The response to stimulation was calculated as the difference between the average of 10 seconds worth of baseline data at the end of the rest period, and the average of 10 seconds of data commencing 20 seconds after the onset of the 4-Letter anagram solving period and the 7-Letter anagram solving period respectively. A ‘Student’s t-test’ was used to assess the significance of these responses (the threshold of significance was set at $p \leq 0.05$ from baseline). Correlations between variables were analysed with the Pearson correlation model.

3. RESULTS

3.1 Activation results

Figure 1 shows the grand average of the NIRS, MBP and scalp flux data from all volunteers during the entire ten minute test. Table 1 shows the mean response of each signal during 4- and 7-Letter anagram solving.

During the 4-Letter anagram task significant changes were observed in the Δ[HbO_2] (n=11, FC $p<0.01$, MC $p<0.01$), Δ[HHb] (n=11, FC p=0.05, MC $p<0.01$) and Δ[HbT] (n=11, FC $p<0.01$, MC $p<0.01$) in both the frontal and motor cortex. These changes were accompanied by significant changes in both MBP (n=11, $p<0.01$) and flux (n=9, p=0.01). During the 7-Letter anagram task significant changes were observed in the Δ[HbO_2] (n=11, FC $p<0.01$, MC $p<0.01$) and Δ[HbT] (n=11, FC $p<0.01$, MC $p<0.01$), which were accompanied by similar significant changes in both MBP (n=11, p=0.05) and flux (n=9, p=0.05). The changes in Δ[HHb] during the 7-letter anagram task were not significant. No significant differences were found between the 4-Letter and 7-Letter anagram activation periods for the NIRS and MBP signals.

Table 1. Response of NIRS signals over the motor and frontal brain regions (MC: motor cortex; FC: frontal cortex) and MBP and Flux during 4- and 7-Letter anagram solving. Data from all volunteers are presented as means±SD. (t-test $^*p<0.01$; $^\dagger p<0.03$; $^\ddagger p\leq 0.05$)

	No Subjects	4-Letters minus Rest		7-Letters minus Rest	
		MC	FC	MC	FC
Δ[HbO_2] (μM)	11	1.55±1.14*	2.04±1.37*	1.34±1.23*	1.83±1.26*
Δ[HHb] (μM)	11	-0.48±0.51*	-0.38±0.62‡	-0.28±0.66	-0.26±0.68
Δ[HbT] (μM)	11	1.08±1.23*	1.65±1.28*	1.07±1.20*	1.57±1.07*
MBP (mmHg)	11	4.7±4.4*		3.3±5.2‡	
ΔFlux (%)	9	50.2±56.5†		18.0±25.2‡	

3.2 Inter-subject correlation

The Δ[HbO_2] and Δ[HHb] signals measured over the frontal and motor cortex regions were found to have a varying association with the MBP and flux signals across different volunteers. In order to investigate this we calculated the correlation coefficient between the filtered Δ[HbO_2] and MBP, Δ[HHb] and MBP; Δ[HbO_2] and flux, and Δ[HHb] and flux for both frontal and motor cortex in all subjects. These results are shown in Figures 2 and 3.

4. DISCUSSION

In this study we observed significant changes in the [HbO_2], [HHb] and [HbT] measured over both the left frontal and motor cortex regions during a 4-letter anagram solving task. We also observed significant changes in the [HbO_2] and [HbT] measurements during a 7-letter anagram solving task. Furthermore, in the group data, we observed a significant increase from rest in both MBP and scalp flux when the subjects were solving the 4- and 7-letter anagrams. We found that the haemoglobin changes measured by NIRS over the frontal and motor cortex during anagram activation were in some volunteers significantly correlated with the changes in MBP and scalp flux.

During the anagram task there is no reason to expect haemodynamic changes over the motor cortex. The task-related changes seen in MBP and flux in this study appear to contribute to the changes in the NIRS haemodynamic signals over the activated and control regions of the cortex. It is possible that the anagram task elicits an emotional response, which produces changes in blood pressure that are likely to cause passive changes in the scalp blood flow as observed in the laser Doppler flux signal. These changes in the scalp blood flow can produce small changes in the [HbO_2] and [HHb] signals as measured by cranial NIRS.

When analysing cerebral haemodynamic activation data using functional neuroimaging the task-specific activation observed is due to the existence of a close coupling between regional changes in brain metabolism and regional cerebral blood flow. In order for this response to be monitored unambiguously it is important that the haemodynamic task-related activity is occurring on top of an unchanged global systemic and brain resting state. The blood pressure and scalp flux changes observed in this study suggest that systemic task related responses may also be present and that they may lead to haemodynamic changes characteristic of functional activation changes in a control region of the brain.

The relatively high correlation coefficient found in some subjects in this study between the NIRS haemodynamic measurements with the MBP and scalp flux signals suggest a global task-related haemodynamic response. In the absence of high resolution maps of haemodynamic response it is difficult to determine whether changes in the NIRS signals are due to the global changes in systemic variables or haemodynamic changes originating from specific regions of the cerebral cortex.

There are numerous recent publications using functional NIRS where differences in response have been reported, for example in frontal and prefrontal activation between healthy volunteers and schizophrenic patients,[10] between healthy volunteers and adults with pervasive developmental disorders,[11] between adults and preschool children,[12] between men and women,[13] and between different age groups from 20 to 90 years old.[14] In none of the studies mentioned above were systemic changes monitored. We suggest that caution should be exercised when analysing quantitatively the cerebrovascular response during frontal and prefrontal activation due to the unknown haemodynamic contribution from systemic alterations occurring during the stimulation.

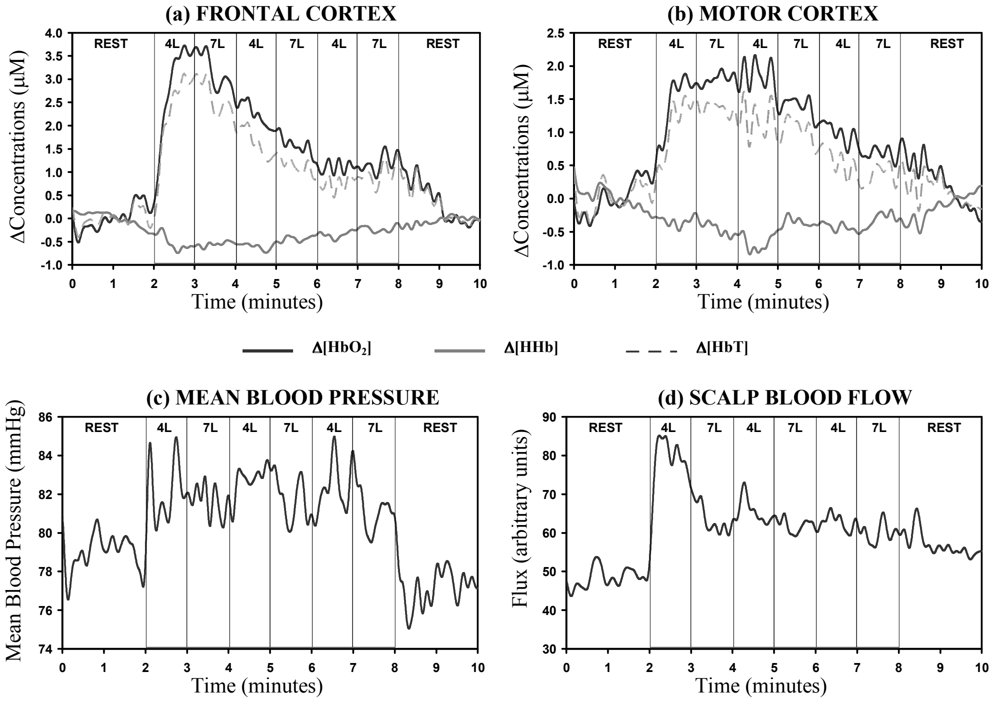

Figure 1. Grand averaged responses for $\Delta[HbO_2]$, $\Delta[HHb]$ and $\Delta[HbT]$ for all 11 subjects measured over the (a) frontal cortex and (b) motor cortex; (c) average (n=11) mean blood pressure; (d) average (n=9) scalp blood flow. (4L: 4-Letter Anagrams, 7L: 7-Letter Anagrams).

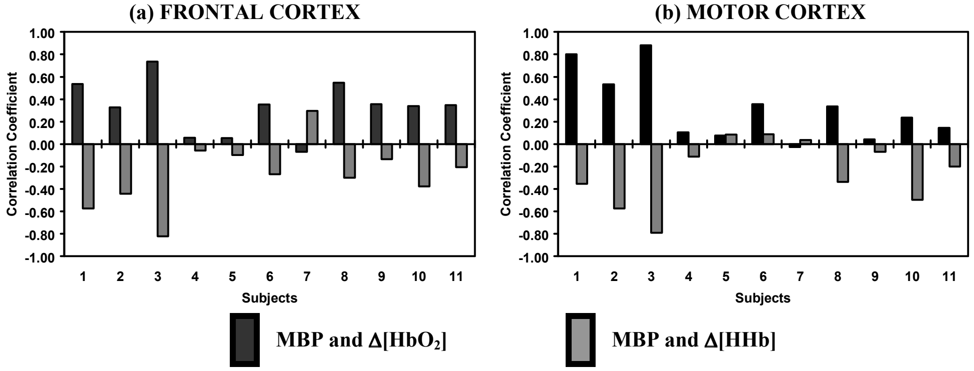

Figure 2. Individual correlation coefficients between MBP and $\Delta[HbO_2]$ and MBP and $\Delta[HHb]$ for each subject for (a) the frontal cortex and (b) the motor cortex.

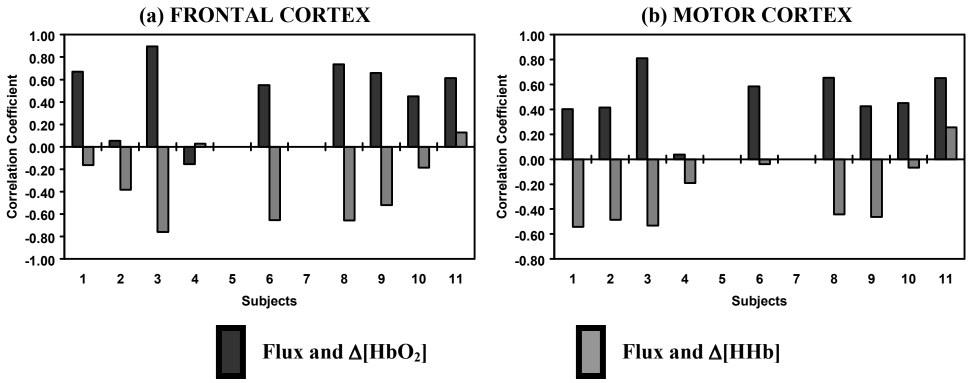

Figure 3. Individual correlation coefficients between flux and $\Delta[HbO_2]$ and flux and $\Delta[HHb]$ for each subject. For subjects 5 and 7 the scalp flux signal was not collected.

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