Chapter 44
Measurement of Frontal Lobe Functional Activation and Related Systemic Effects: A Near-Infrared Spectroscopy Investigation

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Abstract Near-infrared spectroscopy (NIRS) has been used to measure changes in cerebral oxy- and deoxy- haemoglobin ($\Delta[HbO_2]$, Δ[HHb]) in response to functional activation. It has been previously reported that during functional activation of the motor cortex heart rate increases. The aim of this study was to investigate systemic changes during functional activation of the frontal cortex. The responses to anagram presentations with varying difficulty (4-Letters and 7-Letters) over a 6 minute period were recorded. A Hamamatsu NIRO 200 NIRS system recorded $\Delta[HbO_2]$ and Δ[HHb] using the modified Beer Lambert law (MBL) and tissue oxygenation index (TOI) employing spatial resolved spectroscopy (SRS) over the left and right frontal hemisphere. Mean blood pressure (MBP) and heart rate (HR) were measured continuously. Nine young healthy volunteers (mean age 23) were included in the analysis. Significant task related changes were observed in both the NIRS and systemic signals during the anagram solving with increases in $[HbO_2]$ and [HHb] accompanied by changes in MBP and HR. The $[HbO_2]$ and [HHb] signals measured over the frontal region were found to have a varying association with the MBP signal across different volunteers. The effect of these systemic changes on measured NIRS signals must be considered

Keywords: Near-infrared spectroscopy, Frontal lobe activation, Anagrams

44.1 Introduction

Near infrared spectroscopy (NIRS) has been widely used to investigate haemodynamic changes which occur in response to functional activation of specific regions of the cerebral cortex [1]. With conventional continuous wave NIRS

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systems it is not possible to determine exactly where the changes in attenuation have taken place within the illuminated tissue A general assumption is usually made that the changes seen in oxyhaemoglobin (HbO_2) and deoxyhaemoglobin (HHb) which are coincident with the period of stimulation originate from the cortical layers. We have previously reported that significant changes in heart rate occur during a finger tapping protocol for activation of the motor cortex in adults [2]. NIRS is increasingly being used to monitor the haemodynamic response to cognitive tasks by making measurements over the frontal and prefrontal regions [3–5]. It is possible that some mental tasks used in these studies may elicit a systemic response which may affect the measured NIRS signals. The aim of this study was to investigate the systemic changes during functional activation of the frontal cortex by measuring heart rate and mean blood pressure during anagram solving in adult volunteers.

44.2 Method

44.2.1 Subjects

Nine healthy male volunteers all right handed with English as their first language (age 20–25 years; mean 22.9 years) took part in this study.

44.2.2 Instrumentation

A continuous wave near-infrared spectrometer with a sampling rate of 6 Hz (NIRO 200, Hamamatsu Photonics KK) was used to measure changes in tissue oxygenation index (TOI) using spatially resolved spectroscopy and [HbO_2]) and [HHb] using the modified Beer-Lambert law. The optodes from the dual channel system were placed on the left and right forehead respectively (taking care to avoid the midline sinuses) and were shielded from ambient light by using an elastic bandage and a black cloth. An optode spacing of 4cm was used and the differential pathlength factor (DPF) applied was 6.26 [6]. A Portapres® system (TNO Institute of Applied Physics) was used to continuously and non-invasively measure mean blood pressure (MBP) and heart rate (HR) from the finger.

44.2.3 Procedure

All the volunteers were positioned in a sitting position. After 2 minutes of baseline rest measurements activation started with a minute period of solving 4-Letter anagrams (15 anagrams, 4 seconds per anagram) which was followed by a minute period of solving 7-Letter anagrams (6 anagrams, 10 seconds per anagram). Each 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 (e.g. golf–flog; disease–seaside).

44.2.4 Analysis

The NIRS haemoglobin signals were first detrended to remove the slow drift, then all the signals including MBP and HR, were low pass filtered at 0.08 Hz 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 ([HbT]) were calculated from the sum of changes in [HbO_2] and [HHb].

A 'Student t-test' was used to assess the significance of the responses (the threshold of significance was set at $p<0.05$ from baseline). Correlations between variables were analysed with the Pearson correlation model.

44.3 Results

44.3.1 Activation Results

Figure 44.1 shows the grand average of the NIRS, MBP and HR data from all nine volunteers during the entire ten minute test. The response to stimulation was calculated as the difference between the average of 10 seconds worth of baseline rest data, and the average of 10 seconds of data 20 seconds after the onset of the 4-Letter anagram solving period and the 7-Letter anagram solving period respectively. These changes are shown in Table 44.1. There was a significant change in [HbO_2], [HHb] and [HbT] between rest and the 4-Letter anagram solving period and between rest and the 7-Letter anagram solving period. There was no significant difference in the NIRS signals between the 4-Letter anagram solving period and the 7-Letter anagram solving period. The systemic signals (MBP and HR) also showed a significant difference between rest and the 4-Letter anagram solving period and between rest and the 7-Letter anagram solving period.

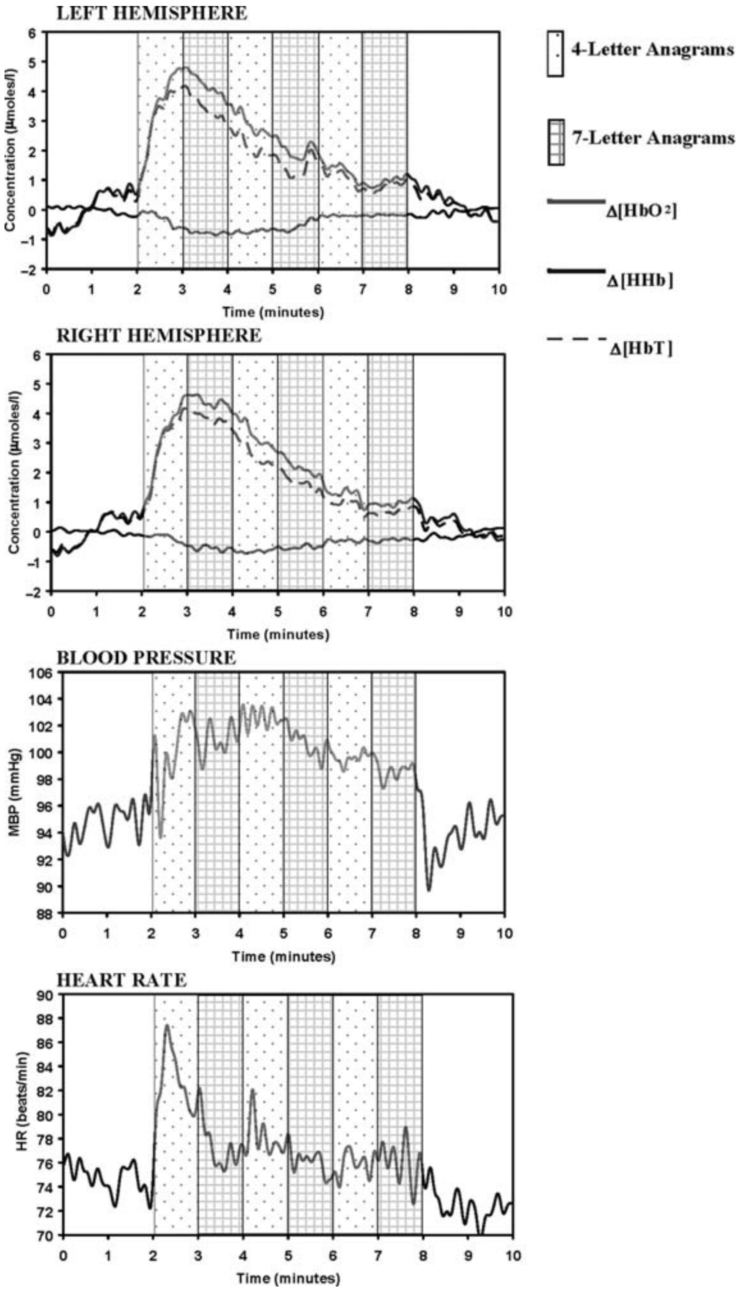

Fig. 44.1 Grand averaged responses from all nine subjects of NIRS haemoglobin signals and systemic measurements for the 10 minute study period.

Table 44.1 Response of NIRS signals over the left and right brain frontal regions and MBP and HR during 4- and 7- Letter anagram solving. Data from nine volunteers is presented as means±SD. (t-test *p<0.01; †p<0.03; ‡p<0.05)

	4-Letters - Rest		7-Letters - Rest	
	LH	RH	LH	RH
$\Delta[HbO_2]$ (μmoles/1)	2.48 ±2.42*	2.41±1.72*	2.19±2.48*	2.30±1.76*
Δ[HHb] (μmoles/1)	−0.28±0.46‡	−0.38±0.33*	−0.46±0.48*	−0.44±0.30*
TOI(%)	−1.03±3.20	−0.29±1.22	0.03±2.01	0.25±1.30
Δ[HbT](μmoles/1)	2.19±2.69†	2.03±1.92*	1.73±2.76‡	1.86±1.92*
MBP (mmHg)	4.6±4.1*		4.8±3.2*	
HR (beats/min)	7.7±5.2*		3.5±3.0*	

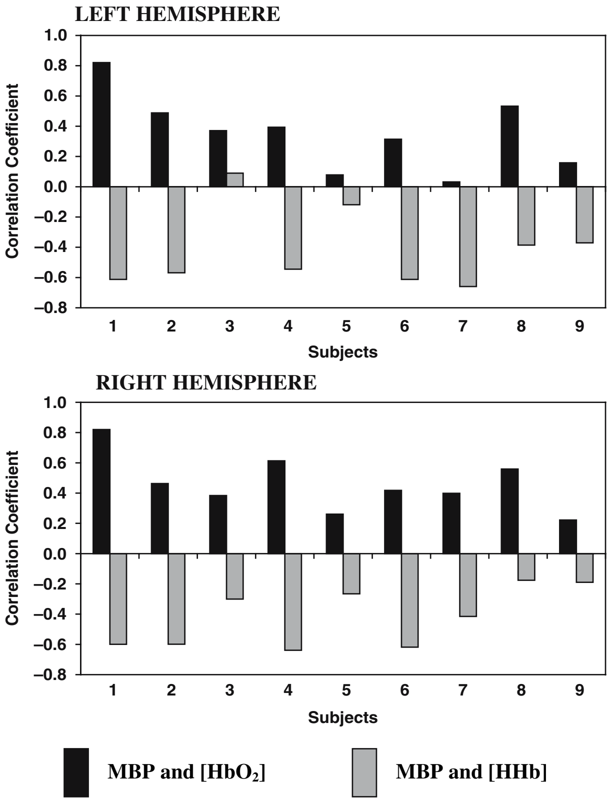

Fig. 44.2 Individual correlation coefficients between MBP and $[HbO_2]$ and MBP and [HHb] for each subject.

44.3.2 Inter-Subject Correlation

The [HbO_2] and [HHb] signals measured over the frontal region were found to have a varying association with the MBP signal across different volunteers. In order to investigate this we calculated the correlation coefficient between the filtered [HbO_2] and MBP and [HHb] and MBP for both hemispheres in all subjects. These results are shown in Fig. 44.2.

44.4 Discussion

In this study we demonstrated significant changes in NIRS variables ([HbO_2], [HHb] and [HbT]) measured over both the right and left frontal region between rest and a 4-letter anagram solving period and between rest and a 7-letter anagram solving period. Furthermore, in the group data, we observed a significant increase from rest in both MBP and HR during periods when the subjects were solving the 4 and 7 letter anagrams. We have found that the haemoglobin changes measured by NIRS during frontal lobe functional activation were in some volunteers significantly correlated with the systemic changes in MBP and HR.

Given that the anagram task involves both language and spatial processing it is reasonable that the response is not lateralised. A previous study by Chance et al.[7] describes a robust prefrontal oxygenation signal in response to anagram solving which also appears to be bilateral. To minimise the likelihood of movement artifact or non stimulation related changes, we chose in this study not to ask the subject to provide the answers to the presented anagrams and we were therefore unable to score the subjects' performance on the task and determine whether the systemic changes were related to this level of performance.

To our knowledge this is the first report of simultaneous measurements of MBP and NIRS variables during a functional activation task of the frontal cortex. In a previous study we reported an increase in heart rate during a finger tapping task in adult volunteers [2]. Obrig et al [8]. measured arterial blood pressure and heart rate in three subjects during visual stimulation (annular checkerboard alternating at 8 Hz) and found a coherence between arterial blood pressure and [HbO_2] at frequencies coinciding with the heart rate and spontaneous low frequency oscillations (centred around 0.1 Hz), but made no specific comment about activation related changes in the systemic variables.

Nearly all studies of task-specific activation using functional neuroimaging rely on the existence of a close coupling between regional changes in brain metabolism and regional cerebral blood flow, sometimes referred to as activation-flow coupling or neurovascular coupling. Regional haemodynamic changes are used as a surrogate marker for changes in regional brain function that occur due to changes in metabolism during excitatory or inhibitory neurotransmission, both of which are energy consuming processes. The relatively high correlation coefficient found in some subjects in this study between [HbO_2] and MBP and [HHb] and MBP suggests a centrally mediated mechanism that might play a role in the overall functional haemodynamic changes seen in the brain in these individuals during stimulation. Caution therefore should be taken when analysing the cerebrovascular response of the activated brain due to the unknown haemodynamic contribution from the systemic alterations occurring during stimulation.

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