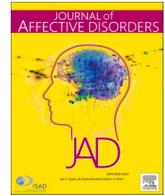


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Research paper

Stress estimation by the prefrontal cortex asymmetry: Study on fNIRS signals

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ABSTRACT

Background: Functional near-infrared spectroscopy (fNIRS) is a non-invasive technique frequently used to measure the brain hemodynamic activity in applications to evaluate affective disorders and stress. Using two wavelengths of light, it is possible to monitor relative changes in the concentrations of oxyhemoglobin and deoxyhemoglobin. Besides, the spatial asymmetry in the prefrontal cortex activity has been correlated with the brain response to stressful situations.

Methods: We measured prefrontal cortex activity with a NIRS multi-distance device during a baseline period, under stressful conditions (e.g., social stress), and after a recovery phase. We calculated a laterality index for the contaminated brain signal and for the brain signal where we removed the influence of extracerebral hemodynamic activity by using a short channel.

Results: There was a significant right lateralization during stress when using the contaminated signals, consistent with previous investigations, but this significant difference disappeared using the corrected signals. Indeed, exploration of the susceptibility to contamination of the different channels showed non-homogeneous spatial patterns, which would hint at detection of stress from extracerebral activity from the forehead.

Limitations: There was no recovery phase between the social and the arithmetic stressor, a cumulative effect was not considered.

Conclusions: Extracerebral hemodynamic activity provided insights into the pertinence of short channel corrections in fNIRS studies dealing with emotions. It is important to consider this issue in clinical applications including modern monitoring systems based on fNIRS technique to assess emotional states in affective disorders.

1. Introduction

Functional near-infrared spectroscopy (fNIRS) is a technique used to estimate the hemodynamics linked to the neuronal activity (Doi et al., 2013). This non-invasive optical technology uses a source to emit near-infrared light into the head, and this light returns to a detector. In order to monitor relative changes in the concentrations of oxyhemoglobin (HbO₂) and deoxyhemoglobin (HbR), the two wavelengths used in this study have been 740 and 850 nm, respectively. This technique has generated increasing interest for several applications where measuring brain activity is essential, including the study of diverse affective disorders, such as borderline personality (Cattarinussi et al., 2022) or attention deficit hyperactivity disorder (Mauri et al., 2020) among

others, thanks to its advantages to be applied in psychiatry (Lai et al., 2017). The applications on neuroergonomics (Curtin and Ayaz, 2018) are also important as they can aid people to prevent situations that can be highly stressful depending on their individual affective reactions. However, the passage of light through skin, muscle, the frontal sinus, and bone to reach the brain can lead to contamination of the brain activity signal because these tissues also have hemodynamic activity (Haeussinger et al., 2014). This concern has been studied from different viewpoints (Kirilina et al., 2012; Tachtsidis and Scholkmann, 2016). Previous investigations have indicated that the extracerebral hemodynamic activity is spatially inhomogeneous (Kirilina et al., 2013; Yücel et al., 2016) and affects HbO₂ and HbR differently (Haeussinger et al., 2014; Kirilina et al., 2013; Tachtsidis and Scholkmann, 2016). These

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facts make it necessary to implement robust methods to control this extracerebral contamination to avoid increasing the false positive rate (Pfeifer et al., 2018) and consequently to guarantee the proper evaluation of emotional disorders.

There are different methods to manage extracerebral contamination (Tachtsidis and Scholkmann, 2016; Yamada et al., 2012). Arguably, one of the most used methods is based on multi-distance channels (Saager et al., 2011; Yücel et al., 2016; Zhang et al., 2015). The term multi-distance refers to the use of two types of channels: short channels (SCs) and long channels (LCs). For an SC, the distance between light emitter and detector is from 0.5 to 1.5 mm (Brigadoi and Cooper, 2015; Haeussinger et al., 2014) and it is supposed to be sensitive only to the extracerebral hemodynamic activity. A LC shows a distance from 30 to 40 mm between the emitter and detector, depending on the device (Li et al., 2011) and, consequently, its signal is composed by both extracerebral and brain cortex hemodynamic activity (Zhang et al., 2015). Hence, with both recordings, it is possible to eliminate the influence of cerebral hemodynamics by means of SC-based regressors (Molina-Rodríguez et al., 2022; Saager et al., 2011).

In several applications, such as affective computing (D'Mello et al., 2018), it is essential to estimate this extracerebral activity or, at least, to quantify its impact. It is important to determine the actual influence of peripheral activity compared with actual prefrontal cortex (PFC) activity, because it could provide different results when using different devices or protocols due to the intricate links between the brain and the physiological response under distinct affective states and for different populations concerning their psychological troubles. Indeed, fNIRS has been used extensively to measure the brain activity related to emotional tasks (Bendall et al., 2016; Harmon-Jones et al., 2010) and affective disorders, such as major depressive disorder, borderline personality or bipolar disorder (e.g. Husain et al., 2020a, 2020b, 2021a, 2021b), but without indicating the specific contribution of extracerebral activity to the activity modulations.

One of the most relevant areas that is accessible from the scalp and involved in the experience and regulation of emotional responses is the PFC (Harmon-Jones et al., 2010). For this reason, it is one of the most studied areas with NIRS (Doi et al., 2013). Among the works that evaluate emotional aspects, a topic of interest is the role of hemispheric lateralization (Doi et al., 2013). Several works have proposed that left/right asymmetry of the PFC is related with specific emotional responses (Davidson, 2004), and for example, patients with Social Anxiety Disorders showed hyperactivity in left frontal cortex under psychosocial stress situations (Kawashima et al., 2016). Based on motivational models, right frontal activity is associated with expression and experience withdrawal-related emotions (anxiety, sadness) or trait avoidance motivations, while left frontal activity is associated with expression and experience approach-related emotion (anger, happiness) or trait approach motivations (Davidson, 2004; Harmon-Jones and van Honk, 2012; Kawashima et al., 2016).

Using fNIRS with a source-detector separation of 30 mm and without an SC, Balconi et al. (2015, 2017) indicated that more lateralized HbO₂ activity is found to the right for the negative valence images and to the left for the positive valence images. They found no significant effects for HbR. Morinaga et al. (2007) reported a greater increase in HbO₂ in the right compared with the left PFC in anticipation of an electric shock. They used a NIRS with a detector emitter distance of 50 mm and without an SC. Tuscan et al. (2013) found a greater increase in blood volume level and oxygenation levels in the right PFC during a social stressor. Furthermore, using a NIRS with a source detector distance of 30 mm and without using SC, Tanida et al. (2004, 2007) found that the HbO₂ activity in the right PFC is positively related to heart rate variability during an arithmetic stressor. In their graphs, there is lateralization of the HbO₂ signal during the stress phase, but they did not provide relative data regarding lateralization of HbO₂. Besides, Hoshi et al. (2011) found that the participants presented a bilateral increase in oxygenation when viewing images, whereas for the pleasant images there was a decrease in

HbO₂ only in the left side. These authors used a NIRS device with a source-detector distance that 30 cm and without SC. They did not report HbR. Herrmann et al. (2003) used a NIRS with a detector emitter distance of 4 cm and without an SC to evaluate the response of the PFC and found greater left activity before visualizing pictures of negative and neutral facial expressions according to HbO₂ values, while there were no significant differences for HbR. Brugnera et al. (2017) evaluated the effect of an arithmetic stressor on lateralization of prefrontal cortex (PFC) by using a NIRS device with a detector emitter distance of 3 cm and without an SC. They did not find asymmetries in the HbO₂ or HbR signals during the stressor.

The effect of the extracerebral hemodynamic activity in the PFC lateralization remains unclear. Given the particular physiological responses during emotional stimulation, it is desirable to quantify the possible influence on the results in healthy participants previously to apply the protocol on people suffering from affective disorders. Therefore, this work has two aims. The first is to determine whether the correction of fNIRS signals by using an SC has a significant effect on the differences between conditions under different levels of stress when computing an asymmetry index. The second is to analyze the susceptibility of different locations on the forehead to extracerebral contamination. Addressing these issues will provide insights into the pertinence of SC corrections in fNIRS studies dealing with emotions and will be useful to design modern systems to characterize affective disorders and to evaluate individual brain and physiological reactions to stress.

2. Materials and methods

2.1. Participants

Seventeen participants recruited at the University of Salamanca (63.2 % female) in the social sciences degree program participated in the present study (18.94 ± 0.96 years old). All participants were right-handed and did not have any psychiatric, psychological, cardiovascular, or neurological disease. Prior to participation, participants signed a written consent form approved by the Ethical Committee.

2.2. Procedure

The experiment took place in a room with low light and a constant temperature. The participants were invited to sit down on a comfortable chair placed 50 cm away from a projector screen; each of the participants could use a mouse and a keyboard. For the realization of the tasks, we used the program Unipark (v. 10.9), an academic program of Questback with online survey software. Before starting, we reassured the participants about the non-invasiveness of fNIRS and placed the device on the forehead according to the international 10–20 system (Jasper, 1958). We also placed a pillow for the neck to increase the comfort of the participant and to avoid movements.

To induce stress in the participants, we used the social and arithmetic components of the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993). These stressors have been used previously in NIRS (Ishikawa et al., 2014; Tanida et al., 2007). In the social stress task, we instructed the participants to make a speech of positive and negative characteristics about themselves in front of an audience and a video camera for 2 min. Sixty seconds passed between the social and numerical task. The arithmetic task consisted of subtracting seven sequentially from a given number. The participants were instructed to respond verbally as quickly as possible from a block of three numbers of increasing size, with a total of 180 s of arithmetic stress. Finally, the subjects were allowed to recover for 180 s. Fig. 1 shows the experimental protocol. Of note, the modality of response could have an influence on the noise contribution in specific brain regions linked to language processing or production. Nonetheless, these regions are out of the area investigated in this study.

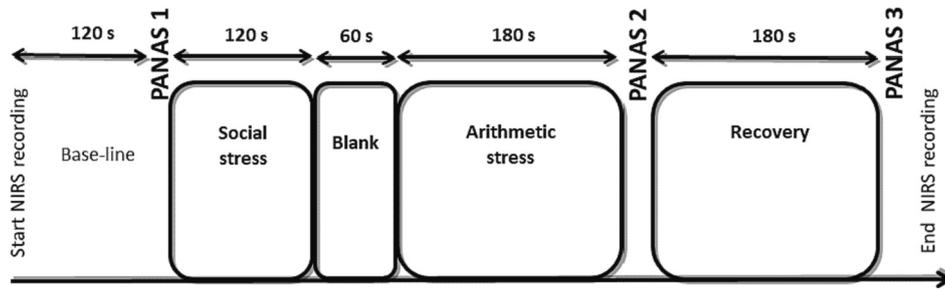


Fig. 1. Schematic representation of experiment protocol. PANAS: Positive and Negative Affect Scale.

2.3. Psychological measures

We use the Spanish version of the Positive and Negative Affect Scale (PANAS; Sandín et al., 1999; Watson et al., 1999) to measure positive affect (PA) and negative affect (NA). Participants responded to 20 items using a seven-point Likert scale, where 1 = “strongly disagree,” 4 = “moderate,” and 7 = “strongly agree.” There were 10 items measuring NA (e.g., “afraid”) and 10 measuring PA (e.g., “inspired”). In the original study the questionnaire showed good psychometric properties (Sandín et al., 1999), with reliabilities of 0.87 and 0.86 for the negative and positive scales, respectively. In our sample both the negative and positive scales at the three timepoints when the PANAS was completed showed high reliability. For the negative scale, Cronbach’s α was 0.80 at timepoint 1, 0.89 at timepoint 2, and 0.81 at timepoint 3. For the positive scale, Cronbach’s α was 0.78 at timepoint 1, 0.87 at timepoint 2, and 0.89 at timepoint 3.

2.4. Instrumentation

We used a continuous wave multi-distance multichannel NIRS system (fNIRS BrainSpy28, NewmanBrain). The device uses four light-emitting diodes (LEDs) as light sources and 10 photodetectors. The LEDs emit infrared light at two wavelengths of 740 and 850 nm. The sampling rate was 10 Hz. Combining light sources and photodetectors, there are 16 SCs (14 mm source-detector separation) and 12 LCs (32 mm source-detector separation) (Fig. 2).

2.5. Signal quality check and channel exclusion criteria

To guarantee adequate signal quality, we performed several preliminary quality tests. To account for instrumental noise (Huppert et al., 2009), we evaluated the raw optical transmission data to identify

channels exhibiting extreme values (below 5 % or above 95 % of the device dynamic range), or a coefficient of variation > 7.5 % (calculated as the percentage ratio between the standard deviation [SD] and the mean [m]; Zimeo Morais et al., 2017). Next, by visual inspection of the accelerometer data, we discarded channels affected by motion artefacts, leading a final sample size of 17.

2.6. fNIRS data processing

We performed all the computations off-line with MATLAB (Version R2019a, MathWorks, Natick, MA, USA), using native functions, self-made scripts, and open-source packages. We carried out optical data preprocessing using the Homer2 NIRS package based on MATLAB. We converted the raw optical data to optical density signals and then digitally band-pass filtered it between 0.005 and 0.2 Hz (zero-phase, 5th-order Butterworth filter) to remove very slow fluctuations and high-frequency components (respiratory, cardiac and instrumental noise; Huppert et al., 2009).

We computed the relative concentration changes in HbO and HbR via the modified Beer–Lambert law (Kocsis et al., 2006). We used a differential path length factor, calculated with the general equation described by Scholkmann and Wolf (2013), which takes into account the participant’s age and the wavelength.

2.7. Neural signal estimation

We used SC signals as reference signals (RS) to remove the extracerebral contamination from LCs. The design of the NIRS device used in this work allows having three SC candidates that meet the proximity requirements to correct the signal: one obtained close to the long-channel detector (SSd), one close to its source (SSs), and one close to its center (SSc) (Fig. 2). For each LS, we estimated the RS as a

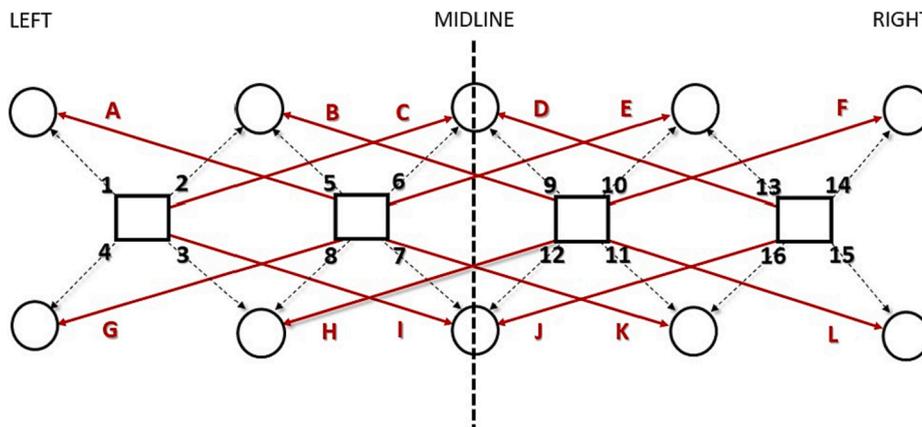


Fig. 2. The optode arrangement of the device. The squares represent the emitters, and the circles represent the detectors. The short channels are represented by black arrows with the numbers 1–16, while the long channels are represented by red arrows with the letters A–L. The montage was placed on the forehead, covering a part of the prefrontal cortex. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

combination of SSd and SSs ($RS = SSd + SSs$). Gagnon et al. (2014) reported that such a “double SS” approach yields a significant improvement in the regression method (Gagnon et al., 2014). Because RS only contains the extracerebral signal and LS includes, in addition, the unknown neural signal (NS), it can be formulated, in terms of linear regression:

$$LS = \beta_0 + \beta_1 RS + NS$$

where β_0 is the y-intercept, β_1 is the regression coefficient, RS is the reference signal, and NS the neural signal (in fact, the regression error term). Assuming that RS and NS are temporally uncorrelated, we can estimate NS as:

$$NS = LS - (\beta_0 + \beta_1 RS)$$

To obtain β_0 and β_1 , we solved linear regression by applying the MATLAB function “robustfit,” which uses an iteratively reweighted least squares algorithm and is less sensitive to outliers than ordinary least-squares (Holland and Welsch, 1977).

2.8. Laterality index (LI)

To calculate the relative prefrontal asymmetry, we used the averaged neural signals of the left and right regions. We calculated an asymmetry value by using the laterality index response (LIR) proposed by Ishikawa et al. (2014). Briefly, $LIR = [(right\text{-ROI activity} - left\text{-ROI activity}) / (right\text{-ROI activity} + left\text{-ROI activity})]$, where ROI is the region of interest. In this way, the relative prefrontal asymmetry (in terms of the LIR) ranges from -1 to $+1$. Positive values indicate that the right is more active than the left PFC, while negative values indicate more activity in the left PFC. This index value should be viewed as a relative measure of activity because it compares the right and left PFC with each other.

2.9. Statistical analysis

To evaluate the presence of psychological stress, we used a repeated measure analysis of variance (ANOVA) with the NA and PA scores in the different phases of the experiment (baseline or initial affective state, induced stress [social and arithmetic], and recovery state).

Second, we performed repeated measures ANOVA, for both HbO2 and HbR, considering the LI-contaminated and LI-corrected values in the different phases of the experiment (baseline, social stress, arithmetic stress, and recovery). We evaluated the effect size by eta square (η^2). We used the Greenhouse–Geisser procedure to correct when sphericity was not assumed.

Third, to evaluate the susceptibility to be contaminated by extracerebral activity of each channel during stress, we used a paired *t*-test to compare the level of contamination between the baseline phase and social and arithmetic stress, for both HbO2 and HbR. Finally, with the aim of evaluating the susceptibility of the channels to decontamination, we used a paired *t*-test to compare the level of contamination of the channels during social and arithmetic stress and the recovery phase, for both HbO2 and for HbR. We used Cohen’s delta (δ) to indicate the effect size and *r* to determine the strength of association.

We used SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA) for all statistical analyses, with $p < 0.05$ considered significant.

3. Results

3.1. Effectiveness of the psychological stress procedure

For the NA scores, there were significant results ($F(1.5, 23.9) = 14.869, p < 0.001, \eta_p^2 = 0.482$) for the comparison between baseline (M: 1.84, SD: 0.89) and induced stress (M: 2.84, SD: 1.33), and between induced stress and recovery (M: 1.61, SD: 0.67). For the PA scores, there were significant results ($F(2, 32) = 13.866, p = 0.000, \eta_p^2 = 0.464$)

between baseline (M: 4.14, SD: 0.73) and induced stress (M: 3.40, SD: 0.90), and between induced stress and recovery (M: 3.86, SD: 0.89).

3.2. Effect of stress manipulation on contaminated and corrected LI-HbO2 and LI-HbR

We performed a repeated measures ANOVA to evaluate the values of HbO2-LI-contaminated for baseline, social and arithmetic stress, and recovery. There were significant results ($F(3, 48) = 4.251, p = 0.010, \eta_p^2 = 0.210$) for the comparison between baseline and social and arithmetic stress, but not for the comparison between social and arithmetic stress and recovery. Indeed, the mean HbO2-LI-contaminated scores were -0.14 (SD: 0.26) at baseline, -0.02 (SD: 0.17) for social stress, 0.00 (SD: 0.14) for arithmetic stress, and 0.00 (SD: 0.13) for recovery (Fig. 3). However, when we performed this same statistical analysis for the HbO2-LI-corrected values, the differences were no longer significant ($F(3, 48) = 0.488, p = 0.692, \eta_p^2 = 0.030$) (Fig. 3).

There were no significant results for HbR-LI-contaminated ($F(3, 48) = 0.618, p = 0.607, \eta_p^2 = 0.037$) or HbR-LI-corrected ($F(3, 48) = 0.370, p = 0.775, \eta_p^2 = 0.023$) (Fig. 3).

3.3. Susceptibility of the channels to be contaminated during stress

During social stress, the HbO2 channels that were susceptible to contamination were B ($T(16) = -2.621, p = 0.019, \delta = 0.635, r = 0.548$) and F ($T(16) = -2.284, p = 0.036, \delta = 0.553, r = 0.495$) (Fig. 4). However, for arithmetic stress the channels susceptible to contamination were F ($T(16) = -2.151, p = 0.047, \delta = 0.521, r = 0.473$) and D ($T(16) = -2.171, p = 0.045, \delta = 0.526, r = 0.477$) (Fig. 4). For HbR, only channel J ($T(16) = -2.328, p = 0.033, \delta = 0.564, r = 0.503$) was susceptible to contamination during social stress, but none during the arithmetic stress.

3.4. Susceptibility of the channel to decontamination during recovery

Regarding HbO2, comparing social stress and the recovery phase, there were significant results for channels C ($T(16) = 2.612, p = 0.019, \delta = 0.633, r = 0.546$), K ($T(16) = 2.848, p = 0.012, \delta = 0.690, r = 0.580$), B ($T(16) = 2.871, p = 0.011, \delta = 0.696, r = 0.583$), F ($T(16) = 2.277, p =$

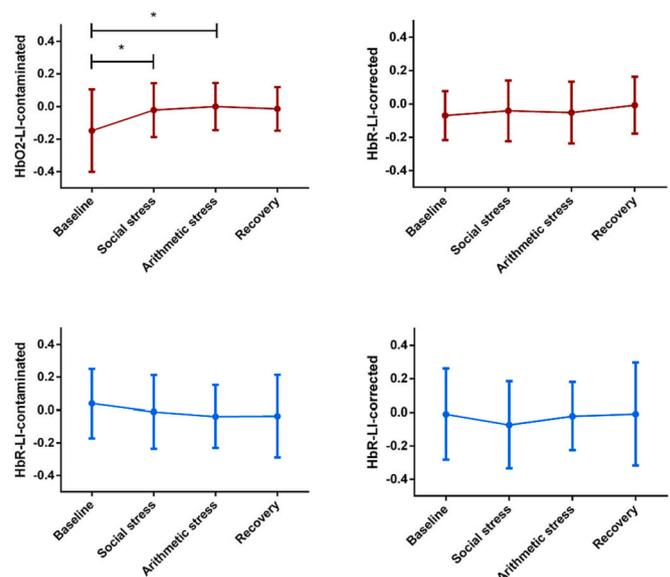


Fig. 3. Effect of stress manipulation contamination on the laterality index for oxyhemoglobin (HbO2-LI; upper) and deoxyhemoglobin (HbR-LI; bottom). The left side shows LI-contaminated and the right side shows LI-corrected. Error bars represent the standard deviation. * $p < 0.05$.

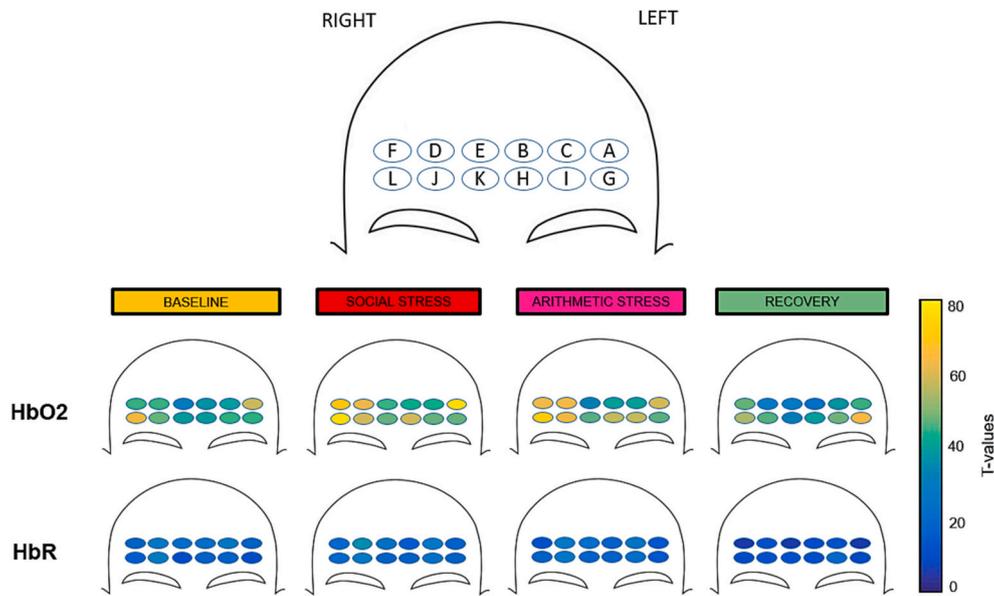


Fig. 4. Susceptibility of the oxyhemoglobin (HbO2) and deoxyhemoglobin (HbR) to contamination for every channel for each condition.

= 0.037, $\delta = 0.552$, $r = 0.494$), and D ($T(16) = 2.716$, $p = 0.015$, $\delta = 0.658$, $r = 0.561$) (Fig. 4). Comparing arithmetic stress and the recovery phase, there were significant results for channels K ($T(16) = 2.827$, $p = 0.012$, $\delta = 0.685$, $r = 0.577$), F ($T(16) = 3.053$, $p = 0.008$, $\delta = 0.740$, $r = 0.606$), and D ($T(16) = 2.742$, $p = 0.014$, $\delta = 0.665$, $r = 0.565$).

Regarding HbR, the comparison between social stress and the recovery phase showed that channels C ($T(16) = 3.080$, $p = 0.007$, $\delta = 0.747$, $r = 0.610$), A ($T(16) = 2.521$, $p = 0.023$, $\delta = 0.611$, $r = 0.533$), K ($T(16) = 2.738$, $p = 0.015$, $\delta = 0.664$, $r = 0.564$), F ($T(16) = 3.198$, $p = 0.006$, $\delta = 0.773$, $r = 0.623$), and H ($T(16) = 2.155$, $p = 0.047$, $\delta = 0.522$, $r = 0.474$) were significantly susceptible to decontamination (Fig. 4). Comparison between arithmetic stress and recovery showed that channels E ($T(16) = 2.189$, $p = 0.044$, $\delta = 0.530$, $r = 0.480$), K ($T(16) = 2.317$, $p = 0.034$, $\delta = 0.561$, $r = 0.501$), F ($T(16) = 2.720$, $p = 0.015$, $\delta = 0.659$, $r = 0.562$), and H ($T(16) = 2.358$, $p = 0.031$, $\delta = 0.571$, $r = 0.507$) were susceptible to decontamination.

3.5. Susceptibility of the hemoglobin species (HbO2 and HbR) to contamination

We performed a two-factor ANOVA (species \times phases) for the contamination values. There were significant results ($F(2.87, 1172) = 26.388$, $p < 0.001$, $\eta_p^2 = 0.061$) for the phases of the experiment, the hemoglobin species ($F(1, 406) = 213.49$, $p < 0.001$, $\eta_p^2 = 0.345$), and the interaction between them ($F(2.87, 1172) = 4.455$, $p = 0.005$, $\eta_p^2 = 0.011$). For both HbO2 and HbR, social and arithmetic stress increased contamination, while in the recovery phase this situation was reversed (Fig. 5). HbO2 showed a higher level of susceptibility to contamination than HbR at the baseline and later phases (Fig. 5).

4. Discussion

In this work, we aimed to explore the suitability and accuracy of the fNIRS technique to detect psychological stress or calmness, as other research works have pointed (Olszewska-Guizzo et al., 2021, 2022). Particularly, we were interested in the effect of extracerebral hemodynamic activity in frontal asymmetry under induced social and arithmetic stress. The results concerning the LI with contaminated HbO2 values showed that left activity was significantly decreased by 21 %, according to the value of the effect size, during social and arithmetic stress. This result is in line with previous research based on the emotional models

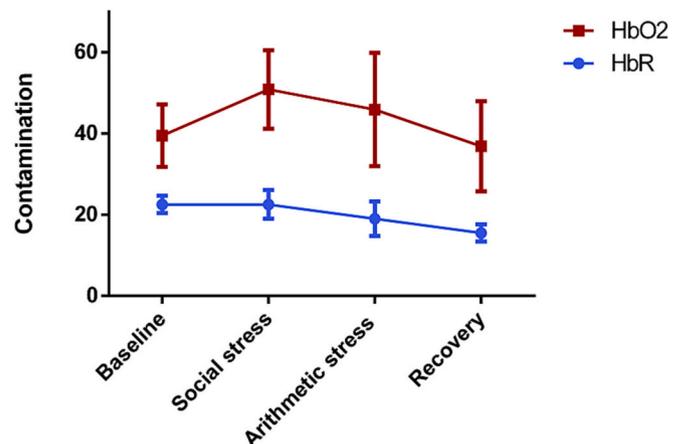


Fig. 5. Susceptibility of hemoglobin to contamination in the different phases of the experiment (t-values). The analysis confirmed significant main effects of phases of the experiment and hemoglobin species (oxyhemoglobin [HbO2] and deoxyhemoglobin [HbR]), and a significant interaction between them. Error bars represent standard deviation.

that propose right frontal activity is associated with expression and withdrawal-related experience emotions (Balconi et al., 2017; Davidson, 2004; Harmon-Jones and van Honk, 2012), and similar results have been reported in other previous investigations (Morinaga et al., 2007; Tanida et al., 2004, 2007; Tuscan et al., 2013). However, some discrepancies exist in the literature. This heterogeneity might be due to technical reasons linked to recording devices—for example, to the variability in the emitter-detector distance—or to issues related to the use of different types of emotional stimuli. Either way, the hypothesis about frontal asymmetry in emotional tasks does not come exclusively from NIRS technology. Indeed, there are data that support the existence of asymmetry using electroencephalography (EEG) (Davidson, 2004; Stewart et al., 2014). In line with Doi et al. (2013), we consider that the relationship between the EEG and neurovascular response (as measured by NIRS) is not straightforward. Thus, it is possible that NIRS technology is less sensitive than EEG with respect to changes in approach/withdrawal motivation in an emotional context.

Previous studies have usually directly linked hemodynamic changes

with changes in neuronal activity, although the authors have not used any method to reduce extracerebral hemodynamic interference. In this sense, when we performed the same analyses but using HbO₂-LI-Corrected, we found that the differences between the different phases of the experiment were not significant. In fact, the effect size was reduced to 0.3 %. These results support the idea that the NIRS signal is very likely contaminated by the extracerebral compartment, as suggested by previous research (Kirilina et al., 2012; Takahashi et al., 2011).

Regarding the susceptibility of the channels to contamination during stress, we found that for the HbO₂ signal, the susceptibility to contamination is not homogeneous for both the social and the arithmetic stressors. Specifically, the susceptibility to contamination during stress is focused on the upper and right forehead area. Concerning the susceptibility of the channels to decontamination, we found that for the HbO₂ signal, decontamination is not homogeneous, especially for the right superior zone and to a lesser extent for the lower-central and upper-left zones.

Previous research had already pointed out the fact that extracerebral hemodynamic activity is spatially non-homogeneous for both HbO₂ and HbR (Kirilina et al., 2013; Yücel et al., 2016). In this sense, there is evidence that the autonomic nervous projections that control blood flow are not distributed homogeneously over the forehead and, therefore, there is an asymmetry in the microvascular facial control (Asthana, 2001; Benedičić et al., 2007; Benedicic et al., 2006). In fact, using Doppler laser flowmetry, researchers have found that the right area of the forehead has a greater flow compared with the left area (Benedicic et al., 2006). This fact is really important when using this technique in psychiatry as pointed in several studies (Ehlis et al., 2014; Ho et al., 2020; Mikawa et al., 2015).

In addition, it seems that the emotional expression on the forehead shows asymmetries with certain differentiated patterns (Fernández-Cuevas et al., 2015; Kashima et al., 2012). Using an infrared camera, Jenkins and Brown (2014) indicated that while performing a cognitively demanding task there is an increase in the temperature of the right forehead, which reflects an increase in blood flow related to the task. Hence, the stress response could probably be related to peripheral extracerebral activity rather than to the real neural substrate.

Regarding the susceptibility of the hemoglobin species to contamination, we found that for both hemoglobin species, social and arithmetic stress increased contamination, while in the recovery phase this situation was reversed. This increased interference from the extracerebral hemodynamic activity may be related to a stress-induced increase in sympathetic activity in the blood vessels of the forehead. Although both HbO₂ and HbR are influenced by extracerebral hemodynamic activity, the degree of influence varies from one to the other (Haeussinger et al., 2014; Kirilina et al., 2013; Tachtsidis & Scholkmann, 2016). In fact, it has been pointed out that the HbO₂ signal is more contaminated than the HbR signal (Kirilina et al., 2013; Zhang et al., 2015). The physiological motive can be found in the difference between the autonomic innervation of venules and arterioles (Sørensen et al., 2012), supporting the need to provide both values to have complete information about the brain cortex hemodynamic activity.

Among the limitations of this research, we highlight that there was no recovery phase between the social and the arithmetic stressor and these phases were not counterbalanced, so there may have been a cumulative effect of one stressor on another. For future research, it would be relevant to check whether these results are confirmed for people suffering from chronic stress or anxiety.

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CRedit authorship contribution statement

Sergio Molina Rodríguez: Data acquisition, data analysis, figure realization and writing
 Antonio R Hidalgo-Muñoz: Data analysis supervision and writing
 Joaquín Ibañez-Ballesteros: Data analysis, figure conception and writing
 Carmen Taberero: Data acquisition, experimental setting and writing.

Conflict of interest

Joaquín Ibañez-Ballesteros reports that he is inventor of patents licensed to Newmanbrain, SL and cofounder and scientific advisor of Newmanbrain S.L., the company responsible of manufacturing the NIRS device used in this research.

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