Behavioural Brain Research

Differences in prefrontal cortex activity based on difficulty in a working memory task using near-infrared spectroscopy

--Manuscript Draft--

Manuscript Number:	BBR_2020_235R1
Article Type:	Research Paper
Keywords:	functional near-infrared spectroscopy.; Sternberg task; Working memory; prefrontal cortex
Corresponding Author:	Anton Aluja University of Lleida Lleida, Catalonia SPAIN
First Author:	Anton Aluja
Order of Authors:	Anton Aluja
	Ignacio Lucas
	Patricia Urieta
	Eduardo Blanco
	Ferran Balada
Abstract:	The Prefrontal cortex (PFC) has been highly related to executive functions such as working memory (WM). This study assesses the activity of the PFC in performing the Sternberg WM task (ST) with three levels of difficulty (easy, medium and hard) using the near-infrared spectroscopy (fNIRS) technique. Participants were 43 young and healthy right-handed women. Nine WM task blocks were pseudo randomly presented, three for each difficulty task. The results showed that the participant's performance was better in the easy trials than in the medium and hard trials. Performance in the medium trials was also better than in the hard ones. Bonferroni-corrected paired post-hoc t-tests indicated higher oxygenation in medium and hard tasks than in the easy ones for times between 13 and 42 seconds in the left lateral PFC and in both, medial and lateral, right PFC. Significant differences in Oxygenated hemoglobin (HbO), Total hemoglobin (HbT) and oxygenation (Oxy) changes depending on the Sternberg WM task were found. Unlike previous studies with fNIRS and WM, the current study uses a highly controlled WM task that differentiates between encoding, retention and retrieval phases, comparing different levels of task load.
Suggested Reviewers:	Yutaro Ogawa ogawa@bmpe.k.u-tokyo.ac.jp Expert in WM and spectroscopy
	Anthony Ruocco anthony.ruocco@gmail.com Expert in frontal spectroscopy
	Hasan Ayaz ayaz@drexel.edu Expert in frontal spectroscopy
Response to Reviewers:	

Differences in prefrontal cortex activity based on difficulty in a working memory task using near-infrared spectroscopy

Ignacio Lucas[1,2], Patrícia Urieta[1,2], Ferran Balada[1,3], Eduardo Blanco[1,2] and Anton Aluja[1,2]

[1] Lleida Institute for Biomedical Research Dr. Pifarré Foundation (IRBLleida), Catalonia, Spain
[2] University of Lleida. Catalonia (Spain).
[3] Dept. Psicobiologia i Metodologia de les Ciències de la Salut. Universitat Autònoma de Barcelona. Catalonia (Spain).

Corresponding author: Anton Aluja (aluja@pip.udl.cat). Lleida Institute for Biomedical Research Dr. Pifarré Foundation (IRBLleida). University of Lleida. Catalonia, Spain

Abstract: The Prefrontal cortex (PFC) has been highly related to executive functions such as working memory (WM). This study assesses the activity of the PFC in performing the Sternberg WM task (ST) with three levels of difficulty (easy, medium and hard) using the near-infrared spectroscopy (fNIRS) technique. Participants were 43 young and healthy right-handed women. Nine WM task blocks were pseudo randomly presented, three for each difficulty task. The results showed that the participant's performance was better in the easy trials than in the medium and hard trials. Performance in the medium trials was also better than in the hard ones. Bonferroni-corrected paired post-hoc t-tests indicated higher oxygenation in medium and hard tasks than in the easy ones for times between 13 and 42 seconds in the left lateral PFC and in both, medial and lateral, right PFC. Significant differences in Oxygenated hemoglobin (HbO), Total hemoglobin (HbT) and oxygenation (Oxy) changes depending on the Sternberg WM task were found. Unlike previous studies with fNIRS and WM, the current study uses a highly controlled WM task that differentiates between encoding, retention and retrieval phases, comparing different levels of task load.

Key words: prefrontal cortex, working memory, Sternberg task, functional near-infrared spectroscopy.

1. INTRODUCTION

The prefrontal cortex (PFC) is a key structure of the brain, involved in numerous cognitive functions [1]. One concept that encompasses several of these functions is Working Memory (WM). It has been defined as the ability to maintain and manipulate a limited amount of task-relevant information [2, 3, 4], and differs from short-term memory, which refers only to the storage of information [5, 6]. WM is essential for decision making and is one of the most important executive functions [7, 8]. Several brain regions are implicated in WM processes, such as the fronto-parietal network, the cingulate cortex, or the dorsolateral and ventrolateral PFC. Additionally, recent studies have implicated the roles of subcortical regions, such as the midbrain and other structures like the cerebellum [9].

Just like other executive functions, WM has limited storage, and its capacity is related to cognitive abilities. In neurological and psychopathological disorders, these abilities decrease [10]. WM performance has been related to higher PFC activity [11]. Engle [12] claimed that WM load is associated with executive attention and distraction avoidance. Excitatory PFC activity could improve mnemonic load by neutralizing inhibition in posterior areas [13]. In fact, PFC activity correlated with WM load in several studies [14, 7]. Many studies have described WM impairments in psychopathological disorders [15] and neurodegeneration [1, 16]. Age interactions with emotion, caffeine and hormones also appear to affect working memory performance at the neurobiological level [17]. Other variables, as sleep deprivation, could also affect WM and frontal activation [18, 19].

Functional magnetic resonance imaging (fMRI) has been frequently used to measure WM-related brain activations. However, fMRI devices are very expensive and researchers require alternative imaging techniques [20]. Functional near-infrared spectroscopy (fNIRS) is an optical method that allows noninvasive measurement of the variations of oxygenated and deoxygenated hemoglobin in cortical zones [21]. The fNIRS has been correlated with fMRI [22].

Furthermore, fNIRS has several unique advantages over functional neuroimaging methodologies, such as fMRI, including fewer limitations for the subject, low susceptibility to movement artifacts and a good temporal sampling rate [20].

Previous studies assessed WM using the fNIRS technique. For example, Molteni et al. [23] applied the fNIRS technique to measure PFC brain activity during an N-back task with different levels of difficulty. The authors observed increases in blood oxygenation associated with task load. Higher levels of difficulty showed increased activation in the PFC compared to the easy ones. The lateral prefrontal cortex plays a major role in WM processes. Moreover, Tanida et al. [24] observed how task performance correlated with lateral PFC activation in a WM paradigm. In another study, Li et al. [25] also compared gender-specific activity during an N-Back task. Besides, Keshmiri et al. [26] also used different WM tests to compare between different analysis methods. Furthermore, Basso et al. [27] showed the potential clinical applicability of this technique by using it during the Logical Memory Test of the Wechsler Memory Scale. However, no previous study has used fNIRS with a WM task that made it possible to differentiate between encoding, retention and retrieval, comparing between different levels of activation.

Of the different experimental paradigms are used to assess WM processes, Sternberg's task (ST) is one of the most widely used. From the initial proposal in the early 1960s, different adaptations have been developed [28]. In general, it consists of the presentation of letters or digits on a screen that must be memorized (encoding), which after a short period of time (retention) are presented individually for the participant to indicate whether or not it was present in the previous presentation (retrieval). Unlike other WM paradigms, ST makes it possible to differentiate time for encoding, retention and retrieval [29]. The original ST was designed to measure how quickly people can search for and retrieve information from short-term memory.

The main objective of this experiment is to check for possible differences between PFC activations depending on WM task load using the fNIRS technique. PFC activation should correlate with task difficulty, as more resources are demanded with the increase in task load. Taking into account previous research on working memory, the PFC structure that should show the highest differences is the lateral PFC. We hypothesize that the activation in both lateral PFC will be higher for the more difficult WM conditions.

METHOD

2.1. Participants

The participants were 43 healthy right-handed women (mean age = 19.6 $\pm$ 1.5). All participants reported no history of neurological or psychopathological disorders or substance abuse. Menstrual cycle phase and hours slept (mean slept = 7.3 $\pm$ 1.0) were controlled. None of the participants were taking psychotropic medication. Another condition for participating in this experiment was no consumption of stimulants or tobacco in the previous 12 hours. Detailed information about the procedure was given to all participants, who signed an informed consent. The study was approved by the University's Ethics Committee.

2.2. Procedure

Participants performed a task based on the classic Sternberg WM paradigm, which involves encoding, maintenance and retrieval phases. Trials consisted of a string of uppercase consonants followed by a mask and then eight probe letters displayed one by one (Figure 1). Subjects had to answer whether the probe letter had been in the previous string or not by pressing the corresponding button. Fifty per cent of the probe letters appeared in the previous string. Three different WM task difficulties were presented to each participant (Easy = 4 letters, Medium = 8, Hard = 12). Nine trials were presented pseudo randomly, three for each difficulty. Variable resting periods (25-35 sec) were performed between trials in order to return to baseline levels of activation.

2.2.2. fNIRS recording

An fNIR 1100 apparatus and COBI software for data collection (Biopac System, Inc.) were used. The system recorded PFC hemodynamic activity (Oxygenated hemoglobin: HbO_2; Reduced hemoglobin: HbR). A time window was selected from 0 to 42 s after stimulus onset. Hemoglobin changes were calculated according to a baseline level taken before stimulus onset (signal change in relation to the baseline). Total hemoglobin (HbT) and oxygenation changes (Oxy) were obtained from HbO_2 and HbR. The PFC parts that were registered included Brodmann areas 9, 10, 45, 46 and 47 [30]. The fNIR apparatus, its functioning and data processing are described in detail elsewhere [31, 32]. The recording sessions took place in an acoustically and electromagnetically isolated room (Faraday cage) with a compartment for the experimental subject and another for the researcher.

2.3. Statistical data analysis

The Sternberg WM execution score was calculated with the formula $\frac{(hits - errors) * 100}{24}$. Paired *t*-tests were performed to analyze differences in task execution and reaction time. Hemodynamic measures recorded from the optodes were grouped into four separate quadrants: lateral left (optodes 1, 2, 3 and 4), central left (optodes 5, 6, 7 and 8), central right (optodes 9, 10, 11 and 12) and lateral right (optodes 13, 14, 15 and 16). Each area was obtained from the mean of the four corresponding channels. A one-way within subject analysis of variance (ANOVA) was conducted to compare hemodynamic changes to task difficulties in the PFC regions. The effects were evaluated with the Greenhouser-Geiser correction for sphericity violations. To evaluate the magnitude of effects, we considered the η_p^2 statistic, which represents the portion of total variability attributable to a given factor while controlling the other ones. Values of $\eta_p^2 < 0.05$ are usually regarded as small, $0.05 \leq \eta_p^2 < 0.15$ as medium, and $\eta_p^2 \geq 0.15$ as large [33].

There are several statistical analysis approaches to extracting the signals related with the neural activity from the data obtained through the fNIRs [34, 26]. Since the Sternberg test allows us to differentiate between encoding, retention and retrieval, we have divided the total recording time of each trial into consecutive, non-overlapping windows, each lasting 5 seconds, in addition to a first segment of 12 seconds corresponding to the coding period. For each segment we extracted the mean. In order to analyse oxygenation changes in response to the Sternberg WM test over time, a repeated measures ANOVA that included two within-group factors (Task load x time) was performed for each quadrant. Within-group factor task load had three levels: easy, medium and hard. The within-group factor time was defined as the mean values of oxygenation changes for forty-two seconds after the beginning of each trial, including seven levels (1-12, 13-17, 18-22, 23-27, 28-32, 33-37 and 38-42).

3. RESULTS

3.1. Task performance

Figure 2 shows the differences in execution scores. As expected, subjects performed better in the easy trials than in the medium ($t_{(42)}$= 9.7; p < 0.001) and hard trials ($t_{(42)}$= 16.4; p < 0.001). Performance in the medium trials was also better than in the hard ones ($t_{(42)}$= 5.8; p < 0.001). Significant differences in reaction time were also observed. Easy trials (878.5 ± 179.1 ms) had a lower reaction time response than medium (1,169.4 ± 247.8 ms) ($t_{(42)}$= 13.6; p < 0.001) and hard ones (1,260.9 ± 253.0 ms) ($t_{(42)}$= 13.1; p < 0.001), and medium trials had a lower reaction time than hard ones ($t_{(42)}$= 3.2; p = 0.002). The comparisons of task performance in function of menstrual cycle did not show statistical differences either for execution (all p > 0.2) or reaction time (all p > 0.08). No statistical differences were found at any level of difficulty in task performance (all p > 0.1) comparing participants who had slept less than 7 hours (10 participants) with the ones who had slept more than 7 hours (33 participants). However, the latter group had slightly better scores in the hard task (46.5 %) than the former (32.5%).

3.2. fNIRS measurements results

Separate analysis of hemodynamic variables presented differences for HbO_2, HbT and Oxy, but not for HbR, in all prefrontal quadrants. Table 1 displays a distinct analysis of hemodynamic variables for each prefrontal quadrant. Analysis of Variance indicated significant differences in HbO, HbT and Oxy changes as a function of Sternberg WM load for all the prefrontal quadrants.

Figure 3 shows the temporal sequence of oxygenation changes for the three difficulties in each channel analyzed. Repeated measures ANOVA shows interaction between task load and time for all the prefrontal quadrants (all $p \leq 0.001$; $\eta_p^2 > .15$ for right medial and lateral PFC; $\eta_p^2 > .12$ for left medial and lateral PFC). Paired post-hoc *t*-tests with a Bonferroni correction indicate higher oxygenation in medium and hard tasks than in the easy ones for times between 13 and 42 seconds in the left lateral prefrontal cortex and in both, medial and lateral, right prefrontal cortex. Significant differences between medium and hard tasks only appeared in the last time lapse for the right medial (($t_{(42)}$= 2.8; $p < 0.01$) and lateral (($t_{(42)}$= 4.0; $p < 0.001$) prefrontal cortex. Figure 4 shows the oxygenation increase (yellow-red) or decrease (green-blue) of the prefrontal cortex in function of working memory load. Each picture represents five-second segments, except the first picture which corresponds to the first 12 seconds. The temporal sequence shows the differences existing according to the load of the working memory, especially in the segments corresponding to the retrieval. Figure 5 displays *p* values of post-hoc paired *t*-test for Oxy changes between difficulties at each time period. Red line indicates a *p* value of 10^{-3}.

4. DISCUSSION

This study was designed to explore the differences in PFC activation in response to different WM loads. PFC activity was expected to be associated with the difficulty of the task load; specifically, it was expected to increase with task difficulty. The activation in both lateral PFC was higher for the more difficult WM conditions. These results confirm the association between WM task load and bilateral PFC activation. Other imaging studies provide evidence that the PFC is quantitatively more activated if the working memory load increases, suggesting that executive functions are involved for highly demanding WM tasks [35, 23, 36].

Results for task execution agree with previous results using similar paradigms. Increasing load in the task impairs execution and increases reaction time. In the current study, the possible interactions of WM with age, emotion, stimulants (caffeine and tobacco), hormones and sleep were controlled to avoid interactions that could have affected our results [17, 37, 19].

PFC oxygenation is related to task load increases, as shown by the results of D'Esposito et al. [35] and Tomasi et al. [36]. The oxygenation increase was evident when comparing the easy condition with the other two conditions, whereas few differences appeared between medium and hard conditions. This effect could be related to the amount of information that we can store. Notice that in our study, 8 and 12 letters were used for medium and hard loads respectively. WM capacity limits of adult humans is set between 5 and 9 elements [38]. Therefore, these conditions would be nearly at the limit of its capacity, or exceed it.

Oxygenation of the PFC increased throughout the blocks, notably in the hard task load, whereas in the easy blocks the increase appeared only at the beginning of each trial, mainly in lateral areas. Sternberg's paradigm made it possible to differentiate between encoding, retention and retrieval. The initial increase observed in all difficulties could indicate that this increase would be more related to encoding and retention than to retrieval. It is important to highlight that, like every hemodynamic variable, the responses recorded with fNIRS have a temporal delay with regard to cortical activation itself [39]. Moreover, we can observe a second oxygenation increase, mainly at the end of the hard blocks, which affected all PFC areas, as we can observe in Figures 3 and 4. This increase would correspond almost completely to the retrieval phase. Statistically significant differences for this phase appeared when comparing easy with both medium and hard loads in bilateral and right medial PFC. In this ST, it could represent an effort to keep the information active in load conditions that would be at the limit of the participants' WM capacity.

Two aspects of the PFC oxygenation increase should be highlighted: both the lateral PFC oxygenation increase and the right medial PFC oxygenation increase. On the one hand, several studies indicate that dorsolateral PFC could be involved in WM, associated with information encoding and response processes [40, 41]. The dorsolateral PFC plays a relevant role in sustaining attention and has been widely related to WM. On the other, ventrolateral PFC (vlPFC) activation has been linked with maintenance periods [42]. It could be related to a greater effort to keep information in a task that would be at the limit of the capacity of working memory. Hard task difficulty would also require recruiting the medial areas of the PFC, mainly the right side, which initially did not require such activation. Results suggest that the observed differences could be due to the use of a different cognitive strategy such as chunking.

The results observed highlight the importance of the PFC lateral structures in the encoding and retrieval phases, in agreement with the results presented by Basso et al. [27]. All three task loads showed activation in these areas at the beginning of the task. However, the easy task showed a drop in this activity in the retrieval phase, which did not happen for the other two difficulties. This could suggest that the activity of the retrieval phase would be highly related to the task load in WM paradigms.

This study has both strengths and limitations. Age interactions with emotion, caffeine and hormones appear to affect WM routines at the neurobiological level [17]. To avoid age effect as much as possible, this study was conducted with young women of a similar age. In addition, to avoid the effect on WM tasks of caffeine or tobacco, participants did not take these substances in a 12-hour period prior to the study. It is well known that women are emotionally more reactive than men [43], and there are some sex differences in working memory performance [44] and prefrontal activity related to WM [25]. Females have been found to consistently activate more limbic and prefrontal structures, while males activate a distributed network inclusive of more parietal regions [45]. This study also controlled the possible phase effect of the menstrual cycle and hours of sleep. Some studies have found restricted working memory in anxiety, while others have not [46]. However, anxiety traits could play a role in WM performance and thus affect the results on higher loads [47], for this reason it is recommended to control anxiety in future studies. Future studies should be designed to control the menstrual cycle and hours of sleep, and also analyze the differences in a sample of men.

In conclusion, this study contributes to a better knowledge of executive functions, such as WM. Activation patterns of the PFC of the brain are in line with previous findings. Unlike previous studies with fNIRS and WM, as far as we know our work was the first to use a highly controlled WM task that differentiates between encoding, retention and retrieval phases, comparing different levels of task load. According to this evidence, fNIRS is a useful tool to measure PFC activation during WM paradigms. The increase of PFC activation was observed controlling possible effects of age, hormones and sleep in females. Cortical activity would be affected by task load, showing higher activations for the most demanding tasks. Both ventrolateral and dorsolateral PFC seem to play a central role in WM processes, highlighting the importance of the lateral areas of the PFC in this type of executive function. Medial PFC also seems to be involved in some kind of cognitive strategy useful for highly demanding WM tasks.

5. REFERENCES

[1] A. Baddeley, Working memory, Science. 255 (5044) (1992) 556–559.

[2] J.G. Hakun, N.F. Johnson, Dynamic range of frontoparietal functional modulation is associated with working memory capacity limitations in older adults, Brain Cognition. 118 (2017) 128-136.

[3] J. Sun, F. Liu, H. Wang, A. Yang, C. Gao, Z. Li, et al., Connectivity properties in the prefrontal cortex during working memory: A near-infrared spectroscopy study, J Biomed Opt. 24 (5) (2019) 051410.

[4] H. Wang, W. He, J. Wu, J. Zhang, Z. Jin, , L. Li, A coordinate-based meta-analysis of the n-back working memory paradigm using activation likelihood estimation, Brain Cognition. 132 (2019) 1-12.

[5] N. Cowan, The magical mystery four: How is working memory capacity limited, and why? Curr Dir Psychol Sci. 19(1) (2010) 51-57.

[6] A. Baddeley, Working memory: Theories, models, and controversies, Annu Rev Psychol. 63 (2012) 1-29.

[7] J.D. Cohen, W.M. Perlstein, T.S. Braver, L.E. Nystrom, D.C. Noll, J. Jonides, et al., Temporal dynamics of brain activation during a working memory task, Nature. 386 (6625) (1997) 604.

[8] A. Diamond, Executive functions, Annu. Rev. Psychol. 64 (2013) 135-168.

[9] L.F. Koziol, D. Budding, N. Andreasen, S. D'Arrigo, S. Bulgheroni, H. Imamizu, et al., Consensus paper: the cerebellum's role in movement and cognition, Cerebellum. 13 (1) (2014), 151-177.

[10] C. Constantinidis, T. Klingberg, The neuroscience of working memory capacity and training, Nat. Rev. Neurosci. 17 (7) (2016) 438.

[11] Y. Ogawa, K. Kotani, Y. Jimbo, Relationship between working memory performance and neural activation measured using near-infrared spectroscopy, Brain Behav. 4 (4) (2014) 544-551.

[12] R.W. Engle, Working memory capacity as executive attention, Curr. Dir. Psychol. Sci. 11 (1) (2002) 19-23.

[13] F. Edin, T. Klingberg, P. Johansson, F. McNab, J. Tegnér, A. Compte, Mechanism for top-down control of working memory capacity, Proc. Natl. Acad. Sci. 106 (16) (2009) 6802-6807.

[14] T.S. Braver, J.D. Cohen, L.E. Nystrom, J. Jonides, E.E. Smith, D.C. Noll, A parametric study of prefrontal cortex involvement in human working memory, Neuroimage. 5 (1) (1997) 49-62.

[15] R. Martinussen, J. Hayden, S. Hogg-Johnson, R. Tannock, A meta-analysis of working memory impairments in children with attention-deficit/hyperactivity disorder, J. Am. Acad. Child. Psy. 44 (4) (2005) 377-384.

[16] C.L. Stopford, J.C. Thompson, D. Neary, A.M. Richardson, J.S. Snowden, Working memory, attention and executive function in Alzheimer’s disease and frontotemporal dementia, Cortex. 48 (4) (2012) 429-446.

[17] W.J. Chai, A.I. Abd Hamid, J.M. Abdullah, Working memory from the psychological and neurosciences perspectives: A review, Front Psychol. 9 (2018) 401.

[18] S.J. Frenda, K.M. Fenn, Sleep less, think worse: The effect of sleep deprivation on working memory, J. Appl. Res. Mem. Cogn. 5 (4) (2016) 436-469.

[19] M.K. Yeung, T.L. Lee, W.L. Cheung, A.S. Chan, Frontal underactivation during working memory processing in adults with acute partial sleep deprivation: a near-infrared spectroscopy study, Front. Psychol. 9 (2018) 742.

[20] H.J. Niu, X. Li, Y.J. Chen, C. Ma, J.Y. Zhang, Z.J. Zhang, Reduced frontal activation during a working memory task in mild cognitive impairment: A non-invasive near-infrared spectroscopy study, CNS Neurosci. Ther. 19 (2) (2013) 125-131.

[21] Y. Yamashita, A. Maki, Y. Ito, E. Watanabe, Y. Mayanagi, H. Koizumi, Noninvasive near-infrared topography of human brain activity using intensity modulation spectroscopy, Opt. Eng. 35 (1996) 1046-9.

[22] X. Cui, S. Bray, D.M. Bryant, G.H. Glover, A.L. Reiss, A quantitative comparison of NIRS and fMRI across multiple cognitive tasks, Neuroimage 54 (4) (2011) 2808-2821.

[23] E. Molteni, M. Butti, A.M. Bianchi, G. Reni, Activation of the prefrontal cortex during a visual n-back working memory task with varying memory load: A near infrared spectroscopy study. In 2008 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (2008) 4024-4027.

[24] M. Tanida, K. Sakatani, T. Tsujii, Relation between working memory performance and evoked cerebral blood oxygenation changes in the prefrontal cortex evaluated by quantitative time-resolved near-infrared spectroscopy, Neurol. Res. 34 (2) (2012) 114-19.

[25] T. Li, Q. Luo, & H. Gong. Gender-specific hemodynamics in prefrontal cortex during a verbal working memory task by near-infrared spectroscopy. Behavioural brain research, 209(1) (2010) 148-153.

[26] S. Keshmiri, H. Sumioka, R. Yamazaki, & H. Ishiguro. Differential entropy preserves variational information of near-infrared spectroscopy time series associated with working memory. Frontiers in neuroinformatics, 12 (2018) 33.

[27] S. Basso, S. Cutini, M. L. Ursini, M. Ferrari & V. Quaresima. Prefrontal cortex activation during story encoding/retrieval: a multi-channel functional near-infrared spectroscopy study. Frontiers in human neuroscience, 7 (2013) 925.

[28] S. Sternberg, High-speed scanning in human memory, Science. 153 (3736) (1965), 652-654.

[29] S. Liu, J.H. Poh, H.L. Koh, K.K. Ng, Y.M. Loke, J.K.W Lim, et al., Carrying the past to the future: Distinct brain networks underlie individual differences in human spatial working memory capacity, Neuroimage. 176 (2018) 1-10.

[30] A.H. Rodrigo, H. Ayaz, A.C. Ruocco, Examining the neural correlates of incidental facial emotion encoding within the prefrontal cortex using functional near-infrared spectroscopy, in Schmorrow, D. Fidopiastis, C. (Eds.), Foundations of Augmented Cognition: Neuroergonomics and Operational Neuroscience, Springer, Cham. (2016) 102-112.

[31] F. Balada, I. Lucas, Á. Blanch, E. Blanco, A. Aluja, Neuroticism is associated with reduced oxygenation levels in the lateral prefrontal cortex following exposure to unpleasant images, Physiol. Behav. 199 (2019) 66-72.

[32] I. Lucas, F. Balada, E. Blanco, A. Aluja, Prefrontal cortex activity triggered by affective faces exposure and its relationship with neuroticism, Neuropsychologia. 132 (2019) 107146.

[33] J. Cohen, *Statistical power analysis for the behavioral sciences* (1988) Second Edition. Hillsdale, NJ: Lawrence Erlbaum Associates Publishers

[34] S. Tak & J. C. Ye. Statistical analysis of fNIRS data: a comprehensive review. Neuroimage, 85 (2014) 72-91.

[35] M. D'Esposito, G.K. Aguirre, E. Zarahn, D. Ballard, R.K. Shin, J. Lease, Functional MRI studies of spatial and nonspatial working memory, Brain Res. Cogn. Brain Res. 7 (1) (1998) 1-13.

[36] D. Tomasi, T. Ernst, E.C. Caparelli, L. Chang, Common deactivation patterns during working memory and visual attention tasks: An intra-subject fMRI study at 4 Tesla, Hum. Brain Mapp. 27 (8) (2006) 694-705.

[37] J. Del Angel, J. Cortez, D. Juarez, M. Guerrero, A. García, C. Ramírez, et al., Effects of sleep reduction on the phonological and visuospatial components of working memory, Sleep Sci. 8 (2) (2015) 68-74.

[38] G.A, Miller, The magical number seven, plus or minus two: Some limits on our capacity for processing information, Psychol. Rev. 101 (2) (1994) 343.

[39] X. Cui, S. Bray, A.L. Reiss, Speeded near infrared spectroscopy (NIRS) response detection, Plos One. 5 (11) (2010) e15474.

[40] A. Bechara, H. Damasio, A.R. Damasio, G.P. Lee, Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making, J. Neurosci. 19 (13) (1999) 5473-5481.

[41] A. Bechara, H. Damasio, D. Tranel, S.W. Anderson, Dissociation of working memory from decision making within the human prefrontal cortex, J. Neurosci, 18 (1) (1998) 428-437.

[42] M. D'Esposito, B.R. Postle, B. Rypma, Prefrontal cortical contributions to working memory: evidence from event-related fMRI studies, Exp. Brain Res. 133 (1) (2000) 3-11.

[43] J.S. Stevens, S. Hamann, Sex differences in brain activation to emotional stimuli: a meta-analysis of neuroimaging studies, Neuropsychologia. 50 (7) (2012) 1578-1593.

[44] J.L. Reed, N.M. Gallagher, M. Sullivan, J.H. Callicott, A.E. Green, Sex differences in verbal working memory performance emerge at very high loads of common neuroimaging tasks, Brain Cognition. 113 (2017) 56-64.

[45] A.C. Hill, A.R. Laird, J.L. Robinson, Gender differences in working memory networks: a Brain Map meta-analysis, Biol. Psychol. 102 (2014) 18-29.

[46] T.P. Moran, Anxiety and working memory capacity: A meta-analysis and narrative review, Psychological Bulletin. 142(8) (2016) 831–864.

[47] R. Takizawa, Y. Nishimura, H. Yamasue & K. Kasai. Anxiety and performance: the disparate roles of prefrontal subregions under maintained psychological stress. *Cerebral Cortex*, *24*(7) (2014) 1858-1866.

ACKNOWLEDGEMENTS

This research was funded by a grant from the Spanish Ministry of Economy, Industry and Competitiveness (PSI2015-63551-P). I. Lucas holds a predoctoral grant from the University of Lleida. P. Urieta holds a predoctoral grant from the AGAUR: Autonomous Government of Catalonia.

Figures and tables

Figure 1. Experimental paradigm for the Sternberg working memory task.

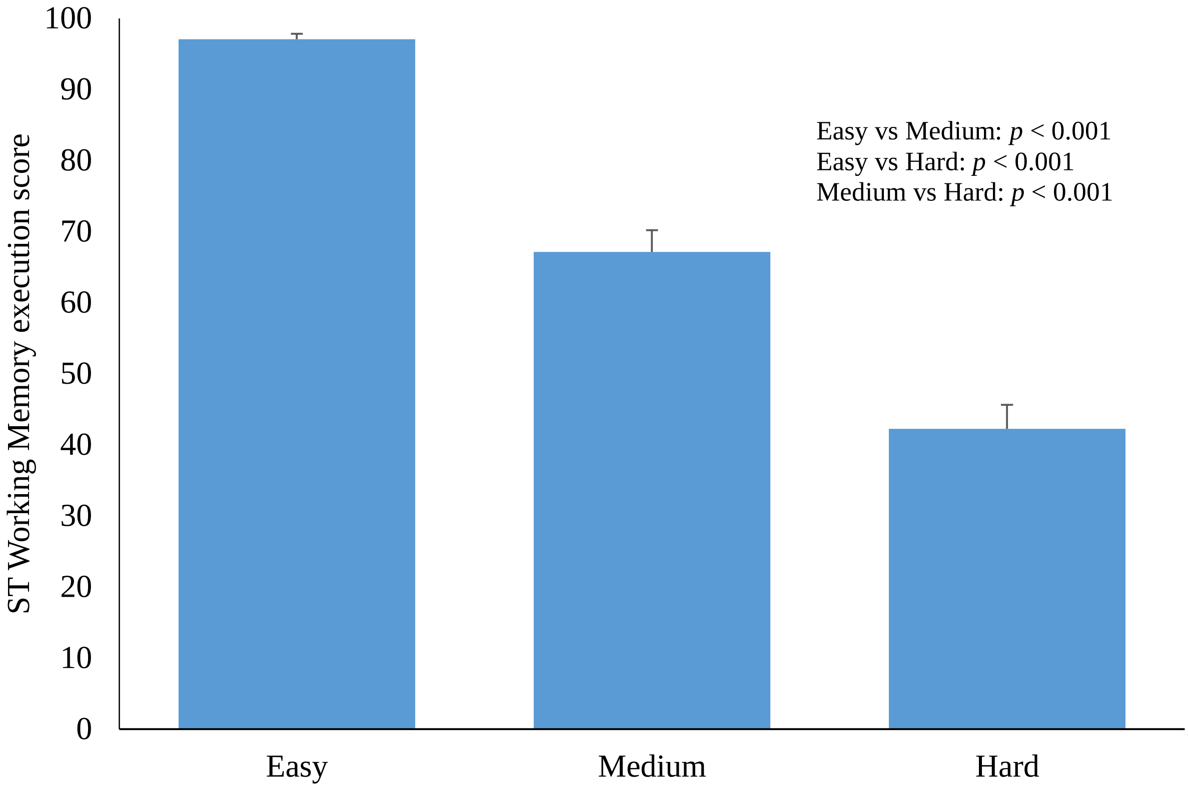

Figure 2. Working Memory task execution score for each load (error bars indicate Standard Error of the Mean).

Table 1.
Hemodynamic means and F values for each prefrontal quadrant.

	HbO_2					HbR					HbT					Oxy				
	Easy	Medium	Hard	F	η_p^2	Easy	Medium	Hard	F	η_p^2	Easy	Medium	Hard	F	η_p^2	Easy	Medium	Hard	F	η_p^2
Q1	-0.05	0.14	0.14	12.94***	.24	-0.07	-0.05	-0.08	0.65	.02	-0.11	0.09	0.06	10.30***	.20	0.01	0.20	0.21	11.76***	.22
Q2	-0.11	0.08	0.07	8.75***	.17	-0.03	-0.01	-0.03	0.31	.01	-0.14	0.07	0.04	7.48**	.15	-0.07	0.10	0.10	6.42**	.13
Q3	-0.17	0.07	0.10	15.50***	.27	-0.04	-0.03	-0.02	0.47	.01	-0.21	0.04	0.08	12.96***	.24	-0.12	0.10	0.13	12.86***	.23
Q4	-0.04	0.15	0.15	15.23***	.27	-0.05	-0.04	-0.06	0.97	.02	-0.10	0.11	0.08	13.49***	.24	0.01	0.19	0.21	12.43***	.23

Note: Q1: Lateral-Left; Q2: Central-Left; Q3: Central-Right; Q4: Lateral-Right; HbO_2: Oxygenated hemoglobin; HbR: Reduced hemoglobin; HbT: Total hemoglobin; Oxy: Oxygenation changes. *$p < 0.01$, ** $p < 0.005$, *** $p < 0.001$. (All significant differences indicate medium & hard > easy).

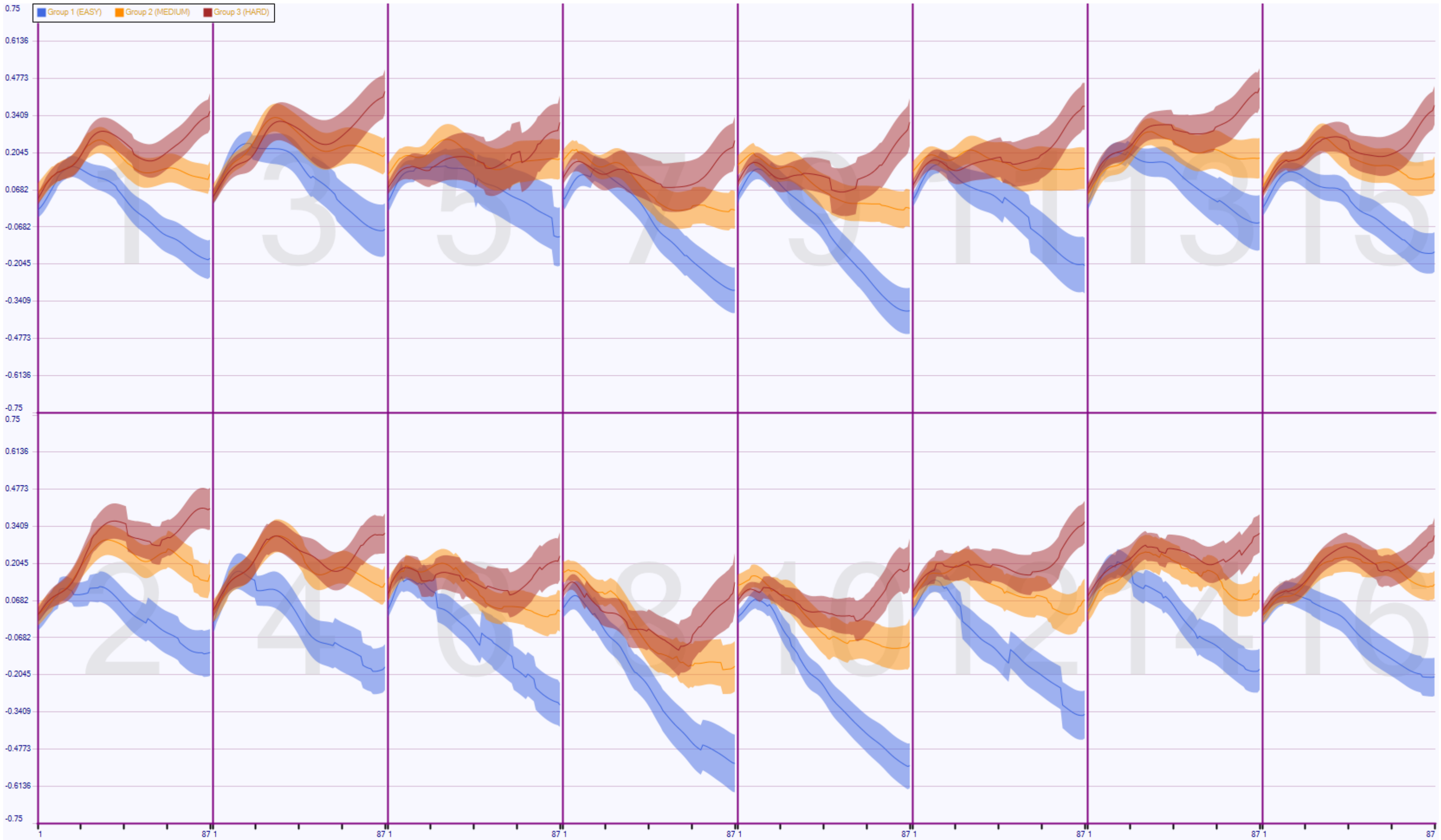

Figure 3. Oxygenation changes in each optode for the three working memory loads. (The 42-s oxy-Hb time-series across all 16 channels for easy, medium and hard conditions with 95 % confidence intervals (CI) shown as shaded areas around the grand mean.

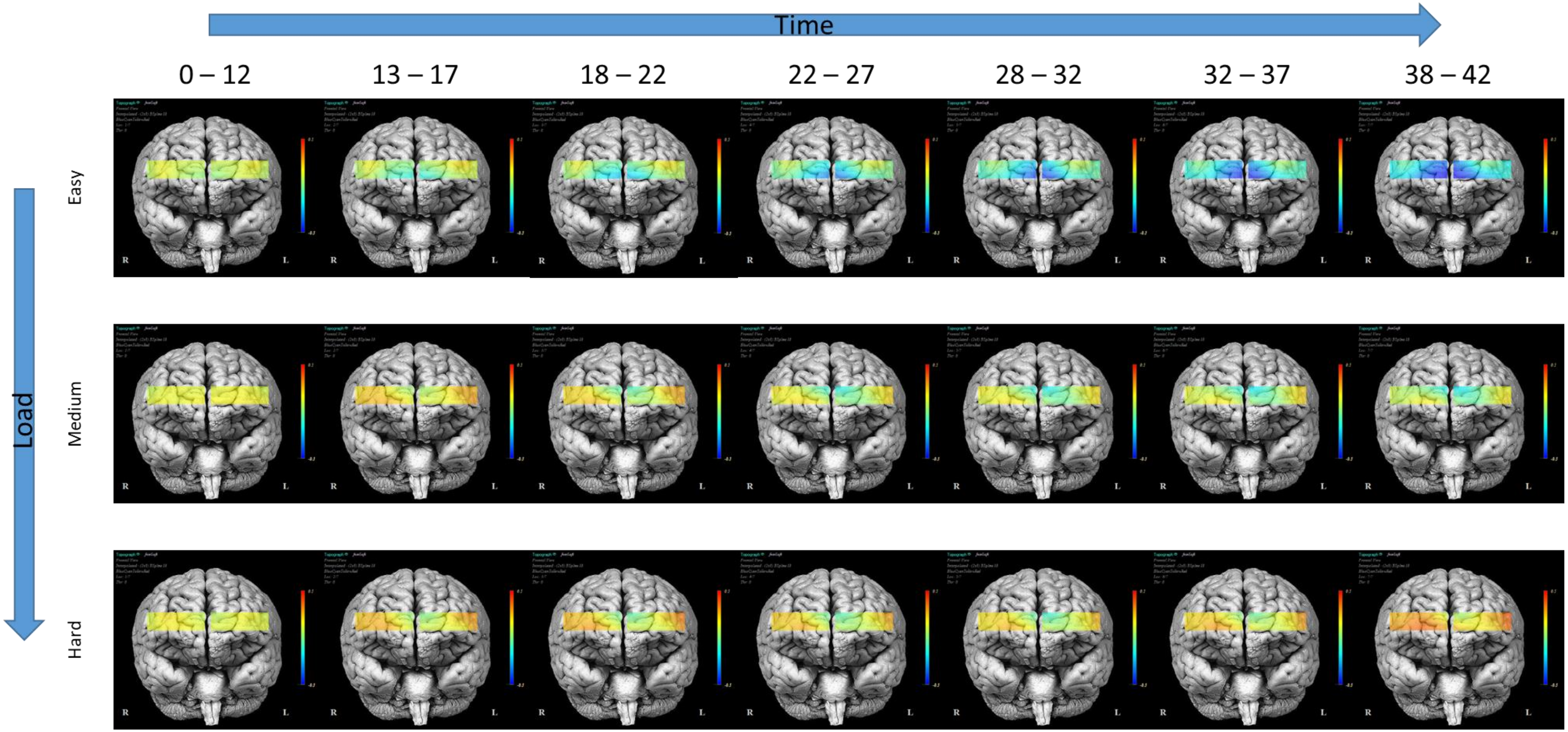

Figure 4. Topographic representation over the Brain Surface Image from Digital Anatomic Project (University of Washington) showing oxygenation levels during easy, medium and hard memory tasks for the first 12 seconds and 5-second intervals for the rest of the block. The color red denotes higher Oxygenation (Color online only).

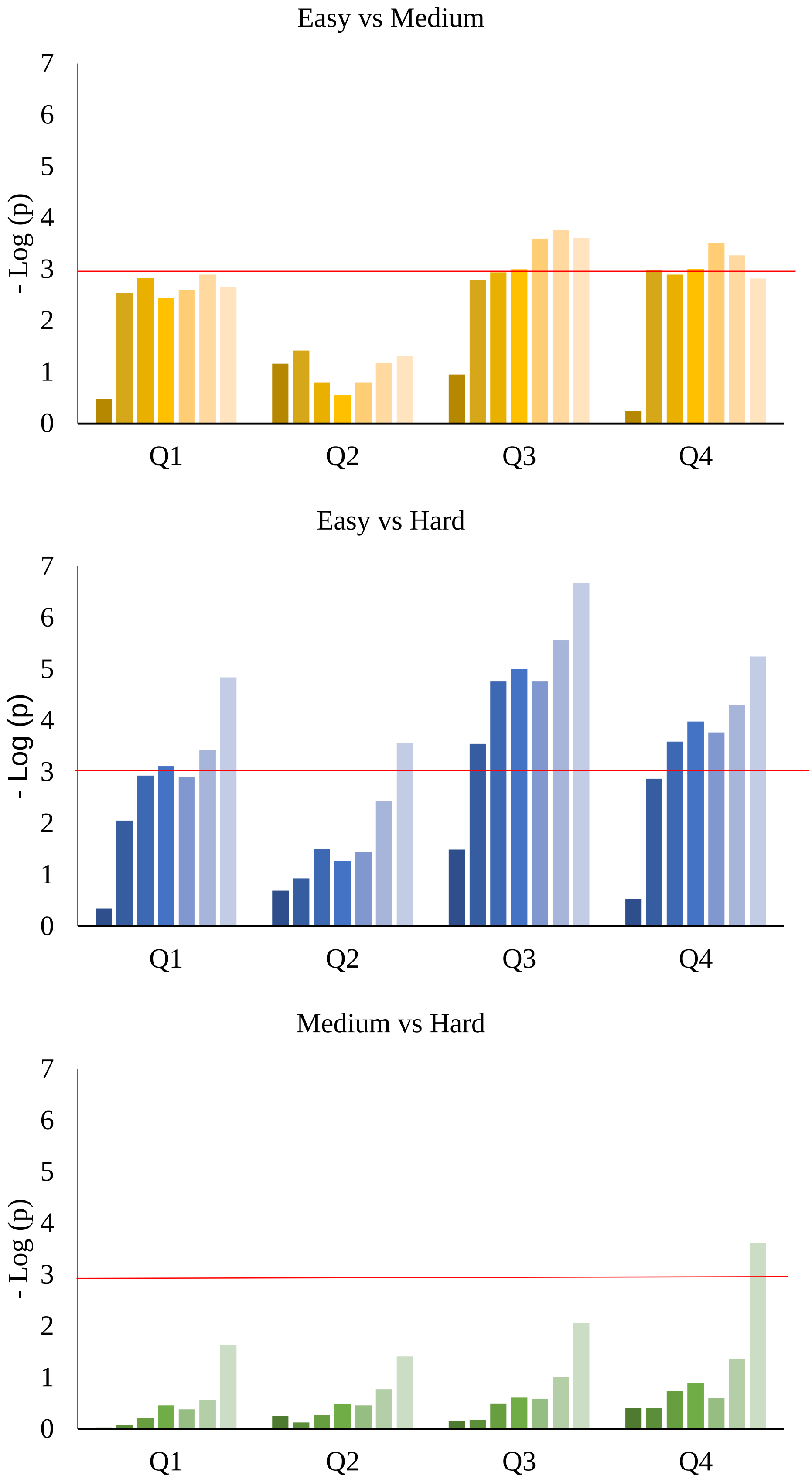

Figure 5. Post-hoc paired *t*-test comparisons (Logarithmic transformation of *p*) of Oxy changes between task loads at each time period. Q1: Lateral-Left; Q2: Central-Left; Q3: Central-Right; Q4: Lateral-Right. Each bar represents different time-periods. From left to right: 1-12; 13-17; 18-22; 23-27; 28-32; 33-37; 38-42 seconds.