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Anticipation of a mentally effortful task recruits Dorsolateral Prefrontal Cortex: An fNIRS validation study

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ABSTRACT

Preparing for a mentally demanding task calls upon cognitive and motivational resources. The underlying neural implementation of these mechanisms is receiving growing attention because of its implications for professional, social, and medical contexts. While several fMRI studies converge in assigning a crucial role to a cortico-subcortical network including Anterior Cigulate Cortex (ACC) and striatum, the involvement of Dorsolateral Prefrontal Cortex (DLPFC) during mental effort anticipation has yet to be replicated. This study was designed to target DLPFC contribution to anticipation of a difficult task using functional Near Infrared Spectroscopy (fNIRS), as a more cost-effective tool measuring cortical hemodynamics. We adapted a validated mental effort task, where participants performed easy and difficult mental calculation, and measured DLPFC activity during the anticipation phase. As hypothesized, DLPFC activity increased during anticipation of a hard task as compared to an easy task. Besides replicating previous fMRI work, these results establish fNIRS as an effective tool to investigate cortical contributions to anticipation of effortful behavior. This is especially useful if one requires testing large samples (e.g., to target individual differences), populations with contraindication for functional MRI (e.g., infants or patients with metal implants), or subjects in more naturalistic environments (e.g., work or sport).

1. Introduction

Humans face cognitively challenging situations on a daily basis. Preparing for such tasks and successfully accomplishing them requires a great deal of cognitive effort, making it a core component of motivated behavior. Several studies investigated cost-benefit trade-offs in decision-making (Apps et al., 2015; Westbrook et al., 2013), and neuroimaging evidence showed that anticipating to have to perform a difficult task relies on a cortical-subcortical brain network, which partially overlaps with regions implicated in anticipation of reward, including the medial Prefrontal Cortex (MPFC, including dorsal Anterior Cingulate Cortex, dACC) and striatum (Chong et al., 2017; Prévost et al., 2010; Westbrook and Braver, 2013, 2015). These regions are implicated in preparing for effortful performance (unconfounded by motor or decision-making factors), showing increased neural activity when preparing for a harder task. For example, this is the case when participants prepare for upcoming mentally demanding arithmetic problems (Vassena et al., 2014) or perceptual discrimination (Krebs et al., 2012). This evidence is often interpreted as indexing proactive control, i.e. top-down deployment of attentional control to ensure successful performance (Braver, 2012). Recently, computational frameworks have been proposed where MPFC activity would reflect the value of engaging in an effortful task to the extent that it can lead to a reward (Holroyd and McClure, 2015; Holroyd and Yeung, 2012; Shenhav et al., 2013; Verguts et al., 2015), or the monitoring processes detecting the frequency of occurrence of motivationally relevant variables (Vassena et al., 2017a). Notwithstanding the different computational implementation, all accounts agree in assigning to MPFC a crucial role in mechanisms underlying effortful behavior. Interestingly, a few studies have also suggested that correctly performing a task (especially when more demanding) may be rewarding in itself (Lutz et al., 2012; Satterthwaite et al., 2012; Schouppe et al., 2014), and that some of the abovementioned regions are implicated in these processes as well, in line with social psychology theory on intrinsic motivation (Bandura and Cervone, 1983).

Dorsolateral Prefrontal Cortex (DLPFC) is also implicated in preparing for cognitively demanding tasks. DLPFC activity is generally observed during higher-level cognitive processing (Miller and Cohen, 2001), such as working memory updating, goal maintenance and task set representation. According to recent theories, DLPFC indeed maintains abstract information about task-related rules, instructions or context (Alexander and Brown, 2015; Koechlin and Summerfield, 2007;

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Nee and Brown, 2012) especially when the appropriate behavioral responses is not a simple reaction to a stimulus, but requires consideration of the current task-set. Furthermore, it has been suggested that DLPFC plays the role of cortical integrator, combining stimulus and context-related information with temporal information about the task, to ensure successful task performance (Badre and Nee, 2018). One recent study showed that MPFC coding of reward expectation seems to drive strategy selection in DLPFC, which in turn regulates MPFC activity (Domenech et al., 2017). This dynamic provides theoretical support for DLPFC role in learning how to deploy control when reward is available. Therefore, as DLPFC and MPFC interact in guiding strategy-selection according to reward prospect, comparable dynamics may be hypothesized in the context of preparing for a more effortful task.

In an earlier study using functional MRI (fMRI) we provided preliminary evidence that effort anticipation implicated DLPFC (Vassena et al., 2014). More specifically, DLPFC was more active when expecting to perform a difficult (i.e., mentally effortful) task, as compared to an easy task. The goal of the current study was to independently replicate anticipation of effort in DLPFC with a novel and promising measurement technique. The use of functional Near-Infrared spectroscopy (fNIRS) is rapidly growing in cognitive and social neuroscience (Balconi and Vanutelli, 2017), as it allows measuring cortical variations in regional blood oxygenation levels in a comparable way to fMRI, but without a number of downsides that MRI has. In particular, fNIRS technology does not involve a strong magnetic field nor gradients. As a consequence, contraindications for participation due to the magnetic field do not apply. Furthermore, the fNIRS machinery (and its use) has a much lower cost than an MRI machine. Because of these two reasons, one can test a larger sample of participants, with lower cost, including patients and other subjects with (non MR-compatible) metal implants, children, and babies (who normally do not undergo fMRI strictly for research purposes), and in more ecological context (as the equipment is portable, Ayaz et al., 2013; Balardin et al., 2017). Finally, motion artifacts are less problematic with fNIRS, which makes it an interesting tool to test hypotheses in domains where movement is required (Metzger et al., 2017; Pinti et al., 2015); a relevant example in the current context would be physical effort (where participants are normally required to move to exert force). One final noteworthy advantage is that subjects can be tested simultaneously and while interacting, making it an ideal tool for social neuroscience experiments (Balconi and Vanutelli, 2017)

Exploiting these advantages to investigate cortical contributions to anticipation of difficulty (and subsequent preparation for mental effort) requires establishing fNIRS as a reliable measurement method of cortical (prefrontal) activity, by replicating cortical hemodynamic effects observed with fMRI. We therefore adopted fNIRS to investigate the contribution of bilateral DLPFC during anticipation of an effortful tasks. We adapted a mental effort task from previous studies (Vassena et al., 2014, 2015). Participants were presented with cues indicating if the upcoming task was going to be easy or hard. We measured oxygenated hemoglobin dynamics in 26 measurement channels covering frontal cortex. Moreover, we tested whether DLPFC sensitivity to task demand during effort anticipation was bilateral or unilateral (lateralized to one hemisphere). Importantly, as a first attempt to validated DLPFC contribution to effort anticipation with fNIRS, difficulty was the only factor manipulated in this design. In contrast, in our previous fMRI study (Vassena et al., 2014) reward magnitude and delay to reward were also investigated. In this sense, the main goal of the current paradigm was to validate fNIRS as a measure of difficulty anticipation, and lay the grounds for using the same technique to study the interaction between difficulty and reward processing (such as magnitude and delay effects) in future studies.

2. Materials and methods

2.1. Participants

Twenty undergraduate students from Ghent University participated in this study (mean age 20.1 ± 2.74 years, 13 females, 9 left handed), receiving one study credit as compensation to participate in the study. Written informed consent was obtained from all participants prior to participation. The study protocol was approved by the Local Ethics Committee of Ghent University. After data collection, one participant was excluded from further analysis due to technical failure. Sample size was determined based on previous studies using fNIRS to investigate cognitive function (Causse et al., 2017; Ferreri et al., 2014; Nakahachi et al., 2008). This was confirmed by an a-priori power calculation, to achieve 80% power to detect a medium-large effect size ($\eta^2 = .10$) for a within-factor comparison in a repeated-measures analysis (Foul and Erdfleder, 2007).

2.2. Experimental procedure

We examined difficulty-related hemodynamic cortical activation while participants performed a task consisting of easy and difficult arithmetic calculations (Fig. 1).

The procedure consisted of one block with 130 trials, of which 65 were easy trials and 65 were difficult trials. Easy and difficult trials were randomly intermixed. At the beginning of every trial, a cue was presented for 1000 ms, indicating if the upcoming trial was going to be easy (a blue square) or difficult (a magenta square), followed by a screen showing the symbol # at fixation with a pseudo-exponentially jittered duration (range 2.2–8 s, mean 4 s). Subsequently, the task was presented. In an easy trial, the task consisted of a sequence of two arithmetic operations, with three small numbers shown on subsequent screens (e.g., 3 + 1 + 1). Each number remained on the screen for 800 ms, and first and second number were followed by a blank screen (600 ms). In a difficult trial, the task consisted of a sequence of more difficult arithmetic operations with three larger numbers shown on subsequent screens (e.g., 8 + 15 – 6, same timing as easy trials, but requiring carrying and borrowing at each operation). We adapted this procedure from previous experiments, as it elicits a reliable and large difficulty effect (Vassena et al., 2014, 2015). After the arithmetic problem, two possible results were presented on the screen, and participants had to select the result they thought to be correct, by pressing either a left or a right button (F or J on the keyboard, response time limit 1500 ms). The response was followed by a feedback screen, which could be correct (showing the Dutch word “correct”), incorrect (showing the Dutch word “fout”) or too late (showing the Dutch words “te laat”). The feedback was followed by a 500 ms blank screen, and a pseudo-exponentially jittered inter-trial interval, with a screen showing the # symbol at fixation (range 2.2–8 s, mean 4 s). Participants were instructed to be as fast and accurate as possible. Before starting the experimental block, 8 training trials were administered. During the training only, at the end of every trial participants were asked to rate the trial on perceived difficulty and pleasantness. The questions were presented on the screen one by one (randomized across participants) and participants were asked to respond by pressing the number corresponding to their response on the keyboard. The difficulty question asked how difficult that trial was for them (on a visual 7-point scale, with 1 meaning very easy and 7 meaning very difficult). The pleasantness question asked how much they liked to perform that trial (on a visual 7-point scale, with 1 meaning not at all and 7 meaning very much). This procedure has been used in previous studies to confirm subjective perception of difficult trials as more difficult (Vassena et al., 2014, 2015).

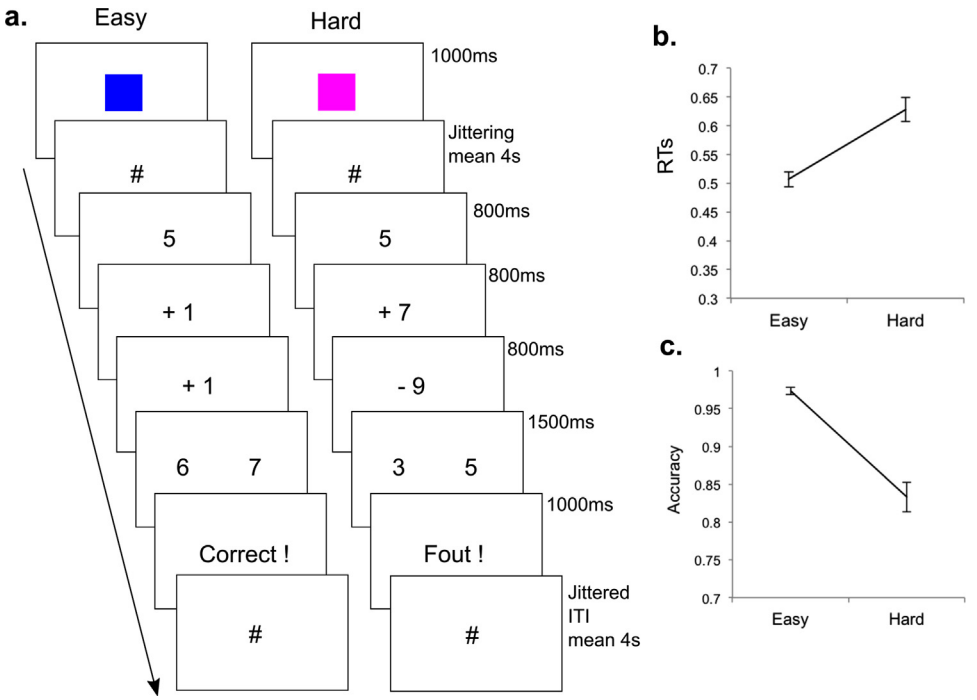

Fig. 1. Task and behavioral performance. a. Task structure. Each trial started with a cue indicating if the upcoming task was going to be easy (blue square) or difficult (magenta square). After a jittered interval, two subsequent operations (additions or subtractions) were presented on the screen, followed by two possible results. Participants had to indicate the response they thought to be correct by pressing right or left response button, and received performance feedback. Subsequent inter-trial interval was also jittered. b. Reaction times for responses in easy as compared to hard trials. c. Accuracy of the responses for easy as compared to hard trials. Error bars represent ± one standard error of the mean. Responses to easy trials were significantly more accurate and faster than hard trials. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

2.3. Questionnaires

Participants filled in the Positive And Negative Affect Scales (PANAS, Watson et al., 1988) twice, before and after the experimental session. The goal of this procedure was to measure changes in affective state, and test whether such changes may be related to task difficulty (by testing the correlation with accuracy and reaction times at the task). At the end of the session, participants also filled in the Need for Cognition scale (short version, Cacioppo et al., 1984), assessing how much participants enjoy engaging in mentally demanding endeavors, and the BIS-BAS scale (Carver and White, 1994), assessing participants' behavioral inhibition and activation tendencies.

2.4. fNIRS methods

We used the continuous-wave NIRS system (NIRScout; NIRx Medical Technologies, Brooklyn, NY) utilizing two wavelengths of near-infrared light (760 and 850 nm). Data were acquired from the prefrontal cortex with 5 sources and 5 detectors per hemisphere, covering the lateral and medial PFC. The distance between each source-detector pair was 3 cm, which provides an adequate compromise between depth sensitivity and signal to noise ratio (Strangman et al., 2013). An a-priori DLPFC region-of-interest (ROI) was anatomically determined, by visual inspection of optode locations projected on a 3D MNI atlas (Fig. 2, Okamoto et al., 2004a), and by convergence of such locations with previously reported DLPFC activity in a comparable task (Vassena et al., 2014). The DLPFC-ROI included the channels F5-F3, F5-FC5, FC3-F3 and FC3-FC5 (the first label of each pair is the sender, the second label is the receiver). This approach had one main limitation: our procedure did not include neuronavigation with the subject-specific MRI scan, thus preventing from projecting specific MNI coordinates to the subject's adapted cortical coordinates. However, given the spatial resolution of the current fNIRS setup, and the large extent of DLPFC activity reported in above-mentioned studies, it seems plausible that a finer anatomical characterization would be difficult to achieve (and not necessary for the current purpose). Fig. 2 shows the channel configuration.

3. Data analysis

3.1. Behavioral data analysis

A paired-sample *t*-test was performed on reaction times (RTs), comparing easy vs. difficult trials. A second paired-sample *t*-test was performed, comparing accuracy in the easy vs. difficult trials. Reported significance values are two-tailed.

We calculated the difference between positive and negative PANAS scores by subtracting scores at the beginning of the session from the scores at the end of session. Subsequently, these differences for positive and negative PANAS separately were correlated with accuracy and RTs at the task, to test potential influences of difficulty (as measured by indexes of task performance) on affective state. Performance was also correlated with difficulty and liking ratings. Furthermore, we calculated Need for Cognition and BIS-BAS scores, to test the relationship between task performance and attitude towards mental effort and behavioral inhibition and activation. One should note that these correlational analyses were exploratory in nature.

3.2. fNIRS data preprocessing

We analyzed the optical data using Homer2 NIRS processing package functions (Huppert et al., 2009) based on MATLAB (Mathworks, MA USA). For every participant, the raw optical intensity data series were converted into changes in optical density (OD). Then PCA was performed, which automatically adjusts the amount of variance to be removed from the data on a subject-by-subject basis. A PCA parameter of 80% was chosen as it is more conservative and removes only the variance supposed to account for the motion artifacts (Brigadoi et al., 2014). Then a motion detection algorithm was applied to the OD time series to identify residual motion artifacts (AMPthresh = .5, SDThresh = 50, tMotion = .5 s, tMask = 1 s). This means that if, over a temporal window of length .5 s, the standard deviation increases by a factor exceeding 50, or the peak-to-peak amplitude exceeds .5, then the segment of data of length 1 s starting at the beginning of that window is defined as motion. Stimuli with artifacts from the HRF calculation were excluded if any artifact appeared 5 s before the stimulus appearance, and 10 s after. Low-pass filtering with a cut-off frequency of .5 Hz was

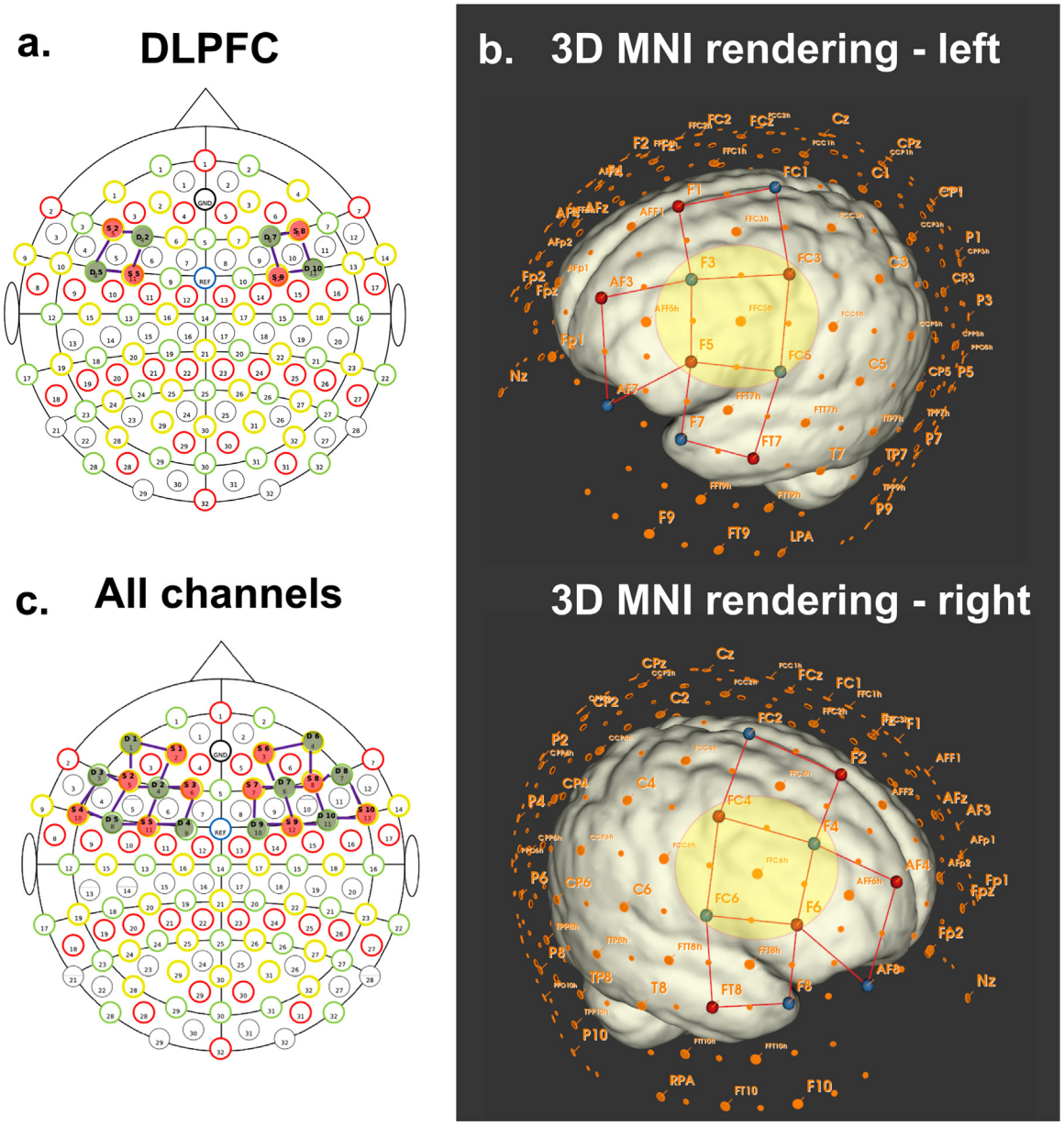

Fig. 2. fNIRS setup a. fNIRS montage visualized on the 10–20 EEG template. Selected optodes and channels covering DLPFC. b. Whole montage visualized on a 3D rendering of MNI space, with optode coordinates projected on the cortex. The yellow circles highlight the channels included in the DLPFC-ROI. c. Whole montage visualized on the 10–20 EEG template. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

applied to the data in order to remove variability due to the cardiac cycle. The OD data were then converted into concentration changes using the modified Beer-Lambert law (Cope and Delpy, 1988; Delpy et al., 1988) with the differential path length factors set to .6. This method enabled us to calculate signals reflecting the oxygenated hemoglobin (OxyHb), deoxygenated hemoglobin (DeoxyHb), and total hemoglobin (Total Hb) signal changes. Afterwards, to recover the mean hemodynamic response we solved the GLM based on ordinary least squares (Ye et al., 2009), modeling the HRF with a modified gamma function convolved with its derivative and 3rd order polynomial for drift correction. Statistics were done outside Homer2 with in-house written scripts in Matlab. Note that we performed all further analysis on the OxyHb signal. Most fNIRS studies focus on OxyHb, as this signal correlates more robustly with the fMRI-BOLD signal in several tasks, possibly due to a higher signal-to-noise ratio as compared to DeoxyHb (Hoge et al., 2005; Huppert et al., 2006; Mehagnoul-Schipper et al., 2002; Okamoto et al., 2004b; Strangman et al., 2002).

3.3. fNIRS statistical analysis

We used a mixed linear modeling (MLM) approach (Baayen et al., 2008) to analyze the relation between the peak OxyHb and task difficulty. All analyses were performed using the package lme4 (version 1.1–13) in R version 3.3.1.

Two sets of analyses were performed: the first set with the signal averaged within the DLPFC-ROI as a dependent variable; the second set with the signal averaged over all channels as a dependent variable. In all analyses, we followed a model building procedure. In a first step, we estimated a benchmark model including a random intercept for channels nested into participants (see Jasinska and Petitto, 2013 for a similar approach) to account for between-subjects variability in OxyHb concentration changes across channels (variability of no interest), plus four covariates. The first covariate was the average RT difference (hard – easy) across subjects, to control for effects of performance on DLPFC activity. The second covariate was the score of the reward responsivity

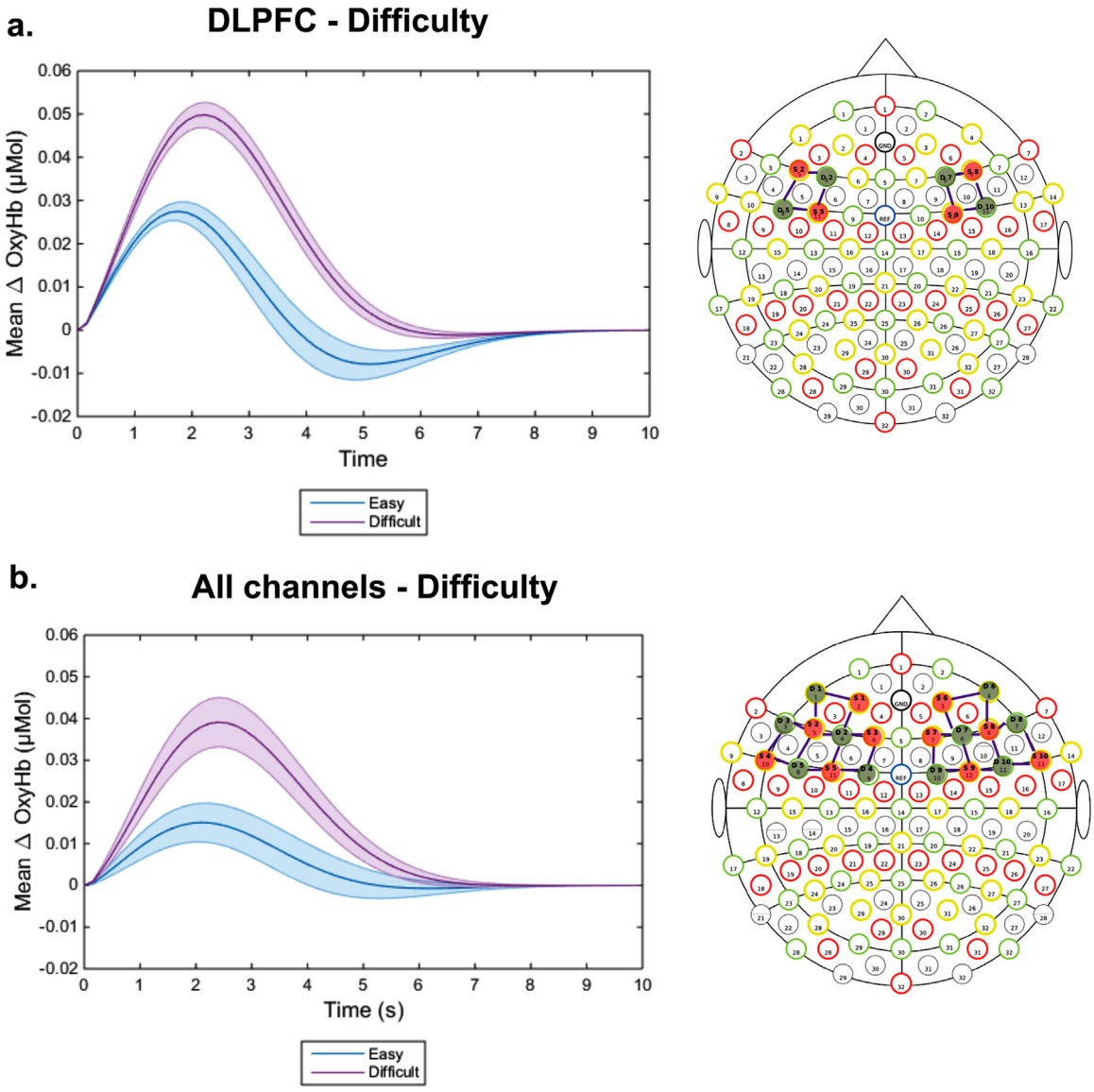

Fig. 3. DLPFC fNIRS results. a. Cortical hemodynamic response of OxyHb within the DLPFC ROI (shown at the top right) time-locked with cue-onset (during task preparation) for easy (blue line) and difficult (pink line) trials. Shades around the lines represent ± standard error of the mean. b. Cortical hemodynamic response of OxyHb averaged over all channels (shown at the bottom right), time-locked with cue-onset (during task preparation) for easy (blue) and difficult (pink) trials. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

scale from the BIS-BAS questionnaire, to target potential effects of incentive motivation. The third and fourth covariates were the average differences in mood before and after the experiment, measured with the PANAS positive and PANAS negative affect scales. The goal of this procedure was to test for additional influences of state and trait individual differences on DLPFC response to difficulty.

Next, two more complex models were created by expanding the benchmark model with one of the fixed effects for Difficulty (Easy vs Difficult), or Hemisphere (Left vs Right). Each expanded model was compared to the benchmark model using a likelihood ratio test (significance level of .05). We introduced the factor Hemisphere to test whether preparation-related activity in PFC would be uni- or bilateral.

In the second step, a new benchmark model was constructed by including the random effects of the original benchmark model, plus each statistically significant fixed effect from the first step, plus the covariates. This benchmark model was then compared to the same model plus the two-way interaction effect. The significance of the interaction of each covariate with the main effect of difficulty was also tested against the benchmark model.

As a control, all analyses were repeated again with the first benchmark model including only a random intercept for participant (thus without nesting channels within participants). This control analysis returned very similar results and therefore will not be reported.

Finally, in order to further explore brain-behavior relationships we correlated the average differences in behavioral performance (RTs and accuracy) with average differences in peak OxyHb within the DLPFC ROI (difficult – easy condition).

4. Results

4.1. Behavioral results

Prior to analysis, RTs were log-transformed. In line with previous reports, participants responded faster to easy trials than to hard trials ($t_{(18)} = -6.47$, $p < .001$, mean difference $-.13$). Responses to easy trials were also more accurate than to hard trials ($t_{(18)} = 6.73$, $p < 0001$, mean difference .14), confirming successful manipulation of task difficulty.

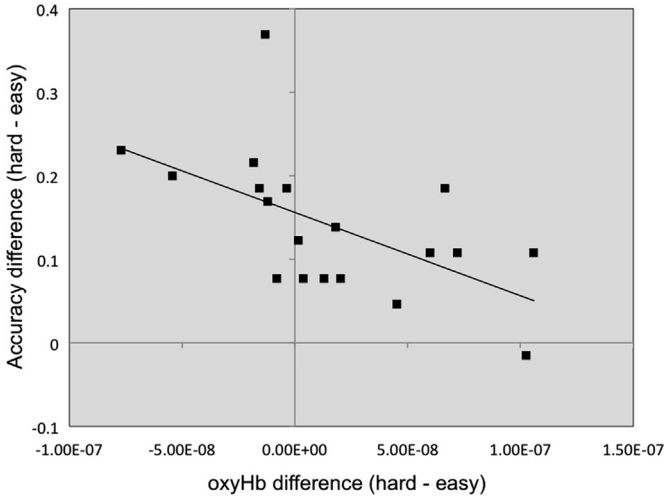

Fig. 4. Correlation between difficulty anticipation in DLPFC and performance accuracy. The x axis shows average differences in oxyHb peak in the hard – easy condition per each participant. The y axis shows differences in performance accuracy (hard – easy). Participants with larger DLPFC difficulty effect showed a smaller difference in accuracy for hard vs. easy trials.

Next we analyzed the ratings about task difficulty and liking, given during the training. Participants judged hard trials as more difficult ($t_{(18)} = 2.31$, $p = .03$). Participants who found hard trials more difficult also liked the easy trials more ($r = .51$, $p = .03$), and showed larger RT differences between hard and easy trials performance ($r = .53$, $p = .02$). Participants who liked easy trials more, also like hard trials less ($r = -.74$, $p < .001$). Participants who liked hard trials more, also found hard trials less difficult ($r = -.45$, $p = .05$). A larger difference in liking ratings between hard and easy trials was associated with smaller difference in RT ($r = -.50$, $p < .04$). A larger difference in difficulty ratings between hard and easy trials was associated with a larger difference in RTs ($r = -.46$, $p = .05$). No significant difference was found in the liking ratings (how much participants reported to like the easy as compared to the hard trials).

Next, we computed the results of the PANAS questionnaire, which was administered before and after the task to check participants' affective state. Both positive ($t_{(18)} = 6.43$, $p < .001$) and negative affect scores ($t_{(18)} = 3.29$, $p = .004$) were significantly lower after the task (possibly due to the long duration of the experiment, which lasted about an hour including set up time and task performance time). Subsequently, we performed an exploratory correlation analysis, correlating the difference between hard and easy condition in RTs and Accuracy with the difference in affective state pre- and post-task (both for negative and positive PANAS). Difference in PANAS-negative scores was larger for participants with higher BIS scores ($r = -.54$, $p = .02$). Larger accuracy difference (hard – easy) was associated with larger difference in PANAS-negative scores ($r = .46$, $p = .05$). No other significant correlations were observed. Performance also did not correlate with other questionnaires measures.

4.2. fNIRS main results

Statistical significance of the results was assessed by likelihood ratio testing. χ^2 and p-values refer to comparisons between the benchmark model and the same model plus the fixed effect or interaction of interest. As the model residuals were right-skewed, a square root transformation was applied to the OxyHb.

The main analysis targeted the effect of task difficulty in the DLPFC-ROI, controlling for average RT difference. As hypothesized, the results revealed a main effect of difficulty ($\chi2(1) = 6.57$, $p = .01$, see Fig. 3a). Specifically, the average OxyHb peak was higher in the hard condition than in the easy condition (Fig. 3). No main effect of hemisphere was observed (Hemisphere: $\chi^2(1) = .07$, $p = .79$). No Difficulty × Hemisphere interaction was observed ($\chi^2(2) = .15$, $p = .93$). The Difficulty × RT interaction was also not significant ($\chi^2(1) = 1.17$, $p = .28$). The Difficulty × reward responsivity interaction did not reach significance ($\chi^2(1) = .23$ $p = .63$), failing to provide evidence for a modulation of individual differences in reward sensitivity (at least as measured by the reward responsivity scale of the BIS-BAS questionnaire). No significant interaction with positive mood was observed (Difficulty × PANAS positive $\chi^2(1) = .05$, $p = .82$). A marginally significant interaction was observed for negative mood (Difficulty × PANAS negative ($\chi^2(1) = 4.06$, $p = .04$)). This was driven by a steeper decrease in negative affect post-experiment in participants showing a smaller difficulty effect in DLPFC ($R^2 = .12$). However, this was the only significant relationship between measures of mood and personality with peak oxyHb, which warrants caution for any interpretation.

Next, we performed the same analysis pipeline on the signal averaged across all channels (whole montage, see Fig. 3b). This analysis revealed a main effect of Difficulty, ($\chi^2(1) = 20.58$, $p < .01$), and no effect of Hemisphere ($\chi^2(1) = .88$, $p = .35$). The Difficulty × Hemisphere interaction was not significant ($\chi^2(2) = 2.77$, $p = .25$). The Difficulty × RT interaction was also not significant ($\chi^2(1) = 2.32$, $p = .13$). Finally, no significant interaction of Difficulty with reward responsivity was observed ($\chi^2(1) = .06$, $p = .81$, nor with positive (Difficulty × PANAS positive $\chi^2(1) = .06$, $p = .80$) or negative mood (Difficulty × PANAS negative $\chi^2(1) = 2.61$, $p = .11$).

Next, we correlated the difficulty effect on the oxyHb peak within the DLPFC ROI (hard > easy) with difference scores of accuracy and RTs. Difference between oxyHb peaks for hard vs. easy trials correlated with differences in accuracy: a larger oxyHb difficulty effect was associated with smaller differences in accuracy ($r = -.57$, $p = .01$. Fig. 4).

Larger oxyHb difficulty effect was also associated with larger differences in liking ratings (between easy and hard, $r = .49$, $p = .03$). Interestingly, participants who liked hard trials more than easy trials also showed a larger DLPFC difficulty effect, potentially reflecting increased interest and engagement in the task. To further explore brain-behavior relationships, we performed the same correlations on the latency of oxyHb response (rather than the peak). Only one significant correlation was observed, between the difficulty effect (latency of oxyHb peak in DLPFC in the hard – easy trials) and the reward responsivity scale of the BIS BAS. Larger difference in latencies was associated with reduced reward responsivity ($r = -.47$, $p = .04$). In participants with lower reward responsivity, the latency of oxyHb response for hard trials was longer.

Finally, for completeness, in Fig. 5 we plot cortical hemodynamic responses for all channels across the whole montage, showing OxyHb, DeoxyHb and total Hb in the hard (Fig. 5a) and easy condition (Fig. 5b), with the light yellow circles delimiting the DLPFC ROI channels. Visual inspection of the signal in the hard condition reveals larger oxyHb peaks in the fronto-lateral channels (including the DLPFC-ROI channels, but also the channels rostral to the ROI), as compared to the fronto-medial and the lateral channels (partially covering frontopolar and temporal regions). Interestingly, in the easy condition, large oxyHb peaks are mainly to be observed in the left hemisphere channels, as compared to the right hemisphere channels in the same condition, potentially suggesting that while these frontal regions are involved in task-preparation in general, anticipation of a difficult task recruits those cortices bilaterally. These speculative interpretations should be investigated in further research.

4.3. fNIRS exploratory results

Previous studies suggest that handedness may interact with functional lateralization: for lateralized cognitive functions, left-reversed laterality occurs more often left-handers (for example, left-handers are

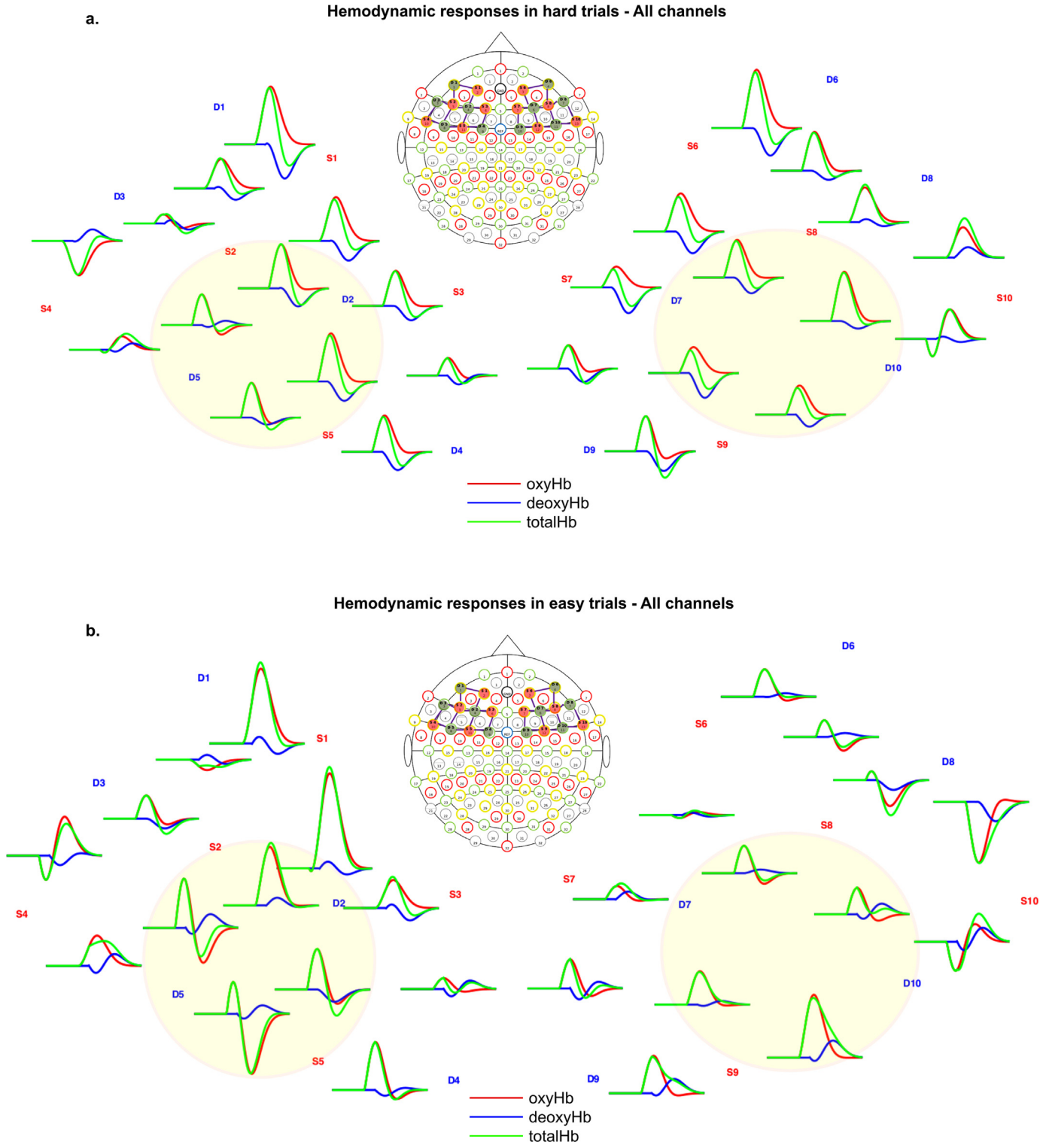

Fig. 5. Hemodynamic responses for all channels separately. a. OxyHb (red), DeoxyHb (blue) and total Hb (green) time-locked with cue onset in the hard trials. b. OxyHb (red), DeoxyHb (blue) and total Hb (green) time-locked with cue onset in the easy trials. In both panels the whole montage is shown. The yellow circles highlight the DLPFC-ROI channels. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

20% more likely to demonstrate right hemisphere dominance for language compared to right-handers, Carey and Johnstone, 2014, Mazoyer et al., 2014, Frässle et al., 2016). To test for this possibility, we performed an additional exploratory analysis adding self-reported handedness as a factor to the MLM model, with DLPFC OxyHb as dependent variable. In this analysis, the main effect of Handedness was marginally significant ($\chi2(1) = 4.1$, $p = .04$). No significant Difficulty × Handedness interaction was observed ($\chi2(4) = .49$, $p = .49$). The Handedness × Hemisphere interaction was marginally significant ($\chi2(2) = 5.67$, $p = .06$). Interestingly, the 3-way interaction Difficulty × Handedness × Hemisphere was significant ($\chi2(3) = 12.53$, $p < .01$), indicating a possible lateralization of the difficulty effect in DLPFC as a function of handedness. However, one should be careful in interpreting these results, as the analysis was exploratory, and the

design was not optimized for this research question, as the sample size in each handedness group was too small. The hypothesis that anticipation of difficulty may be lateralized as a function of handedness should be investigated in future studies, using continuous scales for a more sensitive index of handedness in combination with an appropriately powered design.

5. Discussion

This study investigated the role of DLPFC during anticipation of a mentally effortful task. Our results revealed increased DLPFC when anticipating a difficult task (a harder arithmetic problem), as compared to an easier one. These results confirm a contribution of DLPFC to anticipation of difficulty, as suggested by a previous fMRI study (Vassena et al., 2014), and establish optical imaging with fNIRS as a non-invasive and cost-effective tool to investigate the role of DLPFC this process.

Growing neuroimaging evidence shows that preparing for mentally demanding tasks is associated with activity in medial PFC, especially dorsal ACC (e.g., Parvizi et al., 2013; Vassena et al., 2014). Some studies suggest a crucial contribution of DLPFC to this process as well. For example, Vassena et al. (2014) and Sohn et al. (Sohn et al., 2007) found an effect of task preparation prior to performing hard trials in DLPFC. McGuire & Botvinick (McGuire and Botvinick, 2010) observed that MFC correlated with errors and RTs, but only DLPFC correlated with avoidance ratings when performance (errors and RT) were factored out, suggesting a more general role in strategic preparation. The present results confirm a role of DLPFC in anticipating difficulty. The mechanism underlying such contribution may involve preparation for effort exertion (i.e. allocation of task-related attentional resources, Brown and Alexander, 2017; Verguts et al., 2015), or simply the prediction of the nature of the upcoming task (i.e., is it difficult or not, (Vassena et al., 2017a)). Another possibility is that DLPFC may predict other variables related to task difficulty, such as increased error likelihood (Brown and Braver, 2005) or time-on-task (Grinband et al., 2011). However, these models predict these effects in the dACC rather than DLPFC. In our data, we did not find evidence of a relationship between RT and DLPFC activity, while larger difficulty-related activity in DLPFC was associated with smaller differences in accuracy, potentially suggesting a role of DLPFC-driven top-down control on performance.

Previous fNIRS studies have also investigated DLPFC contribution to several cognitive processes, such as word-encoding in a memory task (Ferreri et al., 2014), inhibitory control in drug users (Roberts and Montgomery, 2015), dual motor and cognitive task-performance (Mandrick et al., 2013). Relevant to the current results, two studies targeted hemodynamic responses in DLPFC in effortful tasks, specifically testing the effect of varying mental load in a working memory task (Molteni et al., 2012), and comparing laboratory measures of load (executive function task) with real-life effort (operating a flight-simulator, Causse et al., 2017). Both studies confirm a PFC contribution to the process. However, in both cases hemodynamic changes were measured *during* task performance, and not during task preparation as in our case. Interestingly, Causse and colleagues found no effects of performance on DLPFC activity, and conclude that this region may play a motivational role in sustaining effort exertion, rather than affecting task performance. Finally, a few studies also investigated the potential of fNIRS signal decoding in PFC as a Brain-Computer Interface, showing reliable decoding of brain activity during mental arithmetic as compared to rest (Bauernfeind et al., 2014; Herff et al., 2013).

The results of the current study thus relate to previous fNIRS evidence on DLPFC involvement during effortful tasks, showing for the first time with fNIRS a clear contribution of DLPFC to anticipation of a difficult cognitive task. Furthermore, they confirm DLPFC involvement as hypothesized on the basis of previous fMRI studies measuring BOLD response to cognitive demand. The BOLD signal is a compound measure, which depends on cerebral blood flow, cerebral blood volume and oxygen metabolism, and in particular oxygenated and deoxygenated hemoglobin ratio. fNIRS measures the changes in oxygen metabolism, a sub-component of the BOLD signal (Buxton, 2013), which in turn can be dissected in oxyHb, deoxyHb, or total Hb. Which of these measure better correlates with BOLD signal seems to be task-dependent (Scarapicchia et al., 2017), and in particular oxyHb seems to be the best index in the context of a cognitive task, as indicated by our results as well. Our results corroborate this link, and suggest oxyHb measured with fNIRS over DLPFC as reliable measure of difficulty anticipation.

Finally, it is important to highlight a few limitations of this study. First, the fNIRS montage used to measured cortical hemodynamics included only frontal channels. Although a similar approach has been adopted in several other studies (Bembich et al., 2014; Ernst et al., 2013; Laguë-Beauvais et al., 2013), other areas must be targeted in future work. In particular parietal cortex has often been found to be co-activated with DLPFC, including during preparation for mental effort (e.g., Boehler et al., 2011). Several studies suggest that DLPFC and parietal cortex form the fronto-parietal network (Dosenbach et al., 2008), implicated in attentional and top-down control, goal-directed behavior and translation of instruction to action (Buschman and Miller, 2007; Farooqui et al., 2012; Hartstra et al., 2012; Muhle-Karbe et al., 2017). On a related note, future studies with the possibility of larger montages should include a functionally dissociable control region. Given our strong a-priori hypothesis, we focused on DLPFC. However, it would be important for future research to investigate the specificity of DLPFC involvement during task preparation, by simultaneously testing regions that should not contribute to the effect, such as the vertex, as typically done when using other modalities (for example neurostimulation).

A second limitation is that the fNIRS technology only allows recording cortical activity; deeper regions such as dACC or subcortical structures cannot be targeted. The contribution of these regions to anticipation of difficulty and mental effort preparation has been reliably observed with fMRI (Kurniawan et al., 2013; Vassena et al., 2014), but cannot be addressed with fNIRS.

Third, in contrast to our fMRI study (Vassena et al., 2014), in this fNIRS study we did not manipulate incentive motivation by delivering rewards of different magnitudes for correct task performance. As a first attempt to validate fNIRS to measure DLPFC contribution to difficulty anticipation, we adopted a simple approach, manipulating only task difficulty, to ensure sufficient data per each design cell. Furthermore, in our fMRI study we did not observe DLPFC involvement for reward anticipation. However, other previous studies did observe modulation of DLPFC activity as a function of reward prospect (Bahlmann et al., 2015; Kouneiher et al., 2009). Therefore, future research should advance these results, by manipulating both anticipated difficulty and reward prospect. On a related note, while the current design provided sufficient power to detect the main effect of interest (i.e., anticipation of difficulty), the interaction with handedness and laterality, and the modulation of reward responsivity (from the BIS BAS questionnaire) should be further tested in a larger sample (as the failure to observe significant effects may be attributed to lack of power).

Finally, future designs should disentangle the mechanism underlying DLPFC contribution to anticipation of difficulty, referring to available computational models of PFC function, which attempt to describe the role of this region to task performance in a mechanistic fashion (Alexander et al., 2017; Koechlin, 2016). Future theorizing efforts should also consider the relative contribution of DLPFC, as opposed to dACC (Vassena et al., 2017b) to develop novel frameworks able to describe the interaction between the two regions (Domenech et al., 2017; Kerns et al., 2004).

The conclusion that DLPFC activation is measurable via fNIRS opens up several avenues for research, given the portability and low price of fNIRS setups. In particular, it allows measurement while engaged in (or preparing for) active tasks, which is not possible with standard (e.g., EEG, fMRI) measurement protocols. This is especially of potential relevance in physical effort tasks, in which movement seems almost by

definition required, for example in the emergent field of sport psychology.

Another group of studies in which fMRI protocols are problematic, and hence fNIRS is an interesting alternative, are those where measurement time is necessarily long, either because a single session is long (e.g., studies on fatigue; Wang et al., 2016) or because several sessions must be administered (e.g., studies on learning or memory). For example, concerning fatigue, (Wang et al., 2016) conducted a Stroop task for 160 min using EEG. They observed an anterior-frontal ERP that increased during the first 80 min of test-taking; during that period, accuracy remained approximately constant. However, as soon as the ERP dropped (after 80 min on the task), also accuracy dropped. They thus interpreted the frontal ERP as a "compensation" signal, reflecting the investment of cognitive effort to maintain task performance at an acceptable level (around 10% errors). fNIRS could be fruitfully used to investigate the spatial localization of this component more precisely. fNIRS also opens up interesting possibilities for studies that require large groups. Examples include between-subject designs, studies on individual differences, or studies where effect sizes are expected to be small. Due to the cost of a single MRI scan, such large-group studies are typically not possible in fMRI. Thus, fNIRS might provide an opportunity to better control Type-I and Type-II errors in neuroimaging (Button et al., 2013). Finally, fNIRS also allows testing in subjects with contra-indications for fMRI (e.g., pregnancy, non-removable ferro-magnetic implants, or pacemakers, children). Based on our findings, one could investigate the development of the difficulty effect in children across the life-span. Finally, one could investigate anticipation of effortful behavior in populations that show clinically impaired motivation and effort exertion.

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Conflict of interests statement

The authors have no competing interests to declare.

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