

# Brain Topography

## Applications of functional near-infrared spectroscopy in fatigue, sleep deprivation, and social cognition --Manuscript Draft--

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<b>Abstract:</b>	<p>Functional near-infrared spectroscopy (fNIRS) is an optical diffusion technique that allows the non-invasive imaging of cortical activity. During the last two decades, rapid technical and methodological advances have made fNIRS a powerful tool to investigate the cerebral correlates of human performance and cognitive functions, including fatigue, sleep deprivation and social cognition. Despite intrinsic limitations such as restricted brain depth and spatial resolution, its applicability, low cost, ecological validity, and tolerance to movements make fNIRS advantageous for scientific research and clinical applications. It can be viewed as a valid and promising brain imaging approach to investigate applied societal problems (e.g., safety, children development, sport science) and complement other neuroimaging techniques. The intrinsic power of fNIRS measurements for the study of social cognition is magnified when applied to the hyperscanning paradigm (i.e., measuring activity in two or more brains simultaneously). Besides consolidating existing findings, future fNIRS research should focus on methodological advances (e.g., artefacts correction, connectivity approaches) and standardization of analysis pipelines, and expand currently used paradigms in more naturalistic but controlled settings.</p>	

## Response to Reviewers

We wish to thank the editor and the reviewer for their positive appreciation of our review paper, as well as for their insightful comments and constructive suggestions concerning our manuscript (**BTOP-D-19-00084**). The manuscript has been revised accordingly (the novel/changed parts are highlighted in bold). In what follows, we respond to all the reviewers' points.

*This is a well-written overview of the current state of brain imaging using fNIRS. It discusses the limitations of the technique in a comprehensive way before showing applications where the main advantage (portability) is demonstrated in different fields. I consider the paper well balanced with an exhaustive literature review that guides the interested reader to the relevant studies in the different fields of application. I have a very few minor comments:*

*1. Page 16: the increasing use of combined EEG fNIRS is mentioned. I recommend to add some sentences about the use of this combination in hybrid brain-computer interfaces to increase classification accuracy.*

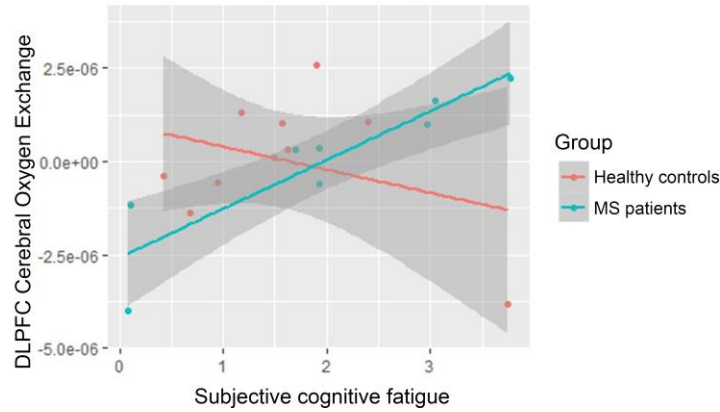
**Response:** We have added several sentences about the use of EEG-fNIRS combination in hybrid BCIs to increase classification accuracy (**pp. 16-17**).

**“Also, hybrid BCI based on simultaneous fNIRS-EEG measurements was shown to significantly improve classification accuracy in auditory and visual perception (Putze et al., 2014), executed movements (Khan et al., 2014) and motor imagery (Fazli et al., 2012; Yin et al., 2015) paradigms.”**

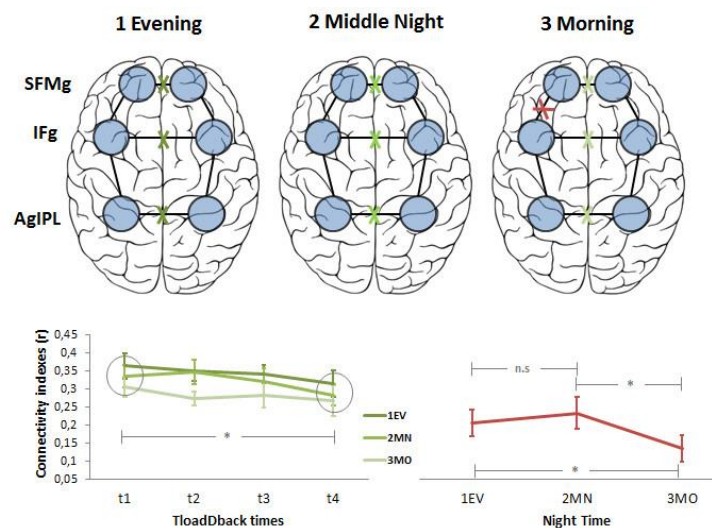
*2. Page 17: I recommend to add an illustration about fNIRS results in MS. Maybe a figure from the work of one of the co-authors (Borrogan et al., 2018a). Likewise, a figure on the effects of sleep deprivation (for example from Borrogan et al., 2019) could be added.*

**Response:** We have added one figure about fNIRS results in Multiple Sclerosis (MS,

**Fig. 4)** and one about the effects of sleep deprivation (**Fig. 5**) as the reviewer suggested.



**Fig. 4.** Association between subjective cognitive fatigue (CF) and dorsolateral prefrontal cortex (DLPFC) Cerebral Oxygen Exchange index. Results disclose a direct relationship, present only in patients with Multiple Sclerosis (MS), between DLPFC Cerebral Oxygen Exchange and the triggering of subjective CF under cognitively demanding conditions. Note that higher Cerebral Oxygen Exchange values denote lower brain activity level (see Borragán et al., 2018 for more details).



**Fig. 5.** Intra- and inter-hemispheric connectivity changes following sleep deprivation. Blue circles indicate the regions of interest where activity was recorded using fNIRS (reproduced from Borragán et al., 2019). Green Xs indicate inter-hemispheric connections in which connectivity decreased from the beginning (t1) to the end (t4) of TloadDback practice (bottom right panel)

during the 3 sessions. Red Xs indicates the intra- hemispheric connection (on the left Superior/Middle Frontal gyrus - Inferior Frontal gyrus) in which connectivity decreased in the morning (3MO) session as compared to the evening (1EV) and middle night (2MN) sessions. Brain connectivity changes might reflect a higher cost of resource consumption when sleep pressure is high. In the cited experiment (for details, see Borragán et al., 2019), performance is readjusted at a lower rate when activity in the left Frontal gyrus starts being desynchronized in the morning as a result of extended sleep deprivation.

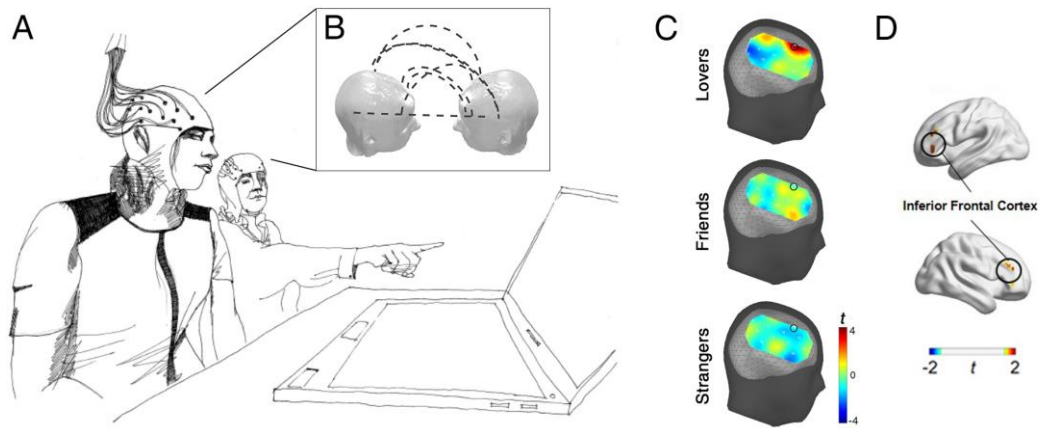
3. *Page 22: Hyperscanning. The problem of the ground/reference in EEG hyperscanning has been discussed and solved in previous literature. I recommend to look at the work of Laura Astolfi in this respect.*

**Response:** Thanks for pointing this out. Following the reviewer’s comment, we checked Laura Astolfi’s work; and acknowledge that the problem of the ground/reference in EEG hyperscanning has been previously discussed and solved. Consequently, we have removed this sentence from page 22.

“Indeed, since fNIRS detectors are individually coupled with a nearby light source and we measure variations in light diffusion over these areas, there is no need to bother with ~~a common ground/reference problem (like with EEG)~~ or coupling two heavy and distant installations (like with fMRI, MEG).”

4. *I recommend to add an illustration of fNIRS hyperscanning results. Maybe from the different studies of the first author.*

**Response:** We have added an illustration of fNIRS hyperscanning results (**Fig. 6**) as the reviewer suggested.



**Fig. 6.** (A) Representative illustration of a fNIRS-based hyperscanning experimental scenario. A teacher is transmitting knowledge to a student, during which their brain activity is recorded by fNIRS simultaneously (Pan et al., 2019). (B) Interpersonal brain synchronization (IBS) emerges as a result of learning interactions within the teacher-student dyad. (C) Maps of IBS in lover-, friend-, and stranger-dyads during a cooperation task (adapted from Pan et al., 2017). Compared to friend- and stranger-dyads, lover-dyads show significantly higher IBS in the superior frontal cortex. (D) Maps of IBS in instructor-learner dyads during a song learning task (adapted from Pan et al., 2018). Interpersonal synchronization of inferior frontal cortices tracks the song learning process.

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1 Running Title: APPLICATIONS OF FUNCTIONAL NEAR-INFRARED  
2 SPECTROSCOPY  
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7 **Applications of functional near-infrared spectroscopy in fatigue, sleep**  
8 **deprivation, and social cognition**  
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30 **Author contributions**  
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32 Y. P., G. B., and P. P. wrote the manuscript.  
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36 **Competing interests**  
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38 The authors declare that they have no actual or potential conflicts of interest  
39 concerning this work.  
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1 **Abstract**

2 Functional near-infrared spectroscopy (fNIRS) is an optical diffusion technique that  
3 allows the non-invasive imaging of cortical activity. During the last two decades,  
4 rapid technical and methodological advances have made fNIRS a powerful tool to  
5 investigate the cerebral correlates of human performance and cognitive functions,  
6 including fatigue, sleep deprivation and social cognition. Despite intrinsic limitations  
7 such as restricted brain depth and spatial resolution, its applicability, low cost,  
8 ecological validity, and tolerance to movements make fNIRS advantageous for  
9 scientific research and clinical applications. It can be viewed as a valid and promising  
10 brain imaging approach to investigate applied societal problems (e.g., safety, children  
11 development, sport science) and complement other neuroimaging techniques. The  
12 intrinsic power of fNIRS measurements for the study of social cognition is magnified  
13 when applied to the hyperscanning paradigm (i.e., measuring activity in two or more  
14 brains simultaneously). Besides consolidating existing findings, future fNIRS research  
15 should focus on methodological advances (e.g., artefacts correction, connectivity  
16 approaches) and standardization of analysis pipelines, and expand currently used  
17 paradigms in more naturalistic but controlled settings.

18 **Keywords:** Functional near-infrared spectroscopy (fNIRS), fatigue, sleep deprivation,  
19 social cognition, hyperscanning, fNIRS application

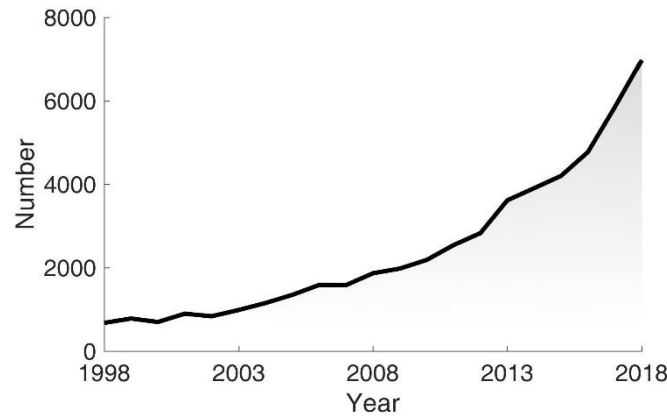
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## 20 1. Introduction

21 Functional near-infrared spectroscopy (fNIRS) is an optical diffusion technique that  
22 allows the non-invasive imaging of cortical activity. Optical diffusion was initially  
23 developed by Jöbsis in 1977, who reported that continuous near infrared light  
24 non-invasively allows the real-time detection of haemoglobin (Hb) levels in the brain  
25 of neonates. In a nutshell, modern fNIRS systems use a system of sources emitting  
26 infrared light at constant frequency and amplitude, coupled with detectors that receive  
27 the light scattered by the intermediate brain tissues. Applying the Modified Beer  
28 Lambert Law (MBLL) allows then to relate light intensity changes to variations in  
29 brain activity (Villringer and Chance, 1997).

30 Within the last two decades, an increasing number of empirical studies used  
31 fNIRS imaging to study the brain mechanisms underlying various cognitive functions  
32 (**Fig. 1**). fNIRS can be advantageous due to a combination of easy applicability, low  
33 cost, sensible temporal resolution, ecological validity and free restraint (i.e., relative  
34 tolerance to movements) (Ehllis et al., 2014). Considering its versatility, fNIRS can be  
35 a good neuroimaging option and bring benefits for studies investigating human  
36 performance in altered conditions such as fatigue and sleep deprivation, as well as for  
37 the study of social cognition, in particular when used in a hyperscanning context (i.e.,  
38 measuring two or more brains simultaneously; Cui et al., 2012; Pan et al., 2017, 2018).  
39 In the present review, we will first provide a brief overview of the principles of fNIRS  
40 with its assets and caveats. We will then focus on fNIRS studies in two main domains.  
41 One, the effects and cortical correlates of fatigue and sleep deprivation. Second, the  
42 neural bases of social cognition and interpersonal relationships using fNIRS and  
43 hyperscanning. Finally, we will discuss current challenges and future prospects of  
44 application for fNIRS.





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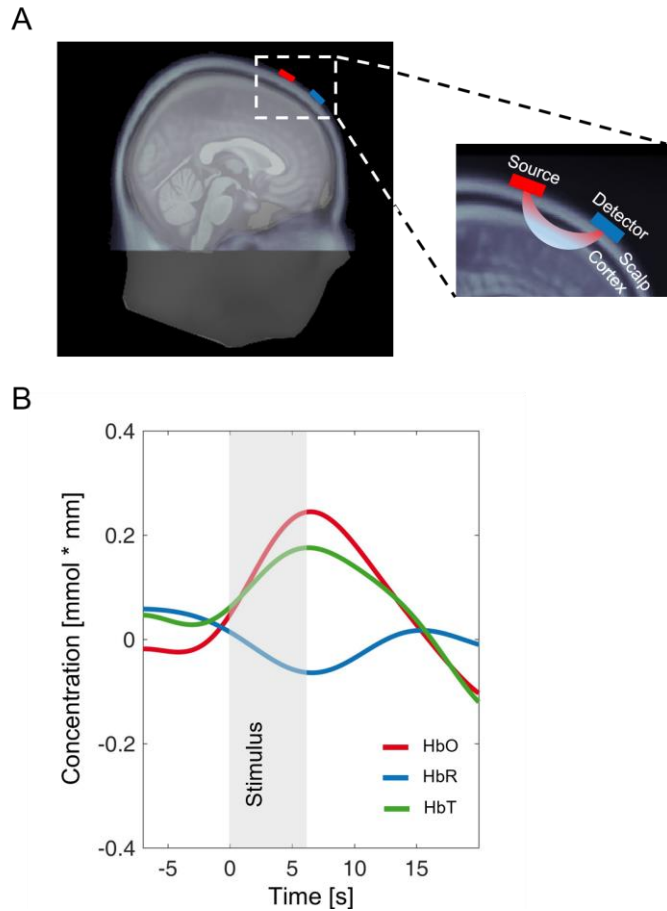
46 **Fig. 1.** Yearly evolution in the number of published fNIRS research articles within the last two decades.  
 47 Data extracted from ScienceDirect (<https://www.sciencedirect.com/>) in May 2019 by performing a  
 48 search using the term “functional near-infrared spectroscopy” as a primary keyword.

49 **1.1. What is functional near-infrared spectroscopy (fNIRS)?**

50 Functional NIRS takes advantage of the diffusion properties of near-infrared light  
 51 through brain tissues to allow the non-invasive and continuous measurement of local  
 52 oxygen-dependent metabolism. Blood oxygen level-dependent (BOLD) changes can  
 53 be quantified looking at the oxidation state of blood haemoglobin. Neuronal activity  
 54 and blood oxygenation changes are interlinked as follows (Scholkmann et al., 2014).  
 55 First, local brain activation causes increased regional metabolism and oxygen  
 56 demands by neurons (i.e., neurometabolic coupling). In a next step, increased oxygen  
 57 consumption induces increased regional cerebral blood flow and volume (i.e.,  
 58 neurovascular coupling). Unlike functional magnetic resonance imaging (fMRI) that  
 59 tracks (de)oxygenation-related changes in blood magnetization to infer variations in  
 60 the BOLD signal, functional NIRS allows the quantitative and separate monitoring of  
 61 both oxy-haemoglobin (HbO) and deoxy-haemoglobin (HbR) levels by detecting  
 62 variations from the source to the detector in specific near-infrared light wavelengths.  
 63 During this process, the near-infrared light emitted from the probe penetrates and  
 64 diffuse into the brain tissues following a characteristic banana-shaped path (**Fig. 2A**).  
 65 Like functional magnetic resonance imaging (fMRI), fNIRS is an indirect measure of

1 66 neuronal activity, with the peak of the hemodynamic response delayed by  
2 67 approximately 5-10 seconds (Ferrari and Quaresima, 2012). Besides measurements of  
3  
4 68 brain activity, the same principle of near infrared light diffusion can be used in other  
5  
6 69 domains, e.g. in motor sciences to assess oxygenation levels in muscle tissues  
7  
8 70 (Volkening et al., 2016).

10 71 As mentioned above, the fNIRS signal can be split into separate HbO and HbR  
11  
12 72 concentrations (**Fig. 2B**). Based on the MBLL, HbO and HbR can be reflected by the  
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14 73 attenuation of specific near-infrared light wavelengths due to absorption changes.  
15  
16 74 Theoretically, these two metrics should be negatively correlated with each other (Cui  
17  
18 75 et al., 2010a) as HbO decreases when HbR increases, and vice versa, but this is not  
19  
20 76 always true in practice for various reasons (see Guerrero-Mosquera et al., 2016;  
21  
22 77 Yamamoto and Kato, 2002; Yuan and Ye, 2013). Focal increase in HbO, along with  
23  
24 78 decreased HbR, is interpreted as a marker of regional brain activation (Fox and  
25  
26 79 Raichle, 1986). The major cause of decreased HbR in venous blood is that the rate of  
27  
28 80 regional cerebral blood flow increase exceeds that of the regional cerebral oxygen  
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30 81 metabolic rate (Sitaram et al., 2009).



82

83 **Fig. 2.** (A) Illustration of the banana-shaped path followed by the NIRS light from source to detector.

84 (B) A representative fNIRS response. The local brain activation is reflected by a decrease in HbR

85 concentration, alongside an increase in HbO concentration. HbT corresponds to the sum of HbO and

86 HbR changes. Note that the peak haemoglobin signal can be observed with a latency of approximately

87 5 – 10 seconds after the onset of a stimulus.

88 It has been argued that global/systemic effects such as heart rate, blood pressure,

89 and respiratory activity influence more HbO, whereas the venous compartment would

90 mostly influence HbR (e.g., Hirsch et al., 2017). HbR has been found principally

91 associated with neurovascular coupling. It exhibits better spatial precision related to

92 neuronal-specific brain activity and fewer confounds from signals due to

93 non-neuronal origins (Hirsch et al., 2017). Thus, HbR was reported to represent a

94 better-defined brain activation than HbO (Kirilina et al., 2012). Compared to HbR,

95 HbO changes typically induce larger amplitudes and involve more widespread brain

1 96 regions. As such, other researchers proposed that in fNIRS measurements, HbO  
2 97 concentration actually is the most sensitive physiological marker of changes in the  
3 98 regional cerebral blood flow (Hoshi, 2007). Whereas functional cortical activity is  
4 99 largely monitored and recorded, non-neuronal brain activity and global/systemic  
5 100 effects can be mitigated via data preprocessing (Zhang et al., 2018; see details in the  
6 101 next section). Therefore, HbO concentrations could feature a high signal-to-noise ratio  
7 102 (Liu et al., 2017). HbO and HbR responses elicited by stimuli can also be determined  
8 103 by assessing the mean activation within a determined window (Watanabe et al., 2008).  
9 104 Another possible indicator of brain activity as assessed by fNIRS is total haemoglobin  
10 105 (HbT, e.g., Nozawa et al., 2016). HbT corresponds to the sum of changes in HbO and  
11 106 HbR, and is thus largely dominated by HbO changes. It was shown that HbT is less  
12 107 sensitive to venous contamination. Consequently, it might provide better spatial  
13 108 specificity than separate HbO and HbR concentrations (Gagnon et al., 2012).  
14 109 Moreover, HbT changes represent changes in blood volume and are related to changes  
15 110 in blood flow (Grubb et al., 1974). Notwithstanding, including both HbO and HbR  
16 111 measures in fNIRS data analyses is certainly useful to obtain a full picture of the  
17 112 underlying brain mechanisms. In this respect, Cerebral Oxygen Exchange (COE),  
18 113 computed as the difference between HbR and HbO, represents another useful  
19 114 indicator of cellular oxygen metabolism (Yoshino et al., 2013). COE indicators can  
20 115 also be generated from an oxyHb and deoxyHb orthogonal coordinate plane using a  
21 116 vector-based analysis perspective (for more details, see Yoshino and Kato, 2012).

22 117 Raw fNIRS signals based on HbO and HbR changes are typically non-stationary,  
23 118 and result from a combination of several components (Scholkmann et al., 2014). The  
24 119 first component is stimulus-/task-evoked neurovascular coupling, directly associated  
25 120 with functional brain activity. The second component is spontaneous neurovascular  
26 121 coupling; it is non-evoked and can be used, e.g., to assess the resting-state functional  
27 122 organization of the brain. Another component is undesired physiological/systemic  
28 123 interferences. These activities entail changes in blood pressure, skin blood  
29 124 flow/volume, heart rate (1 – 2 Hz), respiration (0.1 – 0.3 Hz), Mayer waves (~ 0.1 Hz),

1 125 and very low frequency oscillations ( $< 0.01$  Hz). To remove (or at least mitigate) the  
2 126 effects of these artefacts, several approaches have been proposed. Band-pass filtering  
3  
4 127 is one of the most commonly used methods to remove systemic physiology artefacts  
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6 128 such as cardiac, respiratory, and cardiovascular oscillations (e.g., Yanagisawa et al.,  
7  
8 129 2010). Conventional averaging of fNIRS signals time-locked to the stimuli is also a  
9  
10 130 valid option. Indeed, there is at least two main issues in the pre-processing of fNIRS  
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12 131 data: (1) separation between signal components and (2) correction of motion artefacts.  
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14 132 In order to separate the global (systemic) and local (neuronal) components in fNIRS  
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16 133 signals, Zhang et al. (2016) developed a principal component spatial filter algorithm.  
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18 134 This Gaussian spatial filtering approach significantly improved both temporal  
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20 135 waveforms and spatial pattern consistencies between HbO and HbR concentrations.  
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22 136 Although relatively tolerant to the participants' movements, fNIRS in naturalistic  
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24 137 experiments yet still faces the challenges from motion artefacts. To correct these  
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26 138 artefacts and improve signal quality, Cui et al. (2010a) proposed a  
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28 139 Correlation-Based-Signal-Improvement method based on the negative correlation  
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30 140 between HbO and HbR concentrations (see also Guerrero-Mosquera et al., 2016).  
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32 141 Other artefacts removal methods include discrete wavelet filtering (Molavi and  
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34 142 Dumont, 2012), sliding window motion artefact rejection (Ayaz et al., 2010) and  
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36 143 wavelet-based denoising (Duan et al., 2018). Apart from these univariate methods,  
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38 144 one can also consider multivariate approaches. For instance, one can use additional  
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40 145 channels with, e.g., 1.5-cm source-detector distance to identify and record part of the  
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42 146 global diffusion effects (from extra-cerebral tissue such as scalp and skull) to regress  
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44 147 them from the whole signals. In any case, technical advances concerning artefact  
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46 148 removal and signal quality improvement are still needed.

## 50 149 **1.2. Assets and drawbacks**

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55 150 Both fNIRS and fMRI measure BOLD variations, so why using fNIRS? As compared  
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57 151 to fMRI, fNIRS admittedly suffers specific limitations. The most prominent are  
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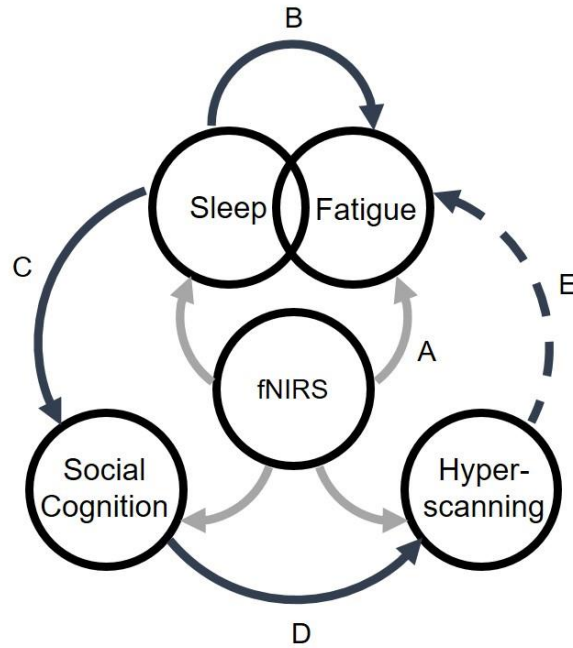
1 152 restricted spatial resolution and measuring brain depth, that limit measurements to the  
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3 153 cortical surface without access to subcortical structures, and the confounding  
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5 154 influence of extracranial signals and anatomical parameters. Regarding spatial  
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7 155 resolution, whereas fMRI can measure activity in the entire brain, fNIRS only monitor  
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9 156 and record cortical activations, penetration depth being 1.5 – 2 cm. This makes a  
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11 157 problem for fNIRS, as sub-cortical structures such as for instance the amygdala  
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13 158 reputedly playing a role in social cognition (Adolphs, 2010), are not detectable.  
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15 159 Furthermore, fNIRS optodes cannot cover the full brain surface at once, limiting to a  
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17 160 partial apprehension of functional activity and connectivity (Lu et al., 2010). This is  
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19 161 due to the fact that a single fNIRS instrument features a limited number of optodes,  
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21 162 but most importantly because the distance between source and detectors cannot be too  
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23 163 close (no diffusion in brain tissues, only skull or leakage effects) or too far away (bad  
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25 164 signal-to-noise ratio). The typical trade-off source-detector distance is 3 – 3.5 cm for  
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27 165 adults and 2 – 2.5 cm for infants. Overall differences in scalp and skulls thickness  
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29 166 between infants and adults (Brigadoi and Cooper, 2015) can explain these differences  
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31 167 in source-detector distance, along with the fact that signal quality is not homogenous  
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33 168 across different brain areas. Indeed, scalp thickness is more important in temporal  
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35 169 than in frontal and parieto-occipital regions (Brigadoi and Cooper, 2015). Besides,  
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37 170 inter-individual differences between participants' skull and scalp thickness may also  
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39 171 lead to dissimilar signal outputs, although it is rare that these differences impede  
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41 172 detecting differential changes in cortical oxygenation (e.g. between conditions in a  
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43 173 within-subject design). A common practice to optimize signal-to-noise ratio is to  
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45 174 determine in advance the regions of interest, and to position the measuring optodes  
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47 175 over these pre-determined regions only. Besides coverage limitation, fNIRS also  
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49 176 suffers from the confounding influence from some artefacts and physiological noises:  
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51 177 (1) artefacts associated with noises of instrumentation, improper optodes fixation and  
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53 178 excessive motion (e.g., body movements, head nodding, mouth opening and shutting,  
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1 179 swallowing); (2) physiological noise related to heartbeats, respiratory activities and  
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3 180 low-frequency fluctuations. Finally, fNIRS cannot obtain structural anatomical images,  
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5 181 something MRI can do.  
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7 182 Considering these drawbacks, what are the assets of fNIRS? First, fNIRS is  
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9 183 inexpensive to use while being able to study the mechanisms underlying the BOLD  
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11 184 signal better than fMRI. Indeed, fNIRS separately captures HbO and HbR changes  
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13 185 (whereas the fMRI BOLD signal results from the contrast between these two  
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15 186 parameters), which allow studying the relationships between these two haemoglobin  
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17 187 concentrations. Relatedly, in contrast to fMRI, fNIRS achieves a better temporal  
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19 188 resolution (e.g., 10-100 Hz) than fMRI, and provides a good option to investigate the  
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21 189 dynamics of the rise and fall of the BOLD signal. Its temporal resolution also makes  
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23 190 fNIRS a good option for real-time neurofeedback and brain computer interface  
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25 191 paradigms (Duan et al., 2013; Erdođan et al., 2019), and functional connectivity  
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27 192 analysis (Tak and Ye, 2014). Due to intrinsic limitations in hemodynamic  
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29 193 measurements, it can be argued that BOLD response as measured by fNIRS remains  
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31 194 quite slow (5 – 8 seconds to peak). Nevertheless, its finer temporal resolution allows  
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33 195 machine-learning algorithms to detect signals with much smaller delay than fMRI  
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35 196 (Cui et al., 2010b). But perhaps one crucial advantage of fNIRS is to allow measuring  
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37 197 cortical hemodynamics in naturalistic conditions (Quaresima and Ferrari, 2019). For  
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39 198 instance, fNIRS has been used to study cortical activity in real-life face-to-face  
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41 199 communication (e.g., Jiang et al., 2012), sports and exercise (e.g., Balardin et al.,  
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43 200 2017), driving (e.g., Liu et al., 2017), singing (e.g., Pan et al., 2018), teaching (e.g.,  
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45 201 Liu et al., 2019), and psychological counselling (e.g., Zhang et al., 2018). Also as  
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47 202 mentioned above, fNIRS is relatively tolerant to body movements as compared to  
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49 203 other motion-sensitive techniques (e.g., fMRI or EEG). This provides a split  
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51 204 advantage since in conventional laboratory studies, participants are often constrained  
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53 205 by experimental settings in which their mental and physical activity differs from real  
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1 206 daily life. To the contrary, modern, small and portable fNIRS equipments can be used  
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3 207 in unconstrained environments. Another asset of fNIRS is that it is quite easy to  
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5 208 combine with other techniques such as electroencephalography (EEG; Leamy et al.,  
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7 209 2011), transcranial Direct Current Stimulation (tDCS; Borragán et al., 2018b),  
8  
9 210 Transcranial Magnetic Stimulation (TMS; Kozel et al., 2009), fMRI (Heinzel et al.,  
10  
11 211 2013, or even magnetoencephalography (MEG; Huppert et al., 2017). Hence, fNIRS  
12  
13 212 is a good tool for a multi-modal imaging approach gathering high temporal, spatial  
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15 213 and frequency information related to neurovascular coupling. Last but not least, easy  
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17 214 applicability and high ecological validity make fNIRS particularly suitable for  
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19 215 studying special populations. Indeed, fMRI is not entirely user-friendly. Strictly  
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21 216 speaking, some persons are prevented to enter fMRI experiments for safety  
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23 217 considerations, or experience claustrophobia in the narrow MRI scanner environment.  
24  
25 218 Likewise, shrapnel and other metal parts in the body, electronic body implants  
26  
27 219 (hearing aids, pacemaker...) or pregnancy are exclusion criteria. In these cases and  
28  
29 220 others, fNIRS is advantageous to investigate hemodynamics within specific  
30  
31 221 populations. Altogether, these assets make fNIRS a promising approach to study the  
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33 222 neural mechanisms underlying human performance and cognitive functions. Hereafter,  
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35 223 we will describe and discuss the use of fNIRS to investigate neural hemodynamic  
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37 224 processes underlying applied societal problems such as fatigue, sleep deprivation and  
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39 225 social cognition (see **Fig. 3**), which are all crucial elements of human living.  
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227 **Fig. 3.** (A) The use of fNIRS in studies of fatigue, sleep deprivation, and social cognition and  
 228 combinability of fNIRS with the hyperscanning approach (i.e., measuring two brains  
 229 simultaneously, Pan et al., 2017, 2018). (B) Sleep deprivation and fatigue partially overlap: a  
 230 portion of fatigue stems from sleep deprivation. (C) Sleep deprivation affects social cognition and  
 231 interaction. (D) The intrinsic power of fNIRS measure in social cognition can be improved by  
 232 combining the hyperscanning approach. (E) Similar approach in the research involving fatigue  
 233 and sleep deprivation is still lacking.

234 **2. Applications of fNIRS in fatigue and sleep deprivation**

235 **2.1. Fatigue**

236 Early fNIRS studies mainly focused on physical fatigue. In a pioneering study,  
 237 Yoshitake et al. (2001) investigated the characteristics of muscle oxygenation on  
 238 lower-back muscle fatigue using a one-channel portable fNIRS system (HEO-100,  
 239 Omron, Japan). Participants were asked to perform isometric back extension at an  
 240 angle of 15 degrees with reference to the horizontal plane, lasting 1 minute.  
 241 Simultaneous electromyography, mechanomyography and fNIRS recordings were  
 242 conducted during the task. Results showed that muscle blood volume and HbO

1 243 concentrations significantly declined at the onset of the contraction, and remained  
2 244 constant throughout the rest of the contraction. Yoshitake et al. (2001) demonstrated  
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4 245 that blood flow restriction due to high intramuscular mechanical pressure was a  
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6 246 crucial factor in muscle fatigue.  
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8 247 Since then, rapid methodological advances allowed for more systematic  
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10 248 investigations of functional activity in the context of fatigue, using multi-channel  
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12 249 fNIRS devices and/or more sophisticated data analysis strategies. Also, there has been  
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14 250 a shift from a restricted focus on physical fatigue to the cerebral correlates of  
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16 251 cognitive or mental fatigue. Cognitive fatigue is characterized by the decline  
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18 252 in cognitive resources that follows sustained cognitive needs irrespective of sleepiness,  
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20 253 typically accompanied with speedily perceived exhaustion (Trejo et al., 2005). Overall,  
21  
22 254 these studies found fatigue-related oxygenation changes mostly within prefrontal and  
23  
24 255 parietal areas during various cognitive tasks (e.g., sustained-attention reaction-time  
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26 256 task, simulated driving, working memory task; De Joux et al., 2013; Derosière et al.,  
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28 257 2013; Liu et al., 2016; Jiao et al., 2012; Zhang et al., 2017; Borragan et al., 2018a,  
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30 258 2018b, 2019; see also a recent review in Qi et al., 2019). These studies generally  
31  
32 259 reported increased hemodynamic responses in prefrontal and parietal cortices in  
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34 260 exhausted as compared to control individuals (e.g., Chuang et al., 2018; De Joux et al.,  
35  
36 261 2013; Derosière et al., 2013; Zhang et al., 2017).  
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39 262 Counteracting fatigue and performance maintenance are often accompanied by  
40  
41 263 increased hemodynamic activity in frontal, primary motor, parieto-occipital and  
42  
43 264 supplementary motor areas (Chuang et al., 2018). For instance, Liu et al. (2014)  
44  
45 265 reported that increased activation in prefrontal regions help maintaining desirable  
46  
47 266 performance levels during a driving task (Liu, 2014). Similarly, Borragán et al. (2019)  
48  
49 267 reported increased fronto-parietal activation during task-related induction of cognitive  
50  
51 268 fatigue. These neurophysiological findings are in line with the patterns of cerebral  
52  
53 269 blood flow changes revealed by other neuroimaging methods such as fMRI (e.g., Gui  
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55 270 et al., 2015), Positron Emission Tomography (e.g., Tajima et al., 2010) or EEG (e.g.,  
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57 271 Wang et al., 2016).  
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1 272 The advantage of using the fNIRS technique to investigate fatigue capitalises on  
2 273 the nature of the phenomenon investigated. Either cognitive or motor, the triggering  
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4 274 of fatigue often entails exposing participants to long-duration (up to more than 1 hour)  
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6 275 paradigms characterised by over-time repeated demands, which represents a limiting  
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8 276 factor given that the longer the task, the higher the probability to capture noise  
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10 277 coming out from external sources such as, for instance, movements. Notwithstanding,  
11  
12 278 relative movement's tolerance in fNIRS technology is a good asset to perform clean  
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14 279 recording within medium-long periods. On the other hand, it was demonstrated that  
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16 280 fatigue can also be initiated in controlled conditions over much shorter periods of time  
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18 281 (e.g., 16 minutes; see Borragán et al., 2017, 2018a, 2018b, 2019; Tak and Ye, 2014),  
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20 282 providing the additional advantage to trigger fatigue without altering arousal. Finally,  
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22 283 fNIRS is optimal to explore the triggering of fatigue and/or other similar situations at  
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24 284 risk to interfere with optimal task performance, such as for instance attentional  
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26 285 overload, stress, drowsiness or sleep deprivation (Borragan et al. 2019) within  
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28 286 realistic environments.

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31 287 **Driving.** According to the U.S. Department of Transportation, almost 1 out of 2  
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33 288 persons commute to work in the U.S. every day, and 86% of these people use a  
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35 289 motorised vehicle. However, driving is not always a safe activity; the World Health  
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37 290 Organisation estimates that road traffic injuries caused 1.35 million deaths worldwide  
38  
39 291 in 2016. Being able to predict attentional lapses and disengagement could be a  
40  
41 292 promising approach to reduce the number of accidents in the future, a task that is well  
42  
43 293 suited to the peculiarities of portable, lightweight fNIRS. Indeed, fNIRS studies have  
44  
45 294 been shown able to detect associations between car driving events and changes in  
46  
47 295 cortical activity (Takahashi et al., 2011). For instance, increased prefrontal activation  
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49 296 was reported during speed deceleration (Yoshino et al., 2013), distraction (Nosrati et  
50  
51 297 al., 2016) or when participants take left as compared to right oriented curves (Oka et  
52  
53 298 al., 2015). An important finding was that fNIRS was able to reveal differential  
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55 299 demands in visual attention, that participants were actually unable to report (Oka et al.,  
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57 300 2015). In the same vein, other fNIRS studies reported how changes in functional  
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1 301 connectivity between fronto-motor areas are associated with decreased performance  
2 302 within time on task or cognitive fatigue (Xu et al., 2017; Borrigan et al. 2019). These  
3  
4 303 studies exemplify how using fNIRS might have useful future applications for road  
5  
6 304 safety.

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8 305 **Piloting.** The capacity of fNIRS to be used in realistic settings such as the cockpit  
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10 306 of a plane put it quickly at the edge of research investigating plane pilot performance  
11  
12 307 (e.g., cognitive fatigue and workload; Gateau et al., 2015). Recent results evidenced  
13  
14 308 that fNIRS has the capacity to detect critical safety aviation issues such as fatigue or  
15  
16 309 inattentional deafness (Verdière et al., 2018). Similar conclusions apply to the railroad  
17  
18 310 area. Increased automation driven by the installation of moderns Automatic Train  
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20 311 Operators (ATO) systems might paradoxically lead to decreased arousal in train  
21  
22 312 operators, making them less prompt to respond if needed. Kojima et al. (2005)  
23  
24 313 showed that fNIRS systems are a viable option to detect exhaustion conditions and  
25  
26 314 differences in brain activity between manual and automatic train operations (Kojima  
27  
28 315 et al., 2005).

29  
30 316 **Sport science.** As mentioned above, optical devices were originally developed to  
31  
32 317 investigate changes in muscle metabolism and muscle oxygenation in exercise and  
33  
34 318 sport science (Chance, 1991). Thanks to its portability and tolerance to movements,  
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36 319 the system is optimal to measure haemoglobin changes in the muscle during/after  
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38 320 specific training (Kounalakis et al., 2008) in a large set of populations from judokas  
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40 321 (Kijach et al., 2016) to handball and hockey players (Jones et al., 2015), cyclists  
41  
42 322 (Wittekind et al., 2012) or climbers (Philippe et al., 2012). Notwithstanding the  
43  
44 323 reliability of fNIRS to assess oxygenation changes during these activities, it must be  
45  
46 324 considered that fatiguing tasks are often accompanied by changes in cardiorespiratory  
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48 325 rhythms (Zhao et al., 2012), which might alter the quality of fNIRS recordings (Zhang  
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50 326 et al., 2016). In addition, fNIRS can be used to investigate the direct/indirect effects of  
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52 327 exercise on cognitive functions (Yanagisawa et al., 2010) or to assess patient's motor  
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54 328 rehabilitation strategies (Lin et al., 2009). Promising results have also been reported  
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56 329 using fNIRS in a Brain Computer Interface (BCI) setting (Rea et al., 2014).

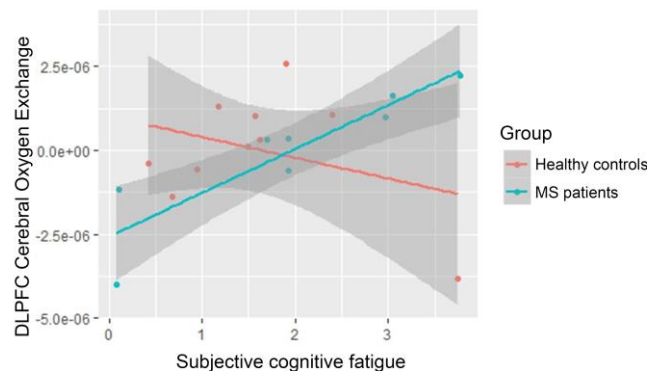
1 330 *Pedestrian safety.* Cities are growing quickly worldwide; the department of  
2 331 Economic and Social Affairs of the United Nations expects that 68% of the world's  
3 332 population will be living in urban nuclei by 2050. Considering this scenario, it is of  
4 333 special interest to understand human dynamics in modern cities (i.e., onset and use of  
5 334 new technologies, new transportation methods...). In addition to a-posteriori  
6 335 descriptive statistics (such as accident incident rates), new portable neuroimaging  
7 336 technologies can be used to identify (and prevent) citizens' risk behaviours or city  
8 337 areas with a higher accident probability. For instance, a study using EEG and a 3D  
9 338 virtual simulator showed that brain activity patterns could be used to identify careless  
10 339 walking in pedestrians using their mobile phone while walking (Erkan, 2017). The  
11 340 fact that fNIRS is less affected by movement artefacts than EEG (Perrey, 2008) is an  
12 341 argument for applications in this area. Besides, methodological improvements are  
13 342 facilitating the analysis of fNIRS data acquired in realistic settings in which the onset  
14 343 of events could not be easily anticipated (Pinti et al., 2017). Furthermore, the fNIRS  
15 344 technique might be also convenient to investigate environmental effects on cognitive  
16 345 function (Bratman et al., 2015).

17 346 *Technical operators.* fNIRS was used to assess the mental state of technical  
18 347 operators in a large variety of settings. For instance, fNIRS proved a reliable  
19 348 technique to measure workload and cognitive fatigue in air traffic controllers (Ayaz et  
20 349 al., 2012), radiologists (Nihashi et al., 2019) or unmanned aerial vehicles (Izzetoglu et  
21 350 al., 2015). Future applications could include the assessment of attentional states in  
22 351 nuclear plant engineers or staff and security guards. Finally, combining fNIRS with  
23 352 EEG is growing rapidly in the domain of human neuroergonomics. Indeed, combining  
24 353 these techniques allow assessing complementary brain signals; i.e., cerebral  
25 354 hemodynamic and neuronal electrical activity. Furthermore, classification accuracy of  
26 355 algorithms detecting attentional disengagement is often better when using both  
27 356 techniques (Nguyen et al., 2017). **Also, hybrid BCI based on simultaneous**  
28 357 **fNIRS-EEG measurements was shown to significantly improve classification**  
29 358 **accuracy in auditory and visual perception (Putze et al., 2014), executed**

359 movements (Khan et al., 2014) and motor imagery (Fazli et al., 2012; Yin et al.,  
360 2015) paradigms.

361 *Patients.* Besides, fNIRS has proven an effective tool to assess fatigue and  
362 attentional disengagement in some neurological conditions; for instance, Multiple  
363 Sclerosis (MS) disease in which fatigue is often viewed as the most debilitating  
364 symptom. In particular, fatigue in MS disease features a cognitive component –  
365 cognitive (or mental) fatigue. Borragán et al. (2018a) exposed patients with MS  
366 disease and healthy controls to a cognitive fatigue-inducing dual working memory  
367 updating task. During the experiment, participants' cortical activity was recorded  
368 using a 24-channel fNIRS system (BrainSight, V2.3b16, Rogue Research Inc.,  
369 Canada) over bilateral fronto-parietal regions (i.e., ventrolateral prefrontal cortex,  
370 dorsolateral prefrontal cortex, and inferior parietal cortex). Results showed  
371 comparable levels of perceived cognitive fatigue, task performance, and brain activity  
372 patterns in patients with MS disease and control participants. Notably, oxygenation  
373 level changes in the dorsolateral prefrontal cortex significantly correlated with  
374 perceived cognitive fatigue in MS patients (Fig. 4). Finally, longer sleep time  
375 positively associated with higher cognitive fatigue the patients with MS disease. This  
376 study therefore provided valuable evidence linking cognitive fatigue, sleep features  
377 and cortical activity patterns in MS disease.

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379  
380 **Fig. 4.** Association between subjective cognitive fatigue (CF) and dorsolateral prefrontal cortex  
381 (DLPFC) Cerebral Oxygen Exchange index. Results disclose a direct relationship, present only in  
382 patients with Multiple Sclerosis (MS), between DLPFC Cerebral Oxygen Exchange and the triggering

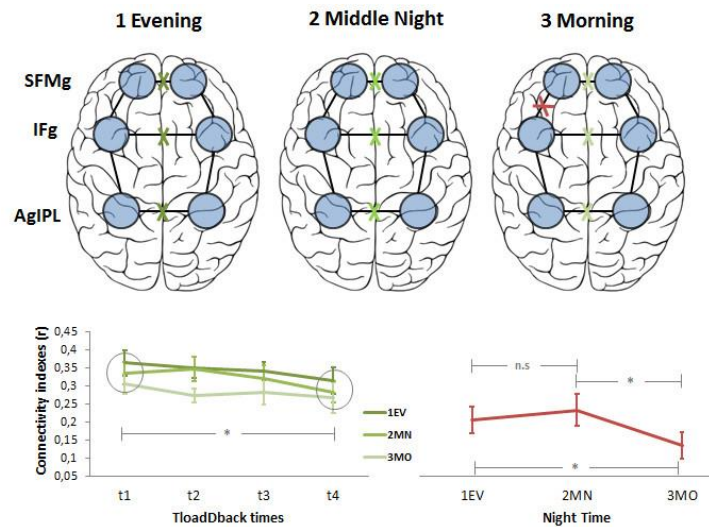
1 383 of subjective CF under cognitively demanding conditions. Note that higher Cerebral Oxygen Exchange  
2 384 values denote lower brain activity level (see Borragán et al., 2018 for more details).

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8 386 **2.2. Sleep deprivation**

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11 387 A portion of human fatigue stems from sleep deprivation or sleep disturbances. fNIRS  
12 388 applications in sleep deprivation conditions have also been of interest for the scientist.  
13 389 More than ten years ago, researchers started to use fNIRS to investigate the brain  
14 390 mechanisms underlying sleep deprivation and complement phenomenological  
15 391 descriptions of sleep complaints. These studies targeted the effect of sleep deprivation  
16 392 on mental fatigue (e.g., Ahn et al., 2016; Borragán et al., 2019), time perception (e.g.,  
17 393 Soshi et al., 2010), driving performance (e.g., Miyata et al., 2010), and working  
18 394 memory (e.g., Yeung et al., 2018). In almost all cases, sleep deprivation was  
19 395 demonstrated to impact cognitive functions, and to be accompanied by alternations of  
20 396 prefrontal oxygenation responses (e.g., Miyata et al., 2010; Yeung et al., 2018), even  
21 397 when participants were not totally sleep deprived (e.g., Yeung et al., 2018). The  
22 398 change of prefrontal activity was either a decrease (e.g., Borragán et al., 2019; Bu et  
23 399 al., 2017; Miyata et al., 2010; **Fig. 5**) which might reflect the cognitive deficit, or an  
24 400 increase (e.g., Honma et al., 2010; Soshi et al., 2010) possibly reflecting  
25 401 compensatory recruitment mechanisms.

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404 **Fig. 5.** Intra- and inter-hemispheric connectivity changes following sleep deprivation. Blue circles  
 405 indicate the regions of interest where activity was recorded using fNIRS (reproduced from Borragán et  
 406 al., 2019). Green Xs indicate inter-hemispheric connections in which connectivity decreased from the  
 407 beginning (t1) to the end (t4) of TloadDback practice (bottom right panel) during the 3 sessions. Red  
 408 Xs indicates the intra- hemispheric connection (on the left Superior/Middle Frontal gyrus - Inferior  
 409 Frontal gyrus) in which connectivity decreased in the morning (3MO) session as compared to the  
 410 evening (1EV) and middle night (2MN) sessions. Brain connectivity changes might reflect a higher  
 411 cost of resource consumption when sleep pressure is high. In the cited experiment (for details, see  
 412 Borragán et al., 2019), performance is readjusted at a lower rate when activity in the left Frontal gyrus  
 413 starts being desynchronized in the morning as a result of extended sleep deprivation.

414

415 Sleep disturbances are also commonly observed in patients suffering from  
 416 psychiatric conditions. For instance, fNIRS was proposed to assist the diagnosis of  
 417 major depressive disorder. Nishida et al. (2017) investigated the possible association  
 418 between sleep assessment and haemoglobin dynamics in major depressive disorder.  
 419 Results showed that (1) self-rated depression negatively correlate with cerebral  
 420 reactivity in the right temporal region (2) and self-rated sleep disturbances negatively  
 421 correlate with HbO changes in the left prefrontal cortex. These findings suggest that  
 422 left prefrontal cortex reactivity is susceptible to sleep complaints in patients with  
 423 major depressive disorder. In another study, Sun et al. (2017) investigated



1 424 haemoglobin response patterns of patients with chronic insomnia disorder using  
2 425 multi-channel fNIRS. Results evidenced reduced prefrontal activation during a verbal  
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4 426 fluency task in chronic insomnia disorders.  
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6 427 Although suffering from sleep deprivation, humans might also demonstrate an  
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8 428 inherent ability to overcome sleepiness and counteract accumulated sleep pressure.  
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10 429 Using fNIRS, Honma et al. (2010) found that activity in the right prefrontal cortex is  
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12 430 associated with the ability to overcome sleepiness during a modified *n*-back (2- and  
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14 431 0-back) working memory task. In this study, participants' right prefrontal activity  
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16 432 correlated with self-rated alertness changes on the 2- and 0-back conditions. Cerebral  
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18 433 activity in the right prefrontal area was proposed to fulfil a functional compensatory  
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20 434 mechanism allowing the participant to meet the task load demands.  
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### 24 435 **3. Applications of fNIRS in social cognition**

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27 436 In the last decade, a growing number of studies aimed at investigating the brain  
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29 437 mechanisms underlying social cognition using fNIRS, capitalizing on its ecological  
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31 438 validity. As discussed section 1.2, fNIRS is advantageous to examine brain activity  
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33 439 patterns under social contexts and naturalistic circumstances, which is of particular  
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35 440 relevance when studying the cerebral correlates of social cognition. Previous fNIRS  
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37 441 studies spanned age groups from infancy (e.g., Lloyd-Fox et al., 2014) to adulthood  
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39 442 (e.g., Egetemeir et al., 2011) and elderly (e.g., Pu et al., 2008), focusing on various  
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41 443 topics including joint action (e.g., Herrmann et al., 2015), joint attention (e.g., Zhu  
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43 444 and Godavarty, 2013), social communication (e.g., Suda et al., 2010) and spontaneous  
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45 445 deception (e.g., Zhang et al., 2016). Additionally, analogous studies were conducted in  
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47 446 patients (e.g., Köchel et al., 2015; Takei et al., 2013; Zhu et al., 2014).  
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50 447 *Joint action.* Much of human daily work requires inter-individual action  
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52 448 coordination. Using fNIRS, Egetemeir et al. (2011) assessed brain activation during  
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54 449 real-life joint action tasks. Joint action (i.e., to cooperate with a partner to perform a  
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56 450 table setting) compared to solo action (i.e., to perform the task alone) induced higher  
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58 451 HbO concentrations in a set of brain areas including the inferior parietal lobule,  
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1 452 reputedly part of the mirror neurons system. Herrmann et al. (2015) further tested the  
2 453 functional role of polymorphism 5-HTTLPR in real-life joint action; they confirmed  
3  
4 454 that participants with the short variant of the polymorphism exhibited increased  
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6 455 parietal brain responses during real-life joint action.  
7

8 456 **Joint attention.** The question of what happens in the brain of participants sharing  
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10 457 an attentional focus on the same object/event during a social interaction is of  
11  
12 458 particular interest. Even by the age of five months, infants are sensitive to social  
13  
14 459 interactions, as shown in an fNIRS study by the recruitment of left dorsal prefrontal  
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16 460 cortex activity when engaged in joint attention with others (Grossmann and Johnson,  
17  
18 461 2010). Other fNIRS studies in healthy children evidenced different HbO  
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20 462 concentrations in frontal regions between joint and non-joint attention interactions  
21  
22 463 (Chaudhary et al., 2011). Zhu and Godavarty (2013) implemented a lagged covariance  
23  
24 464 structural equation model to fNIRS measurements during joint attention tasks in  
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26 465 normal adults, allowing to compute differences in the path coefficients amongst  
27  
28 466 different conditions (i.e., joint attention and non-joint attention) that revealed distinct  
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30 467 interhemispheric connectivity in the frontal region.  
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33 468 **Communication.** The human brain may have evolutionarily adapted to  
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35 469 face-to-face communication, which is a significant feature of all social species. To  
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37 470 examine the brain characteristics of early human social cognitive abilities, Grossmann  
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39 471 et al. (2008) examined cortical specialization for the perception of facial  
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41 472 communication cues in infants. Perceiving facial communication signals resulted in  
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43 473 temporal and prefrontal cortex activation in infants, like in adults. Suda et al. (2010)  
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45 474 validated the potential of fNIRS for studying social interactions in a naturalistic  
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47 475 setting. Specifically, they investigated the haemoglobin dynamics during face-to-face  
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49 476 communication. Speaking compared to mute segments induced higher activity in  
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51 477 frontal and superior temporal regions. Apart from verbal communication, neural  
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53 478 processes underlying non-verbal communication were also tested (i.e., eye-to-eye  
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55 479 contact, Hirsch et al., 2017), and within-individual results revealed that eye-to-eye  
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57 480 contact compared to eye-to-picture gaze induced higher left frontal activation,  
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1 481 synchronized with functional activity in the left superior temporal regions.

2 482 **Deception.** Deception is ubiquitous in human societies, and requires a high level  
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4 483 of social cognition. Using fNIRS, Ding et al. (2013) found that as compared to truth  
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6 484 telling, spontaneous deception (free to choose telling the truth or a lie) triggers larger  
7  
8 485 neural activity in the left superior frontal cortex. Also, the reward system might be  
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10 486 involved in spontaneous deception. In a follow-up study, Ding et al. (2014) examined  
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12 487 the cerebral correlates of second-order deception (i.e., the recipient of deception is  
13  
14 488 fully aware of the deceptive intention of the deceivers and thus the deceiver has to use  
15  
16 489 both lies and truths to deceive). Results demonstrated the involvement of a broad area  
17  
18 490 of the prefrontal cortex in second-order deception (Ding et al., 2014). In a later study  
19  
20 491 (Zhang et al., 2016), graph theory analyses further revealed that spontaneous  
21  
22 492 deception as compared to control deception (instructed to tell the truth or a lie)  
23  
24 493 resulted in greater clustering coefficients, shorter average path lengths, greater  
25  
26 494 average node degrees, and stronger randomness; these results indicate that the  
27  
28 495 functional networks of brain activity for the spontaneous behavior exhibited greater  
29  
30 496 aggregation, efficiency and randomness during deception (Zhang et al., 2016).

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33 497 Several studies using multi-channel fNIRS also probed differences between  
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35 498 psychiatric patients and healthy samples to evidence abnormal brain activity patterns  
36  
37 499 possibly underlying social cognitive deficits. As compared to typically developing  
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39 500 children, children with autism spectrum disorder exhibited reduced interhemispheric  
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41 501 (resting-state functional) connectivity and lower local connectivity in bilateral  
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43 502 temporal cortices (Zhu et al., 2014). Likewise, as compared to healthy controls,  
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45 503 elderly people with late-onset major depression exhibited reduced frontopolar  
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47 504 activation during verbal fluency tasks, associated with poor social functioning (Pu et  
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49 505 al., 2008). Patients with borderline personality disorder showed left medial prefrontal  
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51 506 cortex hyperactivity during social exclusion (Ruocco et al., 2010), and patients with  
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53 507 schizophrenia exhibited decreased HbO changes in both the temporal lobes and the  
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55 508 right inferior frontal gyrus during face-to-face conversation (Takei et al., 2013). In  
56  
57 509 children with attention deficit hyperactivity disorder, there was decreased activity in  
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1 510 the right superior temporal gyrus when processing anger prosody, and increased  
2 511 supramarginal gyrus activity when being exposed to affectively angry sentences  
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4 512 (Köchel et al., 2015). Altogether, these studies suggest the potential of fNIRS for the  
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6 513 investigation of the neural correlates of diverse psychiatric syndromes.  
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#### 9 514 **4. fNIRS-based hyperscanning**

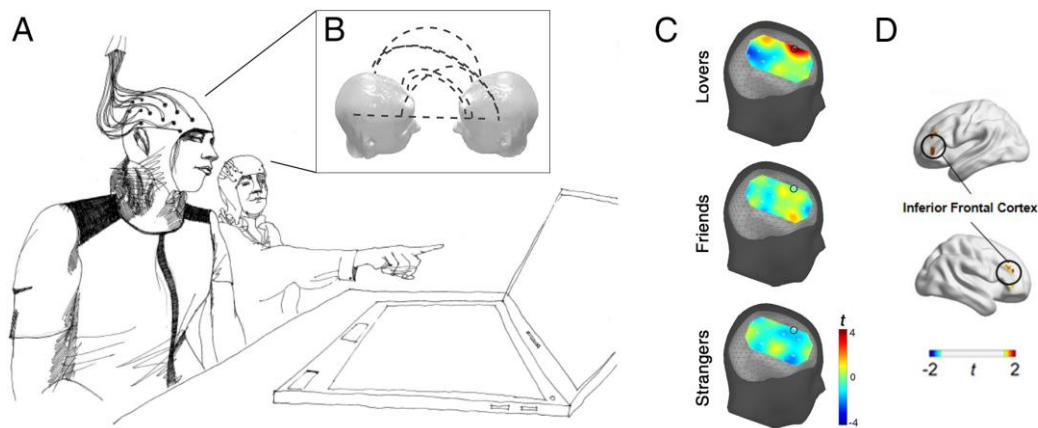
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12 515 Social cognition and interactions typically involve at least two agents. Conventional  
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14 516 fNIRS (and other) studies focused on single person recordings, to some extent  
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16 517 overlooking the interaction between individuals. However, single-person neuroscience  
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18 518 is insufficient to capture the subtle nature of human dynamic interactions (Schilbach  
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20 519 et al., 2013). Recent advances move our focus from single-brain functioning to  
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22 520 two-brain communication using the hyperscanning approach (Pan et al., 2017, 2018).  
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24 521 In this section, we will discuss how fNIRS hyperscanning can boost the intrinsic  
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26 522 power of studying social cognition.  
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28  
29 523 Hyperscanning, i.e., measuring two or more brains simultaneously (Montague et  
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31 524 al., 2002), is a recently developed approach (see an example in **Fig. 6A**). One major  
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33 525 feature distinguishing fNIRS-based hyperscanning from other hyperscanning  
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35 526 modalities (e.g., EEG, Babiloni et al., 2006, and fMRI, Montague et al., 2002) is that,  
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37 527 a single fNIRS acquisition device could be split into two (or more), allowing to use  
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39 528 half of the channels for each participant and record simultaneously their brain activity  
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41 529 (Cui et al., 2012). Indeed, since fNIRS detectors are individually coupled with a  
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43 530 nearby light source and we measure variations in light diffusion over these areas,  
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45 531 there is no need to bother with coupling two heavy and distant installations (like with  
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47 532 fMRI, MEG). Also, the use of a single system for both participants easily solves the  
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49 533 calibration/synchronization problem that often occurs when using two/multi devices.  
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51  
52 534 A crucial aspect of online human-to-human/brain-to-brain investigations relates  
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54 535 to the measure of interpersonal brain synchronization (or inter-brain coherence, or  
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56 536 synchronous brain activity; **Fig. 6B**). Interpersonal brain synchronization as a neural  
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58 537 marker of social interactive activities has been adopted in many studies in the field of  
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538 social neurosciences, including joint action (Cheng et al., 2015; Cui et al., 2012;  
539 Funane et al., 2011; Pan et al., 2017), social communication (Hirsch et al., 2017; Jiang  
540 et al., 2012; Liu et al., 2017), and teaching and learning (Liu et al., 2019; Pan et al.,  
541 2018; Zheng et al., 2018).



543  
544 **Fig. 6.** (A) Representative illustration of a fNIRS-based hyperscanning experimental scenario. A  
545 teacher is transmitting knowledge to a student, during which their brain activity is recorded by fNIRS  
546 simultaneously (Pan et al., 2019). (B) Interpersonal brain synchronization (IBS) emerges as a result of  
547 learning interactions within the teacher-student dyad. (C) Maps of IBS in lover-, friend-, and  
548 stranger-dyads during a cooperation task (adapted from Pan et al., 2017). Compared to friend- and  
549 stranger-dyads, lover-dyads show significantly higher IBS in the superior frontal cortex. (D) Maps of  
550 IBS in instructor-learner dyads during a song learning task (adapted from Pan et al., 2018).  
551 Interpersonal synchronization of inferior frontal cortices tracks the song learning process.

552  
553 The first fNIRS-based hyperscanning study focused on the brain characteristics of  
554 joint action, which requires cooperation/coordination between two partners (Funane et  
555 al., 2011). Participant dyads were required to mentally count 10 seconds after an  
556 auditory cue and press a button as simultaneously as possible. Results disclosed  
557 inter-individual synchronous activity in the prefrontal cortices, associated with their  
558 cooperation performance. Following on, Cui et al. (2012) asked participants to either  
559 press the button as simultaneously as possible (cooperation) or to answer faster than  
560 the partner (competition). Results revealed inter-brain coherence in the right superior

1 561 frontal cortices during cooperation, but not during competition. Increased inter-brain  
2 562 coherence also paralleled better cooperation performance. Further fNIRS-based  
3  
4 563 hyperscanning studies showed that the gender of partner (Cheng et al., 2015) and the  
5  
6 564 inter-partner relationship (Pan et al., 2017) modulate synchronous brain activity in the  
7  
8 565 prefrontal cortices during cooperative exchange (**Fig. 6C**).

10 566       Regarding social communication, Jiang et al. (2012) demonstrated a significant  
11  
12 567 increase in neural synchronization between partners in the left inferior frontal cortex  
13  
14 568 during face-to-face dialog. Furthermore, communication behaviours could be  
15  
16 569 accurately predicted based on neural synchronization levels. Liu et al. (2017) further  
17  
18 570 demonstrated that HbO concentrations in the listener were significantly correlated  
19  
20 571 with HbO concentrations in the speaker with a delay of approximately 5 seconds.  
21  
22 572 Except for live verbal communication, Hirsch et al. (2017) also showed that during  
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24 573 non-verbal eye-to-eye contact, brain-to-brain coherence (based on HbR  
25  
26 574 concentrations) increased within left superior temporal, middle temporal, and  
27  
28 575 supramarginal gyri as well as the pre- and supplementary motor cortices.

31 576       Educational activities such as teaching and learning are a fertile domain to  
32  
33 577 investigate the neurophysiology of social cognition, since they involve a series of  
34  
35 578 social processes including imitation and observation (Pan et al., 2018). Functional  
36  
37 579 NIRS-based hyperscanning allowed focusing on the dyadic interaction between  
38  
39 580 teaching and learning brains. Simultaneous measurements of the brain activity of  
40  
41 581 teacher-student dyads disclosed higher time-lagged brain-to-brain synchronization  
42  
43 582 between the right temporo-parietal junction of the teacher and the anterior superior  
44  
45 583 temporal cortex of the student (Zhang et al., 2018). Pan et al. (2018) reported  
46  
47 584 synchronization between the inferior frontal cortices of teacher and student, when the  
48  
49 585 teacher was teaching a music song to the student (**Fig. 6D**). Also, such interpersonal  
50  
51 586 brain synchronization between teachers and students could be biased by prior  
52  
53 587 knowledge and communication mode, as revealed by fNIRS-based hyperscanning  
54  
55 588 (Liu et al., 2019). Strongly indicating its functional significance, interpersonal brain  
56  
57 589 synchronization with teacher compensated for student's sleep deprivation in an  
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1 590 interactive learning task (Pan et al., 2019). Functional NIRS-based hyperscanning and  
2 591 interpersonal brain synchronization thus provide powerful measures to track  
3  
4 592 interpersonal interactions and social cognition under naturalistic circumstances.  
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## 7 593 **5. Current challenges**

### 10 594 **5.1. Technical and methodological difficulties**

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15 595 Currently, the main challenge in the use of fNIRS is technical and methodological.  
16  
17 596 Concerns include (but are not restricted to) the following aspects.

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19 597 *Unavailable subcortical regions.* As mentioned above, the penetration depth of  
20  
21 598 fNIRS light is typically 1.5 – 2 cm. Theoretically, one can slightly enlarge the distance  
22  
23 599 between fNIRS source and detector to increase the measuring depth, at the cost of  
24  
25 600 reduced signal-to-noise however. Measuring depth limitation in fNIRS prevents the  
26  
27 601 investigation of subcortical regions potentially involved in fatigue, sleep deprivation  
28  
29 602 and social cognition (e.g., the amygdala in social cognition, Adolphs, 2010), and their  
30  
31 603 interactions with cortical structures.

32  
33 604 *Confounds in fNIRS data.* The fNIRS signal is potentially confounded by at least  
34  
35 605 two factors. First, anatomical parameters such as scalp-to-cortex distance may affect  
36  
37 606 the reliability of fNIRS data (e.g., Haeussinger et al., 2011). Second, peripheral  
38  
39 607 hemodynamic parameters such as skin perfusion may cause physiological fluctuations  
40  
41 608 (e.g., Tong et al., 2011). Despite the development of advanced methods such as  
42  
43 609 principal component spatial filtering (Zhang et al., 2016) or  
44  
45 610 Correlation-Based-Signal-Improvement (Cui et al., 2010) to correct systemic effects  
46  
47 611 and motion artefacts, it is yet unclear whether these unwanted components can be  
48  
49 612 completely excluded. Further methodological advances in data pre-processing are  
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51 613 needed here.

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53  
54 614 *Non-standardized analysis pipelines.* Standardized and well-accepted analysis  
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56 615 pipelines are available for many neuroimaging modalities (EEG and fMRI),  
57  
58 616 facilitating the report and replication of findings, and their interpretation. fNIRS data  
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60

1 617 still lacks such a standardized data processing pipeline. Commonly accepted  
2 618 approaches include spatial registration, motion artefact removal, local/global  
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4 619 component separation and data filtering (Cui et al., 2010, 2011; Zhang et al., 2016).  
5  
6 620 However, there is no consensus on empirically based, uniform, and user-friendly  
7  
8 621 analysis guidelines, hampering the comparability and reproducibility between existing  
9  
10 622 studies. Additionally, there is a need to develop more powerful and multivariate  
11  
12 623 fNIRS data analysis approaches, e.g. Multivariable Pattern Analysis (Gemignani et al.,  
13  
14 624 2018).

15  
16  
17 625 ***HbO, HbR or both?*** Functional NIRS nicely provides us concentration changes  
18  
19 626 for two distinct brain signals, i.e., HbO and HbR. Theoretically, regional brain  
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21 627 activation is characterized by concurrent increased HbO and decreased HbR. However,  
22  
23 628 due to physiological interferences and systemic changes, only one concentration  
24  
25 629 (either HbO or HbR) might show significant changes to a task/stimulus in real fNIRS  
26  
27 630 data recordings. As such, previous empirical work often focused on only one  
28  
29 631 concentration, and rarely used both. The consensus is scarce on which concentration  
30  
31 632 to use since both HbO and HbR feature advantages and disadvantages, as discussed  
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33 633 section 1.1. Besides, other studies also took into account their combination by using  
34  
35 634 either the sum (i.e., HbT, Nozawa et al., 2016) or the difference of HbO and HbR  
36  
37 635 (Borragán et al., 2018a). Future studies are still needed to delineate when, why and  
38  
39 636 how to use HbO, HbR or their combination.

## 40 41 42 43 637 **5.2. Interpretation of fNIRS results**

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45  
46 638 A spatial format based on structural features seems natural for interpreting fNIRS data.  
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48 639 However, cortical-level fNIRS results can prove difficult to interpret due to a  
49  
50 640 restricted detection depth and partial coverage over the scalp. For example, Cheng et  
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52 641 al. (2015) reported coherent brain activity in frontopolar, orbitofrontal and left  
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54 642 dorsolateral prefrontal cortices across participant dyads during cooperation. Activity  
55  
56 643 in these areas was previously linked to a series of cognitive functions including social  
57  
58 644 cognition (e.g., Contreras et al., 2012), reward (e.g., Rushworth et al., 2011) and



1 645 meta-cognitive processes (e.g., Amodio and Frith, 2006). Nonetheless, it is difficult to  
2 646 infer from fNIRS data whether these processes have a combined effect or work  
3  
4 647 independently. Besides, cortical-level results can receive various interpretations due to  
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6 648 multiple functional meanings associated with specific cortices, eventually leading to a  
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8 649 relative ambiguity and arbitrariness in the interpretation of fNIRS data. Additionally,  
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10 650 it is not possible using fNIRS to determine the contribution of subcortical structures,  
11  
12 651 and how and to what extent their activity is responsible for variations in cortical  
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14 652 activity in specific contexts. Multimodal imaging is a possible solution to data gained  
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16 653 using fNIRS with other modalities (e.g., EEG or fMRI) and help in their  
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18 654 interpretation.

## 22 655 **6. Conclusions and prospects**

25 656 To sum up, fNIRS is a valid and promising brain imaging tool that can usefully  
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27 657 complement other neuroimaging techniques to study the human brain and cognitive  
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29 658 functions. Despite some limitations, fNIRS has its own assets and can provide  
30  
31 659 valuable contributions to investigations in the fields of fatigue, sleep deprivation and  
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33 660 social cognition, as reviewed here. Functional NIRS may also empower a better  
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35 661 understanding of the neural bases of fatigue, sleep complaints and social deficits. The  
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37 662 intrinsic power of fNIRS measurement can further be improved if combined with  
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39 663 other brain imaging modalities, and even more if applied to the hyperscanning  
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41 664 paradigm. Hopefully, technical and methodological advances will progressively  
42  
43 665 broaden the scope of fNIRS applications to other facets of human performance and  
44  
45 666 cognitive functions.

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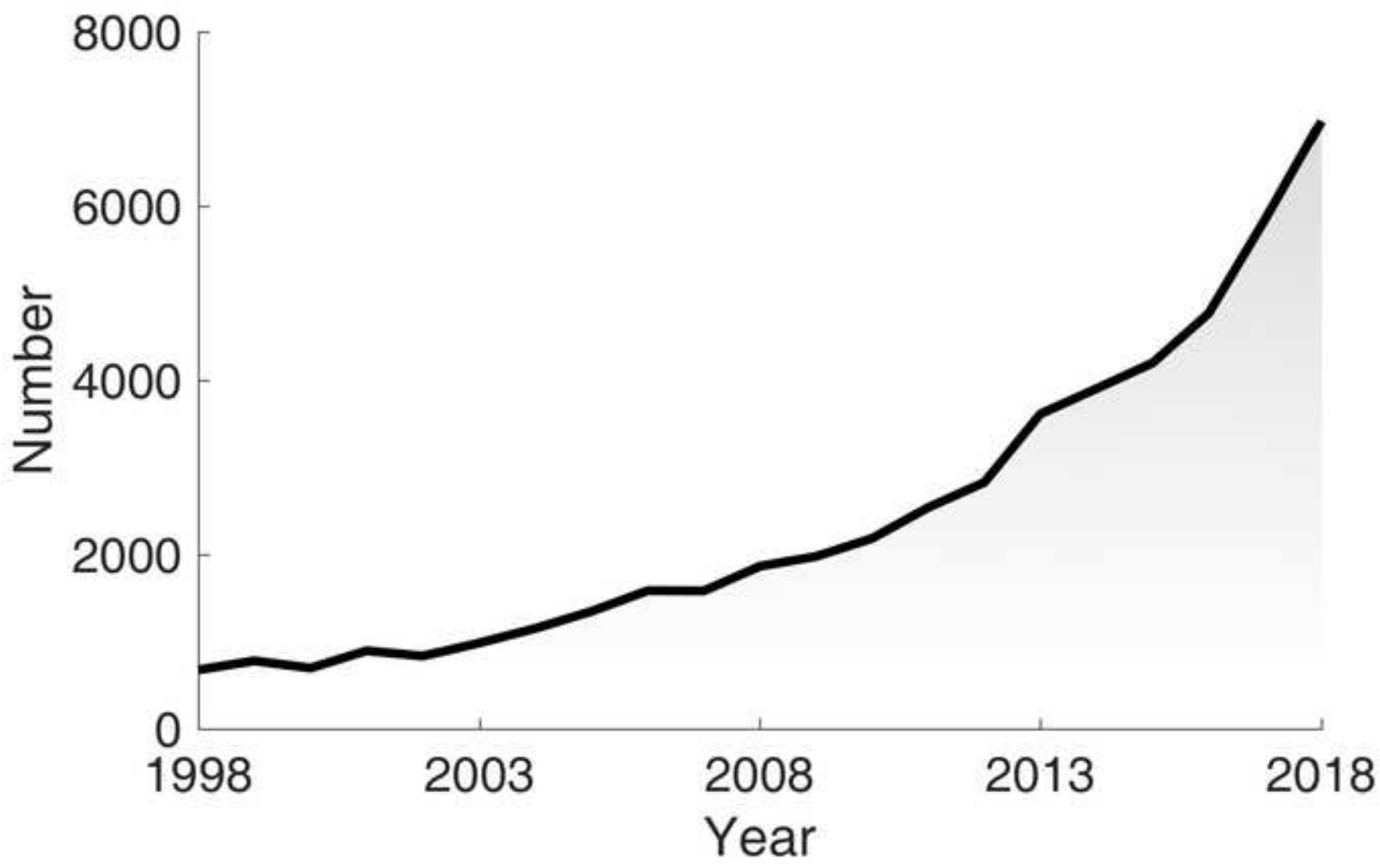
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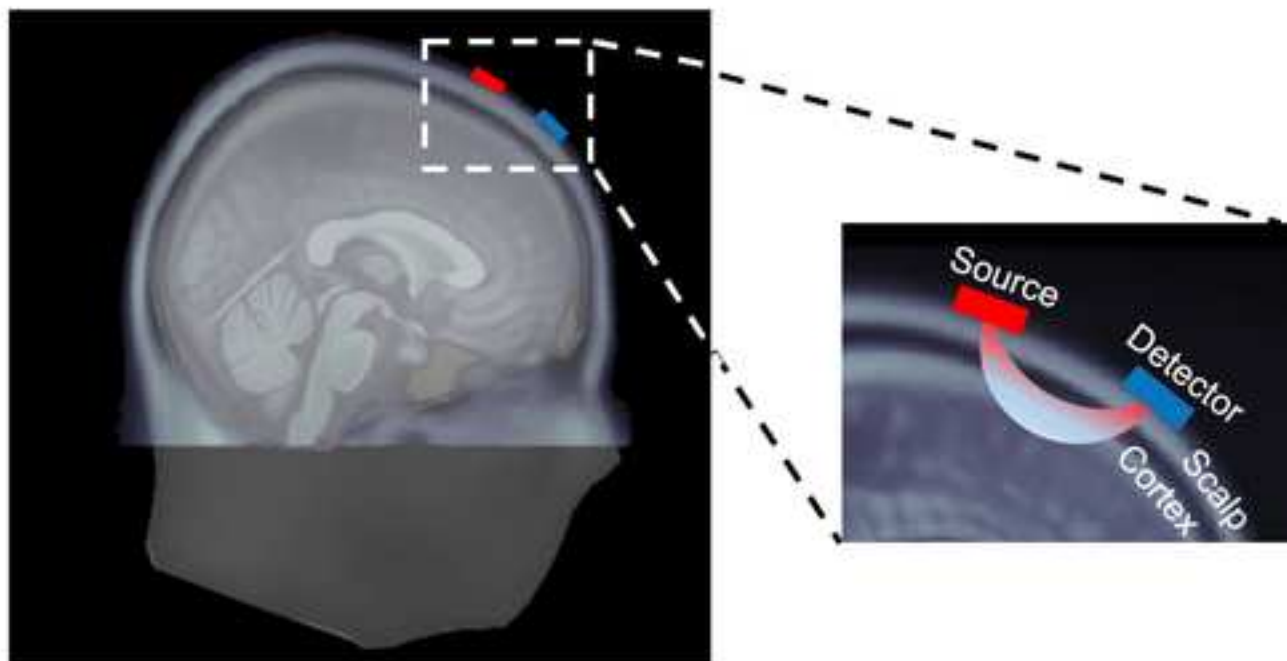
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Figure 1

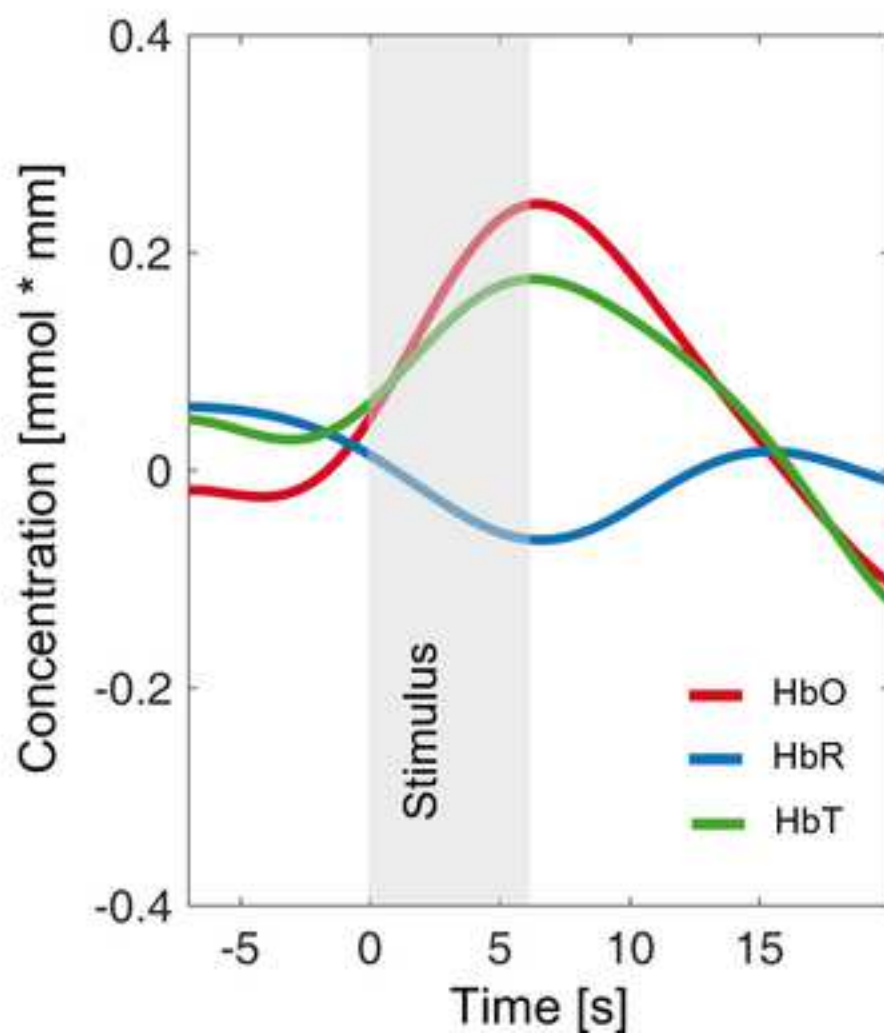




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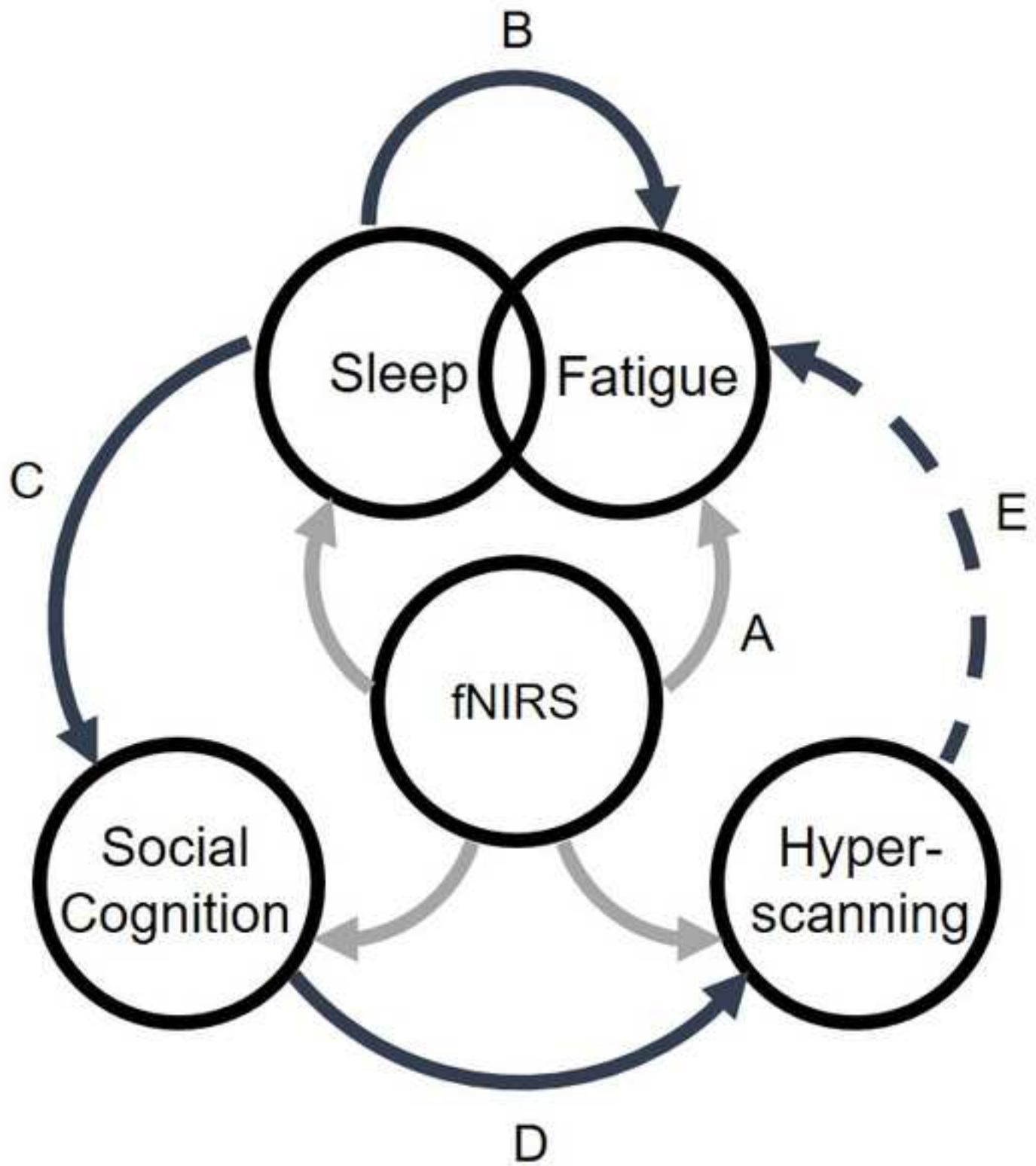


Figure 4

