



Applications of Functional Near-Infrared Spectroscopy in Fatigue, Sleep Deprivation, and Social Cognition

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Abstract

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.

Keywords Functional near-infrared spectroscopy (fNIRS) · Fatigue · Sleep deprivation · Social cognition · Hyperscanning · fNIRS application

Introduction

Functional near-infrared spectroscopy (fNIRS) is an optical diffusion technique that allows the non-invasive imaging of cortical activity. Optical diffusion was initially developed by Jöbsis in Jobsis 1977, who reported that continuous near infrared light non-invasively allows the real-time detection of haemoglobin (Hb) levels in the brain of neonates. In a

nutshell, modern fNIRS systems use a system of sources emitting infrared light at constant frequency and amplitude, coupled with detectors that receive the light scattered by the intermediate brain tissues. Applying the Modified Beer Lambert Law (MBLL) allows then to relate light intensity changes to variations in brain activity (Villringer and Chance 1997).

Within the last two decades, an increasing number of empirical studies used fNIRS imaging to study the brain mechanisms underlying various cognitive functions (Fig. 1). fNIRS can be advantageous due to a combination of easy applicability, low cost, sensible temporal resolution, ecological validity and free restraint (i.e., relative tolerance to movements) (Ehlis et al. 2014). Considering its versatility, fNIRS can be a good neuroimaging option and bring benefits for studies investigating human performance in altered conditions such as fatigue and sleep deprivation, as well as for the study of social cognition, in particular when used in a hyperscanning context (i.e., measuring two or more brains simultaneously; Cui et al. 2012; Pan et al. 2017, 2018). In the present review, we will first provide a brief overview of the principles of fNIRS with its assets and caveats. We will

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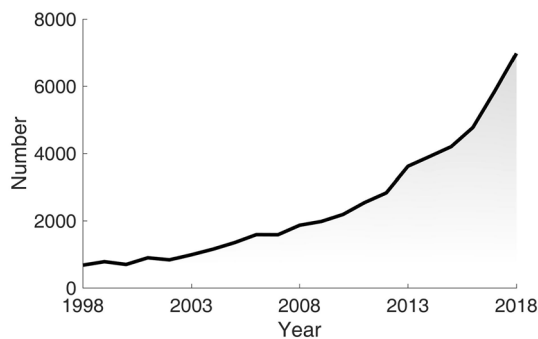


Fig. 1 Yearly evolution in the number of published fNIRS research articles within the last two decades. Data extracted from ScienceDirect (<https://www.sciencedirect.com/>) in May 2019 by performing a search using the term “functional near-infrared spectroscopy” as a primary keyword

then focus on fNIRS studies in two main domains. One, the effects and cortical correlates of fatigue and sleep deprivation. Second, the neural bases of social cognition and interpersonal relationships using fNIRS and hyperscanning. Finally, we will discuss current challenges and future prospects of application for fNIRS.

What is Functional Near-Infrared Spectroscopy (fNIRS)?

Functional NIRS takes advantage of the diffusion properties of near-infrared light through brain tissues to allow the non-invasive and continuous measurement of local oxygen-dependent metabolism. Blood oxygen level-dependent (BOLD) changes can be quantified looking at the oxidation state of blood haemoglobin. Neuronal activity and blood oxygenation changes are interlinked as follows (Scholkmann et al. 2014). First, local brain activation causes increased regional metabolism and oxygen demands by neurons (i.e., neurometabolic coupling). In a next step, increased oxygen consumption induces increased regional cerebral blood flow and volume (i.e., neurovascular coupling). Unlike functional magnetic resonance imaging (fMRI) that tracks (de)oxygenation-related changes in blood magnetization to infer variations in the BOLD signal, functional NIRS allows the quantitative and separate monitoring of both oxy-haemoglobin (HbO) and deoxy-haemoglobin (HbR) levels by detecting variations from the source to the detector in specific near-infrared light wavelengths. During this process, the near-infrared light emitted from the probe penetrates and diffuses into the brain tissues following a characteristic banana-shaped path (Fig. 2a). Like functional magnetic resonance imaging (fMRI), fNIRS is an indirect measure of neuronal activity, with the peak of the hemodynamic response delayed by approximately 5–10 s (Ferrari and Quaresima 2012).

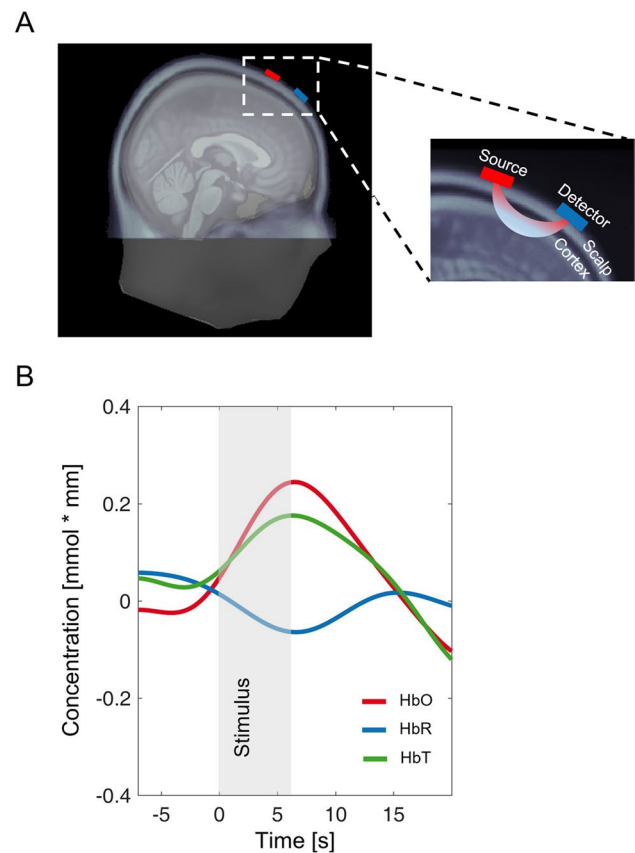


Fig. 2 **a** Illustration of the banana-shaped path followed by the NIRS light from source to detector. **b** A representative fNIRS response. The local brain activation is reflected by a decrease in HbR concentration, alongside an increase in HbO concentration. HbT corresponds to the sum of HbO and HbR changes. Note that the peak haemoglobin signal can be observed with a latency of approximately 5–10 s after the onset of a stimulus (Color figure online)

Besides measurements of brain activity, the same principle of near infrared light diffusion can be used in other domains, e.g. in motor sciences to assess oxygenation levels in muscle tissues (Volkening et al. 2016).

As mentioned above, the fNIRS signal can be split into separate HbO and HbR concentrations (Fig. 2b). Based on the MBLL, HbO and HbR can be reflected by the attenuation of specific near-infrared light wavelengths due to absorption changes. Theoretically, these two metrics should be negatively correlated with each other (Cui et al. 2010a) as HbO decreases when HbR increases, and vice versa, but this is not always true in practice for various reasons (see Guerrero-Mosquera et al. 2016; Yamamoto and Kato 2002; Yuan and Ye 2013). Focal increase in HbO, along with decreased HbR, is interpreted as a marker of regional brain activation (Fox and Raichle 1986). The major cause of decreased HbR in venous blood is that the rate of regional cerebral blood flow increase exceeds that of the regional cerebral oxygen metabolic rate (Sitaram et al. 2009).

It has been argued that global/systemic effects such as heart rate, blood pressure, and respiratory activity influence more HbO, whereas the venous compartment would mostly influence HbR (e.g., Hirsch et al. 2017). HbR has been found principally associated with neurovascular coupling. It exhibits better spatial precision related to neuronal-specific brain activity and fewer confounds from signals due to non-neuronal origins (Hirsch et al. 2017). Thus, HbR was reported to represent a better-defined brain activation than HbO (Kirilina et al. 2012). Compared to HbR, HbO changes typically induce larger amplitudes and involve more widespread brain regions. As such, other researchers proposed that in fNIRS measurements, HbO concentration actually is the most sensitive physiological marker of changes in the regional cerebral blood flow (Hoshi 2007). Whereas functional cortical activity is largely monitored and recorded, non-neuronal brain activity and global/systemic effects can be mitigated via data preprocessing (Zhang et al. 2018; see details in the next section). Therefore, HbO concentrations could feature a high signal-to-noise ratio (Liu et al. 2017a). HbO and HbR responses elicited by stimuli can also be determined by assessing the mean activation within a determined window (Watanabe et al. 2008). Another possible indicator of brain activity as assessed by fNIRS is total haemoglobin (HbT, e.g., Nozawa et al. 2016). HbT corresponds to the sum of changes in HbO and HbR, and is thus largely dominated by HbO changes. It was shown that HbT is less sensitive to venous contamination. Consequently, it might provide better spatial specificity than separate HbO and HbR concentrations (Gagnon et al. 2012). Moreover, HbT changes represent changes in blood volume and are related to changes in blood flow (Grubb et al. 1974). Notwithstanding, including both HbO and HbR measures in fNIRS data analyses is certainly useful to obtain a full picture of the underlying brain mechanisms. In this respect, cerebral oxygen exchange (COE), computed as the difference between HbR and HbO, represents another useful indicator of cellular oxygen metabolism (Yoshino et al. 2013). COE indicators can also be generated from an oxyHb and deoxyHb orthogonal coordinate plane using a vector-based analysis perspective (for more details, see Yoshino and Kato 2012).

Raw fNIRS signals based on HbO and HbR changes are typically non-stationary, and result from a combination of several components (Scholkmann et al. 2014). The first component is stimulus-/task-evoked neurovascular coupling, directly associated with functional brain activity. The second component is spontaneous neurovascular coupling; it is non-evoked and can be used, e.g., to assess the resting-state functional organization of the brain. Another component is undesired physiological/systemic interferences. These activities entail changes in blood pressure, skin blood flow/volume, heart rate (1–2 Hz), respiration (0.1–0.3 Hz), Mayer waves (~0.1 Hz), and very low frequency oscillations (<0.01 Hz).

To remove (or at least mitigate) the effects of these artefacts, several approaches have been proposed. Band-pass filtering is one of the most commonly used methods to remove systemic physiology artefacts such as cardiac, respiratory, and cardiovascular oscillations (e.g., Yanagisawa et al. 2010). Conventional averaging of fNIRS signals time-locked to the stimuli is also a valid option. Indeed, there is at least two main issues in the pre-processing of fNIRS data: (1) separation between signal components and (2) correction of motion artefacts. In order to separate the global (systemic) and local (neuronal) components in fNIRS signals, Zhang et al. (2016b) developed a principal component spatial filter algorithm. This Gaussian spatial filtering approach significantly improved both temporal waveforms and spatial pattern consistencies between HbO and HbR concentrations. Although relatively tolerant to the participants' movements, fNIRS in naturalistic experiments yet still faces the challenges from motion artefacts. To correct these artefacts and improve signal quality, Cui et al. (2010a) proposed a correlation-based-signal-improvement method based on the negative correlation between HbO and HbR concentrations (see also Guerrero-Mosquera et al. 2016). Other artefact removal methods include discrete wavelet filtering (Molavi and Dumont 2012), sliding window motion artefact rejection (Ayaz et al. 2010) and wavelet-based denoising (Duan et al. 2018). Apart from these univariate methods, one can also consider multivariate approaches. For instance, one can use additional channels with, e.g., 1.5-cm source-detector distance to identify and record part of the global diffusion effects (from extra-cerebral tissue such as scalp and skull) to regress them from the whole signals. In any case, technical advances concerning artefact removal and signal quality improvement are still needed.

Assets and Drawbacks

Both fNIRS and fMRI measure BOLD variations, so why using fNIRS? As compared to fMRI, fNIRS admittedly suffers specific limitations. The most prominent are restricted spatial resolution and measuring brain depth, that limit measurements to the cortical surface without access to subcortical structures, and the confounding influence of extracranial signals and anatomical parameters. Regarding spatial resolution, whereas fMRI can measure activity in the entire brain, fNIRS only monitor and record cortical activations, penetration depth being 1.5–2 cm. This makes a problem for fNIRS, as sub-cortical structures such as for instance the amygdala reputedly playing a role in social cognition (Adolphs 2010), are not detectable. Furthermore, in many cases, fNIRS optodes cannot cover the full brain surface at once, limiting to a partial apprehension of functional activity and connectivity (Lu et al. 2010). This is due to the fact that a single fNIRS instrument features a limited

number of optodes, but most importantly because the distance between source and detectors cannot be too close (no diffusion in brain tissues, only skull or leakage effects) or too far away (bad signal-to-noise ratio). The typical trade-off source-detector distance is 3–3.5 cm for adults and 2–2.5 cm for infants. Overall differences in scalp and skulls thickness between infants and adults (Brigadoi and Cooper 2015) can explain these differences in source-detector distance, along with the fact that signal quality is not homogenous across different brain areas. Indeed, scalp thickness is more important in temporal than in frontal and parieto-occipital regions (Brigadoi and Cooper 2015). Besides, inter-individual differences between participants' skull and scalp thickness may also lead to dissimilar signal outputs, although it is rare that these differences impede detecting differential changes in cortical oxygenation (e.g. between conditions in a within-subject design). A common practice to optimize signal-to-noise ratio is to determine in advance the regions of interest, and to position the measuring optodes over these pre-determined regions only. Besides coverage limitation, fNIRS also suffers from the confounding influence from some artefacts and physiological noises: (1) artefacts associated with noises of instrumentation, improper optodes fixation and excessive motion (e.g., body movements, head nodding, mouth opening and shutting, swallowing); (2) physiological noise related to heartbeats, respiratory activities and low-frequency fluctuations. Finally, fNIRS cannot obtain structural anatomical images, something MRI can do.

Considering these drawbacks, what are the assets of fNIRS? First, fNIRS is inexpensive to use while being able to study the mechanisms underlying the BOLD signal better than fMRI. Indeed, fNIRS separately captures HbO and HbR changes (whereas the fMRI BOLD signal results from the contrast between these two parameters), which allow studying the relationships between these two haemoglobin concentrations. Relatedly, in contrast to fMRI, fNIRS achieves a better temporal resolution (e.g., 10–100 Hz) than fMRI, and provides a good option to investigate the dynamics of the rise and fall of the BOLD signal. Its temporal resolution also makes fNIRS a good option for real-time neurofeedback and brain computer interface paradigms (Duan et al. 2013; Erdoğan et al. 2019), and functional connectivity analysis (Tak and Ye 2014). Due to intrinsic limitations in hemodynamic measurements, it can be argued that BOLD response as measured by fNIRS remains quite slow (5–8 s to peak). Nevertheless, its finer temporal resolution allows machine-learning algorithms to detect signals with much smaller delay than fMRI (Cui et al. 2010b). But perhaps one crucial advantage of fNIRS is to allow measuring cortical hemodynamics in naturalistic conditions (Quaresima and Ferrari 2019). For instance, fNIRS has been used to study cortical activity in real-life face-to-face communication (e.g., Jiang et al. 2012), sports and exercise (e.g., Balardin et al.

2017), driving (e.g., Liu et al. 2017b), singing (e.g., Pan et al. 2018), teaching (e.g., Liu et al. 2019), and psychological counselling (e.g., Zhang et al. 2018). Also as mentioned above, fNIRS is relatively tolerant to body movements as compared to other motion-sensitive techniques (e.g., fMRI or EEG). This provides a split advantage since in conventional laboratory studies, participants are often constrained by experimental settings in which their mental and physical activity differs from real daily life. To the contrary, modern, small and portable fNIRS equipments can be used in unconstrained environments. Another asset of fNIRS is that it is quite easy to combine with other techniques such as electroencephalography (EEG; Leamy et al. 2011), transcranial Direct Current Stimulation (tDCS; Borragán et al. 2018b), Transcranial Magnetic Stimulation (TMS; Kozel et al. 2009), fMRI (Heinzel et al. 2013, or even magnetoencephalography (MEG; Huppert et al. 2017). Hence, fNIRS is a good tool for a multi-modal imaging approach gathering high temporal, spatial and frequency information related to neurovascular coupling. Last but not least, easy applicability and high ecological validity make fNIRS particularly suitable for studying special populations. Indeed, fMRI is not entirely user-friendly. Strictly speaking, some persons are prevented to enter fMRI experiments for safety considerations, or experience claustrophobia in the narrow MRI scanner environment. Likewise, shrapnel and other metal parts in the body, electronic body implants (hearing aids, pacemaker) or pregnancy are exclusion criteria. In these cases and others, fNIRS is advantageous to investigate hemodynamics within specific populations. Altogether, these assets make fNIRS a promising approach to study the neural mechanisms underlying human performance and cognitive functions. Hereafter, we will describe and discuss the use of fNIRS to investigate neural hemodynamic processes underlying applied societal problems such as fatigue, sleep deprivation and social cognition (see Fig. 3), which are all crucial elements of human living.

Applications of fNIRS in Fatigue and Sleep Deprivation

Fatigue

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

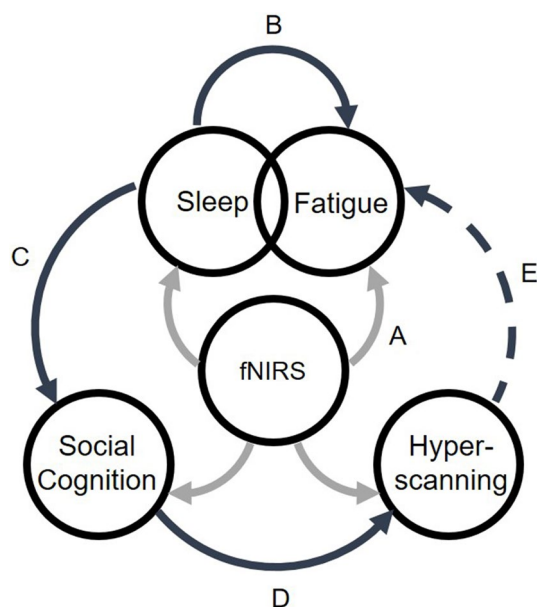


Fig. 3 **a** The use of fNIRS in studies of fatigue, sleep deprivation, and social cognition and combinability of fNIRS with the hyper-scanning approach (i.e., measuring two brains simultaneously, Pan et al. 2017, 2018). **b** Sleep deprivation and fatigue partially overlap: a portion of fatigue stems from sleep deprivation. **c** Sleep deprivation affects social cognition and interaction. **d** The intrinsic power of fNIRS measure in social cognition can be improved by combining the hyper-scanning approach. **e** Similar approach in the research involving fatigue and sleep deprivation is still lacking

muscle blood volume and HbO concentrations significantly declined at the onset of the contraction, and remained constant throughout the rest of the contraction. Yoshitake et al. (2001) demonstrated that blood flow restriction due to high intramuscular mechanical pressure was a crucial factor in muscle fatigue.

Since then, rapid methodological advances allowed for more systematic investigations of functional activity in the context of fatigue, using multi-channel fNIRS devices and/or more sophisticated data analysis strategies. Also, there has been a shift from a restricted focus on physical fatigue to the cerebral correlates of cognitive or mental fatigue. Cognitive fatigue is characterized by the decline in cognitive resources that follows sustained cognitive needs irrespective of sleepiness, typically accompanied with speedily perceived exhaustion (Trejo et al. 2015). Overall, these studies found fatigue-related oxygenation changes mostly within prefrontal and parietal areas during various cognitive tasks (e.g., sustained-attention reaction-time task, simulated driving, working memory task; De Joux et al. 2013; Derosière et al. 2013; Liu et al. 2016; Jiao et al. 2012; Zhang et al. 2017; Borragan et al., 2018a, b, 2019; see also a recent review in Qi et al. 2019). These studies generally reported increased hemodynamic responses in prefrontal and parietal cortices in exhausted as compared to control individuals (e.g., Chuang

et al. 2018; De Joux et al. 2013; Derosière et al. 2013; Zhang et al. 2017).

Counteracting fatigue and performance maintenance are often accompanied by increased hemodynamic activity in frontal, primary motor, parieto-occipital and supplementary motor areas (Chuang et al. 2018). For instance, Liu et al. (2014) reported that increased activation in prefrontal regions help maintaining desirable performance levels during a driving task (Liu 2014). Similarly, Borragan et al. (2019) reported increased fronto-parietal activation during task-related induction of cognitive fatigue. These neurophysiological findings are in line with the patterns of cerebral blood flow changes revealed by other neuroimaging methods such as fMRI (e.g., Gui et al. 2015), Positron Emission Tomography (e.g., Tajima et al. 2010) or EEG (e.g., Wang et al. 2016).

The advantage of using the fNIRS technique to investigate fatigue capitalises on the nature of the phenomenon investigated. Either cognitive or motor, the triggering of fatigue often entails exposing participants to long-duration (up to more than 1 h) paradigms characterised by over-time repeated demands, which represents a limiting factor given that the longer the task, the higher the probability to capture noise coming out from external sources such as, for instance, movements. Notwithstanding, relative movement's tolerance in fNIRS technology is a good asset to perform clean recording within medium-long periods. On the other hand, it was demonstrated that fatigue can also be initiated in controlled conditions over much shorter periods of time (e.g., 16 min; see Borragan et al. 2017, 2018a, b, 2019; Tak and Ye 2014), providing the additional advantage to trigger fatigue without altering arousal. Finally, fNIRS is optimal to explore the triggering of fatigue and/or other similar situations at risk to interfere with optimal task performance, such as for instance attentional overload, stress, drowsiness or sleep deprivation (Borragan et al. 2019) within realistic environments.

Driving

According to the U.S. Department of Transportation, almost 1 out of 2 persons commute to work in the U.S. every day, and 86% of these people use a motorised vehicle. However, driving is not always a safe activity; the World Health Organisation estimates that road traffic injuries caused 1.35 million deaths worldwide in 2016. Being able to predict attentional lapses and disengagement could be a promising approach to reduce the number of accidents in the future, a task that is well suited to the peculiarities of portable, lightweight fNIRS. Indeed, fNIRS studies have been shown able to detect associations between car driving events and changes in cortical activity (Takahashi et al. 2011). For instance, increased prefrontal activation was reported during speed deceleration (Yoshino et al. 2013), distraction (Nosrati

et al. 2016) or when participants take left as compared to right oriented curves (Oka et al. 2015). An important finding was that fNIRS was able to reveal differential demands in visual attention, that participants were actually unable to report (Oka et al. 2015). In the same vein, other fNIRS studies reported how changes in functional connectivity between fronto-motor areas are associated with decreased performance within time on task or cognitive fatigue (Xu et al. 2017; Borrigan et al. 2019). These studies exemplify how using fNIRS might have useful future applications for road safety.

Piloting

The capacity of fNIRS to be used in realistic settings such as the cockpit of a plane put it quickly at the edge of research investigating plane pilot performance (e.g., cognitive fatigue and workload; Gateau et al. 2015). Recent results evidenced that fNIRS has the capacity to detect critical safety aviation issues such as fatigue or inattentive deafness (Verdière et al. 2018). Similar conclusions apply to the railroad area. Increased automation driven by the installation of modern Automatic Train Operators (ATO) systems might paradoxically lead to decreased arousal in train operators, making them less prompt to respond if needed. Kojima et al. (2005) showed that fNIRS systems are a viable option to detect exhaustion conditions and differences in brain activity between manual and automatic train operations (Kojima et al. 2005).

Sport Science

As mentioned above, optical devices were originally developed to investigate changes in muscle metabolism and muscle oxygenation in exercise and sport science (Chance 1991). Thanks to its portability and tolerance to movements, the system is optimal to measure haemoglobin changes in the muscle during/after specific training (Kounalakis et al. 2008) in a large set of populations from judokas (Kujach et al. 2016) to handball and hockey players (Jones et al. 2015), cyclists (Wittekind et al. 2012) or climbers (Philippe et al. 2012). Notwithstanding the reliability of fNIRS to assess oxygenation changes during these activities, it must be considered that fatiguing tasks are often accompanied by changes in cardiorespiratory rhythms (Zhao et al. 2012), which might alter the quality of fNIRS recordings (Zhang et al. 2016b). In addition, fNIRS can be used to investigate the direct/indirect effects of exercise on cognitive functions (Yanagisawa et al. 2010) or to assess patient's motor rehabilitation strategies (Lin et al. 2009). Promising results have also been reported using fNIRS in a Brain Computer Interface (BCI) setting (Rea et al. 2014).

Pedestrian Safety

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

Technical Operators

fNIRS was used to assess the mental state of technical operators in a large variety of settings. For instance, fNIRS proved a reliable technique to measure workload and cognitive fatigue in air traffic controllers (Ayaz et al. 2012), radiologists (Nihashi et al. 2019) or unmanned aerial vehicles (Izzetoglu et al. 2015). Future applications could include the assessment of attentional states in nuclear plant engineers or staff and security guards. Finally, combining fNIRS with EEG is growing rapidly in the domain of human neuroergonomics. Indeed, combining these techniques allow assessing complementary brain signals; i.e., cerebral hemodynamic and neuronal electrical activity. Furthermore, classification accuracy of algorithms detecting attentional disengagement is often better when using both techniques (Nguyen et al. 2017). 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.

Patients

Besides, fNIRS has proven an effective tool to assess fatigue and attentional disengagement in some neurological conditions; for instance, Multiple Sclerosis (MS) disease in which fatigue is often viewed as the most debilitating symptom. In

particular, fatigue in MS disease features a cognitive component—cognitive (or mental) fatigue. Borragán et al. (2018a) exposed patients with MS disease and healthy controls to a cognitive fatigue-inducing dual working memory updating task. During the experiment, participants' cortical activity was recorded using a 24-channel fNIRS system (BrainSight, V2.3b16, Rogue Research Inc., Canada) over bilateral fronto-parietal regions (i.e., ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, and inferior parietal cortex). Results showed comparable levels of perceived cognitive fatigue, task performance, and brain activity patterns in patients with MS disease and control participants. Notably, oxygenation level changes in the dorsolateral prefrontal cortex significantly correlated with perceived cognitive fatigue in MS patients (Fig. 4). Finally, longer sleep time positively associated with higher cognitive fatigue the patients with MS disease. This study therefore provided valuable evidence linking cognitive fatigue, sleep features and cortical activity patterns in MS disease.

Sleep Deprivation

A portion of human fatigue stems from sleep deprivation or sleep disturbances. fNIRS applications in sleep deprivation conditions have also been of interest for the scientist. More than 10 years ago, researchers started to use fNIRS to investigate the brain mechanisms underlying sleep deprivation and complement phenomenological descriptions of sleep complaints. These studies targeted the effect of sleep deprivation on mental fatigue (e.g., Ahn et al. 2016; Borragán et al. 2019), time perception (e.g., Soshi et al. 2010), driving performance (e.g., Miyata et al. 2010), and working memory (e.g., Yeung et al. 2018). In almost all cases, sleep

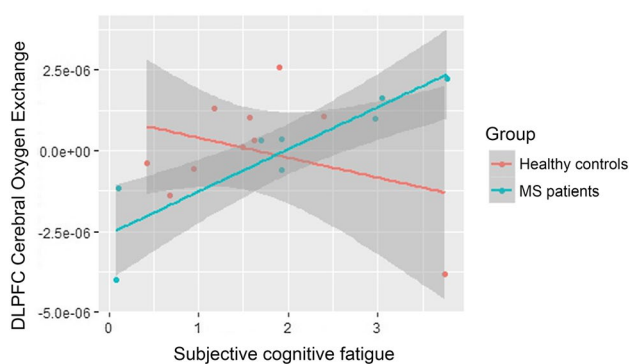


Fig. 4 Association between subjective cognitive fatigue (CF) and dorsolateral prefrontal cortex (DLPFC) cerebral oxygen exchange index. Results disclose a direct relationship, present only in patients with Multiple Sclerosis (MS), between DLPFC cerebral oxygen exchange and the triggering of subjective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

deprivation was demonstrated to impact cognitive functions, and to be accompanied by alternations of prefrontal oxygenation responses (e.g., Miyata et al. 2010; Yeung et al. 2018), even when participants were not totally sleep deprived (e.g., Yeung et al. 2018). The change of prefrontal activity was either a decrease (e.g., Borragán et al. 2019; Bu et al. 2017; Miyata et al. 2010; Fig. 5) which might reflect the cognitive deficit, or an increase (e.g., Honma et al. 2010; Soshi et al. 2010) possibly reflecting compensatory recruitment mechanisms.

Sleep disturbances are also commonly observed in patients suffering from psychiatric conditions. For instance, fNIRS was proposed to assist the diagnosis of major depressive disorder. Nishida et al. (2017) investigated the possible association between sleep assessment and haemoglobin dynamics in major depressive disorder. Results showed that (1) self-rated depression negatively correlate with cerebral reactivity in the right temporal region (2) and self-rated sleep disturbances negatively correlate with HbO changes in the left prefrontal cortex. These findings suggest that left prefrontal cortex reactivity is susceptible to sleep complaints in patients with major depressive disorder. In another study, Sun et al. (2017) investigated haemoglobin response patterns of patients with chronic insomnia disorder using multi-channel fNIRS. Results evidenced reduced prefrontal activation during a verbal fluency task in chronic insomnia disorders.

Although suffering from sleep deprivation, humans might also demonstrate an inherent ability to overcome sleepiness and counteract accumulated sleep pressure. Using fNIRS, Honma et al. (2010) found that activity in the right prefrontal cortex is associated with the ability to overcome sleepiness during a modified *n*-back (2- and 0-back) working memory task. In this study, participants' right prefrontal activity correlated with self-rated alertness changes on the 2- and 0-back conditions. Cerebral activity in the right prefrontal area was proposed to fulfil a functional compensatory mechanism allowing the participant to meet the task load demands.

Applications of fNIRS in Social Cognition

In the last decade, a growing number of studies aimed at investigating the brain mechanisms underlying social cognition using fNIRS, capitalizing on its ecological validity. As discussed "[Assets and Drawbacks](#)", fNIRS is advantageous to examine brain activity patterns under social contexts and naturalistic circumstances, which is of particular relevance when studying the cerebral correlates of social cognition. Previous fNIRS studies spanned age groups from infancy (e.g., Lloyd-Fox et al. 2014) to adulthood (e.g., Egetemeier et al. 2011) and elderly (e.g., Pu et al. 2008), focusing on various topics including joint action (e.g., Herrmann et al. 2015), joint attention (e.g., Zhu and Godavarty 2013), social

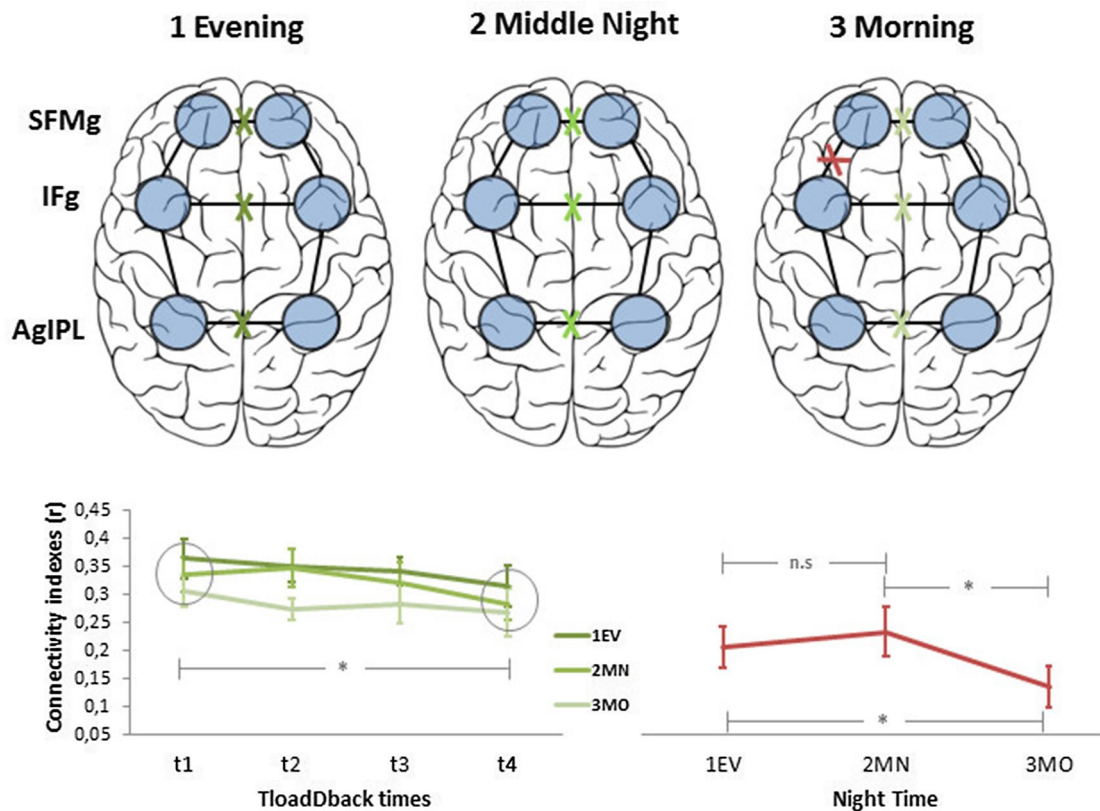


Fig. 5 Intra- and inter-hemispheric connectivity changes following sleep deprivation. Blue circles indicate the regions of interest where activity was recorded using fNIRS (reproduced from Borragán et al. 2019). Green Xs indicate inter-hemispheric connections in which connectivity decreased from the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

communication (e.g., Suda et al. 2010) and spontaneous deception (e.g., Zhang et al. 2016a). Additionally, analogous studies were conducted in patients (e.g., Köchel et al. 2015; Takei et al. 2013; Zhu et al. 2014).

Joint Action

Much of human daily work requires inter-individual action coordination. Using fNIRS, Egetemeir et al. (2011) assessed brain activation during real-life joint action tasks. Joint action (i.e., to cooperate with a partner to perform a table setting) compared to solo action (i.e., to perform the task alone) induced higher HbO concentrations in a set of brain areas including the inferior parietal lobule, reputedly part of the mirror neurons system. Herrmann et al. (2015) further tested the functional role of polymorphism 5-HTTLPR in real-life joint action; they confirmed that participants with the short variant of the polymorphism exhibited increased parietal brain responses during real-life joint action.

Joint Attention

The question of what happens in the brain of participants sharing an attentional focus on the same object/event during a social interaction is of particular interest. Even by the age of 5 months, infants are sensitive to social interactions, as shown in an fNIRS study by the recruitment of left dorsal prefrontal cortex activity when engaged in joint attention with others (Grossmann and Johnson 2010). Other fNIRS studies in healthy children evidenced different HbO concentrations in frontal regions between joint and non-joint attention interactions (Chaudhary et al. 2011). Zhu and Godavarty (2013) implemented a lagged covariance structural equation model to fNIRS measurements during joint attention tasks in normal adults, allowing to compute differences in the path coefficients amongst different conditions (i.e., joint attention and non-joint attention) that revealed distinct interhemispheric connectivity in the frontal region.

Communication

The human brain may have evolutionarily adapted to face-to-face communication, which is a significant feature of all social species. To examine the brain characteristics of early human social cognitive abilities, Grossmann et al. (2008) examined cortical specialization for the perception of facial communication cues in infants. Perceiving facial communication signals resulted in temporal and prefrontal cortex activation in infants, like in adults. Suda et al. (2010) validated the potential of fNIRS for studying social interactions in a naturalistic setting. Specifically, they investigated the haemoglobin dynamics during face-to-face communication. Speaking compared to mute segments induced higher activity in frontal and superior temporal regions. Apart from verbal communication, neural processes underlying non-verbal communication were also tested (i.e., eye-to-eye contact, Hirsch et al. 2017), and within-individual results revealed that eye-to-eye contact compared to eye-to-picture gaze induced higher left frontal activation, synchronized with functional activity in the left superior temporal regions.

Deception

Deception is ubiquitous in human societies, and requires a high level of social cognition. Using fNIRS, Ding et al. (2013) found that as compared to truth telling, spontaneous deception (free to choose telling the truth or a lie) triggers larger neural activity in the left superior frontal cortex. Also, the reward system might be involved in spontaneous deception. In a follow-up study, Ding et al. (2014) examined the cerebral correlates of second-order deception (i.e., the recipient of deception is fully aware of the deceptive intention of the deceivers and thus the deceiver has to use both lies and truths to deceive). Results demonstrated the involvement of a broad area of the prefrontal cortex in second-order deception (Ding et al. 2014). In a later study (Zhang et al. 2016a), graph theory analyses further revealed that spontaneous deception as compared to control deception (instructed to tell the truth or a lie) resulted in greater clustering coefficients, shorter average path lengths, greater average node degrees, and stronger randomness; these results indicate that the functional networks of brain activity for the spontaneous behavior exhibited greater aggregation, efficiency and randomness during deception (Zhang et al. 2016a).

Several studies using multi-channel fNIRS also probed differences between psychiatric patients and healthy samples to evidence abnormal brain activity patterns possibly underlying social cognitive deficits. As compared to typically developing children, children with autism spectrum disorder exhibited reduced interhemispheric (resting-state functional) connectivity and lower local connectivity in bilateral temporal cortices (Zhu et al. 2014). Likewise, as

compared to healthy controls, elderly people with late-onset major depression exhibited reduced frontopolar activation during verbal fluency tasks, associated with poor social functioning (Pu et al. 2008). Patients with borderline personality disorder showed left medial prefrontal cortex hyperactivity during social exclusion (Ruocco et al. 2010), and patients with schizophrenia exhibited decreased HbO changes in both the temporal lobes and the right inferior frontal gyrus during face-to-face conversation (Takei et al. 2013). In children with attention deficit hyperactivity disorder, there was decreased activity in the right superior temporal gyrus when processing anger prosody, and increased supramarginal gyrus activity when being exposed to affectively angry sentences (Köchel et al. 2015). Altogether, these studies suggest the potential of fNIRS for the investigation of the neural correlates of diverse psychiatric syndromes.

fNIRS-Based Hyperscanning

Social cognition and interactions typically involve at least two agents. Conventional fNIRS (and other) studies focused on single person recordings, to some extent overlooking the interaction between individuals. However, single-person neuroscience is insufficient to capture the subtle nature of human dynamic interactions (Schilbach et al. 2013). Recent advances move our focus from single-brain functioning to two-brain communication using the hyperscanning approach (Pan et al. 2017, 2018). In this section, we will discuss how fNIRS hyperscanning can boost the intrinsic power of studying social cognition.

Hyperscanning, i.e., measuring two or more brains simultaneously (Montague et al. 2002), is a recently developed approach (see an example in Fig. 6a). One major feature distinguishing fNIRS-based hyperscanning from other hyperscanning modalities (e.g., EEG, Babiloni et al. 2006, and fMRI, Montague et al. 2002) is that, a single fNIRS acquisition device could be split into two (or more), allowing to use half of the channels for each participant and record simultaneously their brain activity (Cui et al. 2012). 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 coupling two heavy and distant installations (like with fMRI, MEG). Also, the use of a single system for both participants easily solves the calibration/synchronization problem that often occurs when using two/multi devices.

A crucial aspect of online human-to-human/brain-to-brain investigations relates to the measure of interpersonal brain synchronization (or inter-brain coherence, or synchronous brain activity; Fig. 6b). Interpersonal brain synchronization as a neural marker of social interactive activities has been adopted in many studies in the field of social

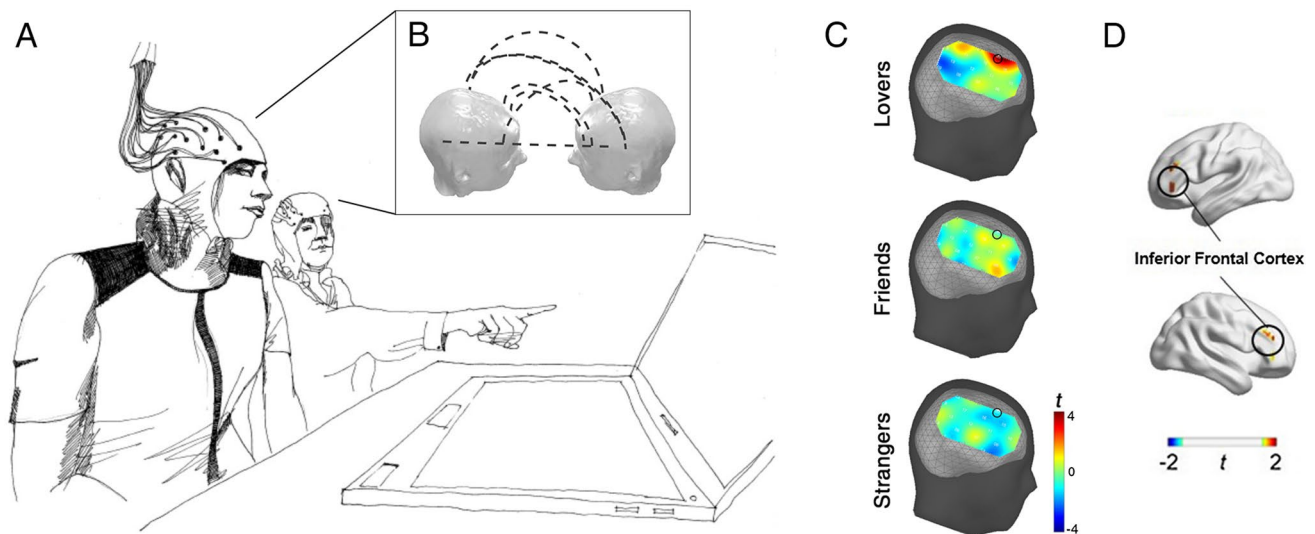


Fig. 6 **a** Representative illustration of a fNIRS-based hyperscanning experimental scenario. A teacher is transmitting knowledge to a student, during which their brain activity is recorded by fNIRS simultaneously (Pan et al. 2019). **b** Interpersonal brain synchronization (IBS) emerges as a result 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 (Color figure online)

neurosciences, including joint action (Cheng et al. 2015; Cui et al. 2012; Funane et al. 2011; Pan et al. 2017), social communication (Hirsch et al. 2017; Jiang et al. 2012; Liu et al. 2017a), and teaching and learning (Liu et al. 2019; Pan et al. 2018; Zheng et al. 2018). The first fNIRS-based hyperscanning study focused on the brain characteristics of joint action, which requires cooperation/coordination between two partners (Funane et al. 2011). Participant dyads were required to mentally count 10 s after an auditory cue and press a button as simultaneously as possible. Results disclosed inter-individual synchronous activity in the prefrontal cortices, associated with their cooperation performance. Following on, Cui et al. (2012) asked participants to either press the button as simultaneously as possible (cooperation) or to answer faster than the partner (competition). Results revealed inter-brain coherence in the right superior frontal cortices during cooperation, but not during competition. Increased inter-brain coherence also paralleled better cooperation performance. Further fNIRS-based hyperscanning studies showed that the gender of partner (Cheng et al. 2015) and the inter-partner relationship (Pan et al. 2017) modulate synchronous brain activity in the prefrontal cortices during cooperative exchange (Fig. 6c).

Regarding social communication, Jiang et al. (2012) demonstrated a significant increase in neural synchronization between partners in the left inferior frontal cortex during face-to-face dialog. Furthermore, communication behaviours could be accurately predicted based on neural synchronization levels. Liu et al. (2017a) further demonstrated that

HbO concentrations in the listener were significantly correlated with HbO concentrations in the speaker with a delay of approximately 5 s. Except for live verbal communication, Hirsch et al. (2017) also showed that during non-verbal eye-to-eye contact, brain-to-brain coherence (based on HbR concentrations) increased within left superior temporal, middle temporal, and supramarginal gyri as well as the pre- and supplementary motor cortices.

Educational activities such as teaching and learning are a fertile domain to investigate the neurophysiology of social cognition, since they involve a series of social processes including imitation and observation (Pan et al. 2018). Functional NIRS-based hyperscanning allowed focusing on the dyadic interaction between teaching and learning brains. Simultaneous measurements of the brain activity of teacher-student dyads disclosed higher time-lagged brain-to-brain synchronization between the right temporo-parietal junction of the teacher and the anterior superior temporal cortex of the student (Zhang et al. 2018). Pan et al. (2018) reported synchronization between the inferior frontal cortices of teacher and student, when the teacher was teaching a music song to the student (Fig. 6d). Also, such interpersonal brain synchronization between teachers and students could be biased by prior knowledge and communication mode, as revealed by fNIRS-based hyperscanning (Liu et al. 2019). Strongly indicating its functional significance, interpersonal brain synchronization with teacher compensated for student's sleep deprivation in an interactive learning task (Pan et al. 2019). Functional NIRS-based hyperscanning and

interpersonal brain synchronization thus provide powerful measures to track interpersonal interactions and social cognition under naturalistic circumstances.

Current Challenges

Technical and Methodological Difficulties

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

Unavailable Subcortical Regions

As mentioned above, the penetration depth of fNIRS light is typically 1.5–2 cm. Theoretically, one can slightly enlarge the distance between fNIRS source and detector to increase the measuring depth, at the cost of reduced signal-to-noise however. Measuring depth limitation in fNIRS prevents the investigation of subcortical regions potentially involved in fatigue, sleep deprivation and social cognition (e.g., the amygdala in social cognition, Adolphs 2010), and their interactions with cortical structures.

Confounds in fNIRS Data

The fNIRS signal is potentially confounded by at least two factors. First, anatomical parameters such as scalp-to-cortex distance may affect the reliability of fNIRS data (e.g., Haussinger et al. 2011). Second, peripheral hemodynamic parameters such as skin perfusion may cause physiological fluctuations (e.g., Tong et al. 2011). Despite the development of advanced methods such as principal component spatial filtering (Zhang et al. 2016b) or Correlation-Based-Signal-Improvement (Cui et al. 2010a) to correct systemic effects and motion artefacts, it is yet unclear whether these unwanted components can be completely excluded. Further methodological advances in data pre-processing are needed here.

Non-Standardized Analysis Pipelines

Standardized and well-accepted analysis pipelines are available for many neuroimaging modalities (EEG and fMRI), facilitating the report and replication of findings, and their interpretation. fNIRS data still lacks such a standardized data processing pipeline. Commonly accepted approaches include spatial registration, motion artefact removal, local/global component separation and data filtering (Cui et al. 2010a, Cui et al. 2012; Zhang et al. 2016b). However, there is no consensus on empirically based, uniform, and user-friendly analysis guidelines,

hampering the comparability and reproducibility between existing studies. Additionally, there is a need to develop more powerful and multivariate fNIRS data analysis approaches, e.g. Multivariable Pattern Analysis (Gemignani et al. 2018).

HbO, HbR or Both?

Functional NIRS nicely provides us concentration changes for two distinct brain signals, i.e., HbO and HbR. Theoretically, regional brain activation is characterized by concurrent increased HbO and decreased HbR. However, due to physiological interferences and systemic changes, only one concentration (either HbO or HbR) might show significant changes to a task/stimulus in real fNIRS data recordings. As such, previous empirical work often focused on only one concentration, and rarely used both. The consensus is scarce on which concentration to use since both HbO and HbR feature advantages and disadvantages, as discussed Sect. 1.1. Besides, other studies also took into account their combination by using either the sum (i.e., HbT, Nozawa et al. 2016) or the difference of HbO and HbR (Borragán et al. 2018a). Future studies are still needed to delineate when, why and how to use HbO, HbR or their combination.

Interpretation of fNIRS Results

A spatial format based on structural features seems natural for interpreting fNIRS data. However, cortical-level fNIRS results can prove difficult to interpret due to a restricted detection depth and partial coverage over the scalp. For example, Cheng et al. (2015) reported coherent brain activity in frontopolar, orbitofrontal and left dorsolateral prefrontal cortices across participant dyads during cooperation. Activity in these areas was previously linked to a series of cognitive functions including social cognition (e.g., Contreras et al. 2011), reward (e.g., Rushworth et al. 2011) and metacognitive processes (e.g., Amodio and Frith 2006). Nonetheless, it is difficult to infer from fNIRS data whether these processes have a combined effect or work independently. Besides, cortical-level results can receive various interpretations due to multiple functional meanings associated with specific cortices, eventually leading to a relative ambiguity and arbitrariness in the interpretation of fNIRS data. Additionally, it is not possible using fNIRS to determine the contribution of subcortical structures, and how and to what extent their activity is responsible for variations in cortical activity in specific contexts. Multimodal imaging is a possible solution to data gained using fNIRS with other modalities (e.g., EEG or fMRI) and help in their interpretation.

Conclusions and Prospects

To sum up, fNIRS is a valid and promising brain imaging tool that can usefully complement other neuroimaging techniques to study the human brain and cognitive functions. Despite some limitations, fNIRS has its own assets and can provide valuable contributions to investigations in the fields of fatigue, sleep deprivation and social cognition, as reviewed here. Functional NIRS may also empower a better understanding of the neural bases of fatigue, sleep complaints and social deficits. The intrinsic power of fNIRS measurement can further be improved if combined with other brain imaging modalities, and even more if applied to the hyperscanning paradigm. Hopefully, technical and methodological advances will progressively broaden the scope of fNIRS applications to other facets of human performance and cognitive functions.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no actual or potential conflicts of interest concerning this work.

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