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Review

Functional near infrared optical imaging in cognitive neuroscience: an introductory review

Simone Cutini,[a,*] Sara Basso Moro[a] and Silvia Bisconti[b]

[a]Department of General Psychology, University of Padova, Padova, Italy. E-mail: simone.cutini@unipd.it

[b]Department of Health Sciences, University of L'Aquila, L'Aquila, Italy

Cognitive neuroscience is a multidisciplinary field focused on the exploration of the neural substrates underlying cognitive functions; the most remarkable progress in understanding the relationship between brain and cognition has been made with functional brain imaging. Functional near infrared (fNIR) spectroscopy is a non-invasive brain imaging technique that measures the variation of oxygenated and deoxygenated haemoglobin at high temporal resolution. Stemming from the first pioneering experiments, the use of fNIR spectroscopy in cognitive neuroscience has constantly increased. Here, we present a brief review of the fNIR spectroscopy investigations in the cognitive neuroscience field. The topics discussed encompass the classical issues in cognitive neuroscience, such as the exploration of the neural correlates of vision, language, memory, attention and executive functions. Other relevant research topics are introduced in order to show the strengths and the limitations of fNIR spectroscopy, as well as its potential in the biomedical field. This review is intended to provide a general view of the wide variety of optical imaging applications in the field of cognitive neuroscience. The increasing body of studies and the constant technical improvement suggest that fNIR spectroscopy is a versatile and promising instrument to investigate the neural correlates of human cognition.

Keywords: cognitive neuroscience, near infrared spectroscopy, fNIRS, optical imaging, cognition, psychology, human brain mapping

Introduction

Cognitive neuroscience is a multidisciplinary field focused on the exploration of the neural substrates underlying cognitive functions; it originated in the early 1980s from the connection between neuroscience and cognitive science although over the years it has constantly been enriched by an increasing interaction with several other disciplines,[1] such as neurophysiology, neuroanatomy, neuropsychology, psychophysiology and computational modelling. Nowadays, cognitive neuroscience represents a prominent field in the investigation of the human brain. Due to its multidisciplinary nature, cognitive neuroscience adopts several investigation methods, such as lesion studies, multi-unit and single-cell recording; nevertheless, the most remarkable progress in understanding the relationship between brain and cognition has been made with functional brain imaging methods.

Before the advent of brain imaging, the association between brain regions and cognitive functions was mainly provided by clinical neuropsychological investigations of brain-damaged patients and post-mortem examination. When brain imaging was introduced, cognitive scientists were given the chance to investigate the human brain in a wide variety of actions, from perception to higher order mental activities. With brain

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imaging, scientists started to address not only which brain areas were necessary for a specific cognitive function, but also the neural circuitry involved in a particular mental activity (e.g. when reading a word[2]). The wide variety of brain imaging methods available can provide different measurements of the neural correlates of cognitive processes: for instance, some methods record the magnetic (magnetoencephalography) or electrical (electroencephalography, EEG) fluctuations occurring in relation to neural activity, while other methods, such as functional magnetic resonance imaging (fMRI) and functional near infrared spectroscopy (fNIR spectroscopy, or fNIRS) measure local changes in cerebral haemodynamic activity that can be used to infer information on the underlying neural activity (Figure 1). In this respect, the term "neurovascular coupling"[3–5] indicates the well-known link (both in terms of space and amplitude) between neural activity and the local change in cerebral blood flow (CBF). Since neither glucose nor oxygen reserves are present in neurons, an increase in neural activity is accompanied by an increase in regional CBF, providing additional glucose and oxygen to the area of active neurons. Given that the increase in CBF is significantly higher than the corresponding oxygen consumption, the resulting effect leads to the haemodynamic response (Figure 1): a net increase in the amount of oxygenated haemoglobin (HbO) and a net decrease of deoxygenated haemoglobin (HbR). Such an over-supply of oxygen, generated by CBF, is the basis of the blood-oxygenation level dependent (BOLD) signal used in fMRI,[6,7] which broadly corresponds to the HbR response.[8]

Among all the brain imaging techniques, fMRI is considered as the "gold standard" technique for non-invasive functional mapping of the human brain. Nevertheless, the use of fNIR optical imaging in the cognitive neuroscience field has increased significantly in recent years. Similar to fMRI, fNIR spectroscopy monitors haemodynamic changes in the brain;[9] however, unlike the BOLD signal of fMRI, which derives contrast from the paramagnetic properties of HbR, brain optical imaging is based on: (i) high near infrared (650–1000 nm) light propagation into scattering tissues and (ii) absorption by the main chromophores (HbO and HbR of the red blood cells). Using light sources with two or more different wavelengths (e.g. 690 nm and 830 nm), fNIR spectroscopy can simultaneously record HbO and HbR [as well as total haemoglobin (HbT) given by the sum of HbO and HbR] concentration changes with high temporal resolution (typically > 10 Hz). Cortical haemodynamic activity can be recorded by locating a set of optodes (i.e. optical fibres) over the scalp: sources emit the near infrared light which is conveyed to the scalp by means of optical fibres, while other optical fibres collect the photons emerging from the scalp and convey them to be measured by near infrared detectors. Each source–detector pair is considered a measurement point (i.e. channel). Multi-channel fNIR spectroscopy, obtained by using arrays of multiple optodes (sources and detectors) placed on the scalp [Figure 2(a)], represents the current standard technology. Some typical instruments are shown in Figure 2(b).

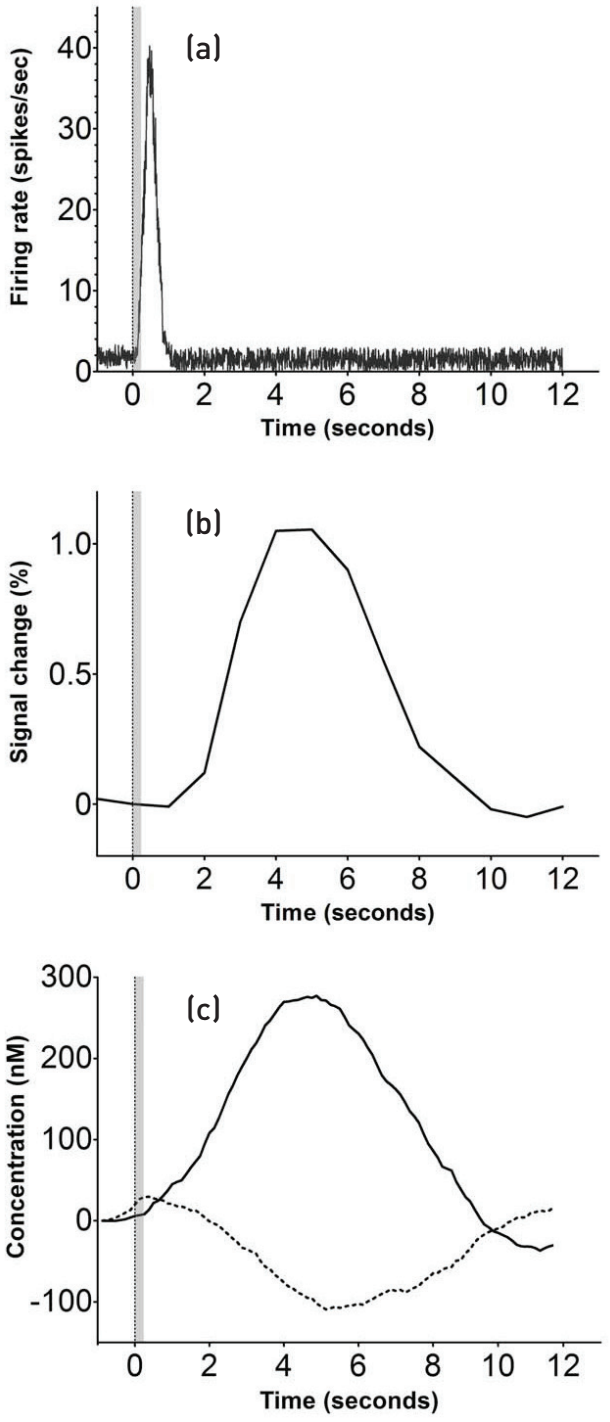

Figure 1. Illustration of the connection between neural activity and haemodynamic response in an event-related paradigm. (a) Neural response. (b) BOLD response. (c) HbO (solid line) and HbR (broken line) responses obtained with fNIR spectroscopy. In all panels, the dotted vertical line indicates the onset of the stimulus, whereas the grey rectangle indicates the stimulus duration. The (fictitious) neural and haemodynamic data highlight (i) the temporal difference between neural firing and the correspondent haemodynamic response, (ii) the lower temporal resolution exhibited by the fMRI signal with respect to the fNIR spectroscopy signal, and (iii) the different shape of HbO and HbR response profiles.

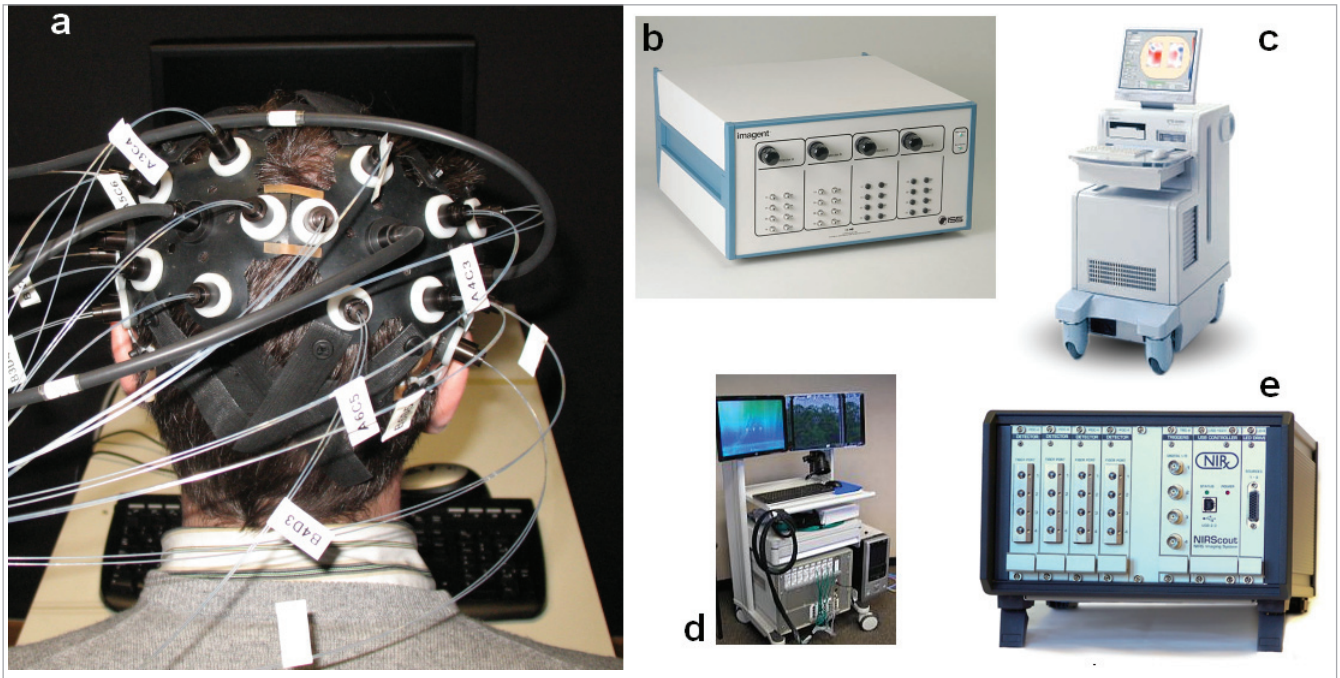

Figure 2. (a) A typical example of an fNIR spectroscopy probe holder placed on the head of a participant (bilateral parietal lobe). In this set-up, thin optical fibres (diameter 0.4 mm) convey near infrared light to the participant's head (note that each location comprises two optical fibres, one for each wavelength), whereas optical fibre bundles (diameter 3 mm) capture the light that is scattered through the brain tissue. (b) to (e) Various fNIR spectroscopy instruments. (b) The ISS Imagent: http://www.iss.com/biomedical/instruments/imagent.html; (c) the Hitachi ETG 4000: http://www.hitachi-medical-systems.eu/products-and-services/optical-topography/etg-4000.html; (d) the Nirsoptix Brain Monitor: http://www.techen.com/index.cfm?event=brainmonitor and (e) the NIRScout: http://www.nirx.net/imagers/nirscout-xtended.

Today, fNIR spectroscopy users can choose between several commercial fNIR spectroscopy instruments with different characteristics, as shown, for example, in Figure 2(b). A recent study[9] provided an exhaustive list of the currently available fNIR spectroscopy instruments with the main technical details (the complete list can be found on the website of the industries). The increasing number of commercial fNIR spectroscopy instruments available is related to the promising results obtained with fNIR spectroscopy in cognitive neuroscience: even if fNIR spectroscopy has some peculiar disadvantages with respect to fMRI (for example, fNIR spectroscopy measurements are limited to cortical activity), it might potentially provide a richer picture of cortical haemodynamics compared with fMRI. Furthermore, fNIR spectroscopy imposes negligible physical/motor constraints on participants, so that movements and the experimental setting can be ecologically sound, thus providing some advantages that could be very beneficial for the biomedical field.

Although NIR spectroscopy as a non-invasive instrument for brain haemodynamic monitoring was introduced more than 30 years ago,[10] its use for functional brain mapping was applied for the first time in the early 1990s: pioneering works[11–14] demonstrated the possibility of functional brain mapping with NIR spectroscopy. For instance, one of the first investigations[11] found that there was an increase of HbO and a decrease in HbR across the frontal and occipital cortices in response to cognitive tasks and visual stimulation, respectively. In the same year, another study[14] showed that cerebral blood volume increased in the occipital cortex (but not in the frontal cortex) during photic stimulation in five adult volunteers tested with fNIR spectroscopy. Subsequent studies[15,16] found that during mental arithmetic and problem solving tasks, some parts of the prefrontal cortex (PFC) exhibited a modulation of HbO and HbR concentrations depending on the task.

Starting from these experiments, the use of fNIR spectroscopy in cognitive neuroscience has constantly increased. Here, we present a brief review of the fNIR spectroscopy investigations in the field of cognitive neuroscience. The topics presented in the following sections encompass the classical issues investigated in cognitive neuroscience, such as the neural correlates of vision, language, memory and attention, as well as some more recent themes, such as functional connectivity and brain–computer interface. The objective of the present review is to provide a general picture of the applications of fNIR spectroscopy and its potential in cognitive neuroscience (obviously, it is not an exhaustive list of all the fNIR spectroscopy investigations in the field of cognitive science). The topics investigated with fNIR spectroscopy discussed below are divided into paragraphs to provide improved readability.

Executive functions

Executive functions include a broad category of cognitive operations that drive complex behaviour, such as selection of the appropriate action, inhibition of inappropriate actions or irrelevant information, planning, conflict resolution, cognitive flexibility; the neural correlates of executive functions are thought to be located in the PFC.[17] One of the first studies that investigated the field of the executive functions with fNIR spectroscopy[18] aimed at detecting the small metabolic changes in the frontal cortex when performing cognitive tasks, as already observed in previous studies.[11,13,16] The authors adopted the continuous performance test (a repetitive task where participants must respond to targets and inhibit the response to non-targets) to examine the involvement of the frontal brain regions with 2-channel fNIR spectroscopy. The main result they observed was a difference in the course of HbR, but not HbO, between the right and left hemisphere. In contrast to left frontal areas, in which HbO and HbR increased at the beginning and decreased at the end with the same curve, right frontal areas showed a significantly smaller initial increase of HbR followed by a decrease on baseline level. Another study[19] introduced a motor control task within a response inhibition paradigm, investigating brain oxygenation of PFC with a 24-channel fNIR spectroscopy instrument. In this experiment, participants were asked to perform a "go/no-go" task in which the "no-go condition" was the experimental condition and the "go condition" was the control condition. A significantly higher increase in HbO in the most inferior part of the PFC was found by analysis for the "no-go condition" in comparison with the "go condition". In addition to the go/no-go task,[20] inhibitory processes[21] also have been investigated with fNIR spectroscopy by using the stop signal task,[22] which is widely adopted to assess motor inhibition performance and is considered more demanding than a go/no-go paradigm.[23] A recent study[24] investigated the involvement of PFC in such a task. In some trials, participants were asked to reconfigure their (already initiated) response, thus providing a different response from that already programmed. The results were very interesting. First, the authors localised the neural correlates of response inhibition in the inferior PFC; second, they found a strong increase in the right PFC during successful inhibition of already initiated responses, as well as a bilateral increase of activity in PFC when the inhibition was unsuccessful. These studies, together, bring evidence in favour of the feasibility of functional fNIR spectroscopy to measure the changes in cortical blood oxygenation due to the inhibition of prepotent and/or already initiated responses.

Other trends in research confirm the appropriateness of fNIR spectroscopy to assess executive functions. The Stroop effect[25] is considered a prominent behavioral demonstration of cognitive conflict processing. In Stroop tasks, a stimulus with at least two dimensions is presented. Participants are instructed to give a behavioural response on the basis of the task-relevant stimulus dimension and neglect the other dimension. In the incongruent condition of Stroop tasks, in each trial the task-relevant stimulus dimension prompts a certain behavioural response while the task-irrelevant stimulus dimension prompts a different behavioural response. In contrast, in the congruent condition, the task-relevant and task-irrelevant stimulus dimensions prompt the same behavioural response. Interestingly, there has been a massive investigation of the Stroop effect with optical imaging (which has been briefly reviewed in a recent work[26]). For instance, one[27] of those investigations showed how the interference during the incongruent trials of a colour–word matching Stroop task causes stronger bilateral brain activity in the lateral PFC. The increase of HbO and the decrease of HbR were significantly higher in the incongruent condition with respect to the neutral condition in the superior-lateral PFC. Another study[28] that investigated the frontal oxygenation in response to a Stroop colour–word task was conducted utilising multi-channel fNIR spectroscopy. In incongruent trials, a specific increase in HbO and HbT in the left inferior-frontal brain areas was observed, although the haemodynamic modulation of superior-frontal areas due to Stroop interference was less pronounced in comparison with previous results.[27]

Interestingly, a seminal fNIR spectroscopy study[29] comparing young versus older people during Stroop task has shown that the haemodynamic activity of the lateral PFC is significantly influenced by age. It is also worth mentioning that some studies have focused on the Stroop task in clinical populations such as patients with cerebral microangiopathy[30] or children with attention deficit disorder.[31] Notably, fNIR spectroscopy has been successfully used in clinical populations also with other paradigms, highlighting the potential use of fNIR spectroscopy in the medical area. Patients that are hard to test with other neuroimaging techniques, such as impulsive children,[32] patients with Parkinson's disease or patients with dementia[33] have been successfully tested with fNIR spectroscopy.

Several other experimental paradigms concerning executive functions have been used with fNIR spectroscopy. For instance, in a recent fNIR spectroscopy investigation,[34] the PFC of the participants was monitored using a computerised version of the Trail Making Test; during the performance, the researchers observed a bilateral frontal increase in HbO and a decrease in HbR. In another optical imaging study,[35] concentration changes of HbO and HbR were monitored during the digit span task using multi-channel fNIR spectroscopy. The digit span task is widely used in neuropsychological research and clinical evaluation: it involves remembering a set of numbers in the standard order (digit span forward) or in the reverse order (digit span backward). While in the digit span forward no significant difference was observed in the concentrations of HbO during the performing phase compared to the resting phase, the digit span backward performance caused a significant increase in HbO with respect to the rest interval. Thus, the digit span backward task required greater PFC activation than the digit span forward. The results replicated those carried out earlier with other imaging techniques[36] and are consistent with a previous fNIR spectroscopy study,[37] which described an

activation of the right dorso-lateral prefrontal cortex (DLPFC) when the digit span backward task was performed.

Another fNIR spectroscopy experiment[38] aimed at isolating the neural correlates of task-switching.[39] In a typical task-switching paradigm, subjects are instructed to repeat the same task over a variable number of trials and switch to a different task at some point during the trial sequence. Each task often involves a rapid response and a reaction time is usually recorded. The finding of interest is that the mean reaction times in switch trials are longer than those in repetition trials. Such a difference is attributed to the task-set reconfiguration,[39] which consists of enabling a different response set and adjusting response criteria. There is no substantial agreement about the neural correlates of task-set reconfiguration: although most brain imaging studies on task-switching found a co-activation of two key regions [the DLPFC and the superior frontal gyrus (sFG)], an influential fMRI study[40] investigated the possible functional dissociation between these two regions. According to this account, both the DLPFC and sFG would be engaged while carrying out a task-switching paradigm, but only the sFG would be determinant for switching between tasks *per se*: whereas the DLPFC would be primarily involved in the maintenance and coordination of the different stimulus–response mapping rules in working memory, the sFG would be more directly related to reconfiguring the cognitive parameters demanded by the execution of a specific task upon detection of a stimulus feature associated with the task-switch. The authors performed a sophisticated fMRI investigation, showing that these two regions are interdependent but functionally separable. The aforementioned fNIR spectroscopy experiment[38] was aimed at providing additional evidence with regard to the functional dissociation of these two regions. In order to exclude potential confounds, the task-switching paradigm was designed with an equal number of switch and repetition trials and with an unpredictable occurrence of switch trials. The results of the optical investigation indicated that both the DLPFC and sFG were actively engaged during the execution of the task-switching paradigm but, most importantly, only the activity of the sFG was significantly higher in switch trials with respect to repetition trials.

Emotions

In recent years, the neural correlates of emotion in humans have been intensely investigated. The amygdala is a subcortical structure which is well known to be crucially involved in emotion processing; nevertheless, several studies investigated whether emotion might also be related to cortical activity. For instance, an fMRI study revealed that the PFC is involved in emotional regulation,[41] showing a broad hemispherical asymmetry between left and right PFC for positive and negative emotions, respectively (for details see a recent review[42]). An fNIR spectroscopy investigation[43] used 2-channel fNIR spectroscopy to measure the brain activity of the left and right medial PFC, while participants were presented with a set of pictures. The paradigm had two conditions in which the self-monitoring requirement was manipulated: low self-monitoring (i.e. just look at the emotional pictures presented) or high self-monitoring (i.e. try to feel like the emotion expressed by the stimulus presentation). The results showed that the assignment type influenced the blood oxygenation of the frontal lobe: when the task required more self-monitoring processes, there were significantly higher HbO concentrations in the frontal left hemisphere, especially when highly emotional pictures were viewed. This result suggests that self-monitoring processes are tightly involved in certain aspects of emotional induction and might contribute to frontal activation. It should also be noted that the frontal cortex is tightly involved in the maintenance of attentional demands of a task[44] and action monitoring.[45] The relationship between prefrontal activation and processing of emotional stimuli was investigated in a recent fNIR spectroscopy experiment,[46] which revealed that prefrontal activation is present both in emotion induction and emotion regulation. Notably, the effect was located in the left PFC and it was limited to HbR (with no HbO difference).

Another fNIR spectroscopy investigation[47] examined the influence of emotional content on the occipital cortex during visual stimulation. Interestingly, emotionally positive and negative stimuli produced a larger decrease of HbR in specific areas of the occipital cortex in comparison with the decrease induced by neutral stimuli. A recent fNIR spectroscopy study[48] showed that the haemodynamic response peak latency of the visual cortex is modulated by the emotional valence of the stimuli. Specifically, the processing of positive pictures caused reduced haemodynamic response peak latency with respect to negative pictures. Besides the theoretical implications of these results, it is worth noting that fNIR spectroscopy was able to capture a temporal difference that might be hardly detectable with fMRI, confirming that the higher temporal resolution of fNIR spectroscopy can be effectively used under the right circumstances and with the appropriate objectives. Another recent fNIR spectroscopy study[49] examined the modulation of auditory cortex by emotional auditory stimuli, finding that pleasant and unpleasant sounds produced stronger auditory cortex activity as compared to neutral sounds; the results suggest that human auditory cortex activity is modulated by complex emotional sounds.

Vision

The neural correlates of vision have been extensively investigated with fNIR spectroscopy since the first optical imaging experiments (see Introduction) and nowadays the activity of the occipital lobe continues to be investigated in optical studies.[50] A recent fNIR spectroscopy study of the visual cortex[51] was aimed at dissociating the task-related activity from the effect of attentional load, in order to exclude a potential confound in the interpretation of the results. Not surprisingly, the authors found that the amount of attention paid during the execution

of the task significantly affected the HbO concentration, thus proving that the occipital activity can be influenced by attentional processes (this suggestion could well be extended to other brain regions).

Visual tasks can be adopted to investigate the neural activity of brain areas close to the visual cortex. For instance, an fNIR spectroscopy study[52] investigated the haemodynamic activity of the parieto-occipital areas during a visuo-spatial task. In the experimental condition (line orientation), participants had to discriminate the orientation of a line, whereas in the control condition (colour naming) they had to identify the colour of the line. Interestingly, the line orientation task led to a significantly higher HbO concentration of the bilateral parieto-occipital cortex than that observed in the line colour naming condition. The HbO difference between the two conditions was likely to be specifically linked to the higher cognitive demands in the spatial domain during the line orientation task. An investigation[53] tested the feasibility of event-related design with multi-channel fNIR spectroscopy. The authors measured brain activity during the performance of a simple motor and visual task and they were able to show that event-related paradigms can provide valid estimations of the haemodynamic concentrations and that they have considerable advantages (for example, optimally controlled experimental structure, reduced impact of low-frequency signal components due to physiological artefacts).[54,55] Similarly, visual and motor cortices were the main topic of a 52-channel fNIR spectroscopy study[56] aimed at exploring the regional specificity of cortical activation. It was possible to detect dissociable patterns of haemodynamic activity due to different tasks. As expected, during visual and motor tasks, the activations were observed in occipital and motor cortices, respectively, demonstrating the sensitivity of multi-channel fNIR spectroscopy in detecting cortical activation in humans. Besides these generic studies, there are also intriguing investigations specifically focused on the functional organization of the occipital lobe.

Indeed, the visual cortex is an ideal region for testing innovative brain mapping approaches because: (i) it has been used as a platform for the first experiments with fMRI;[57] (ii) its organisation has been precisely described with invasive methods in humans;[58] (iii) its activity is usually characterised by high reliability at group level.[50] The human visual cortex is retinotopically structured: it is segregated into four quadrants [Figure 3(a)], which are contralaterally organised and reversed on the vertical dimension [for example, lower left visual quadrant is coded in the upper right visual cortex quad-

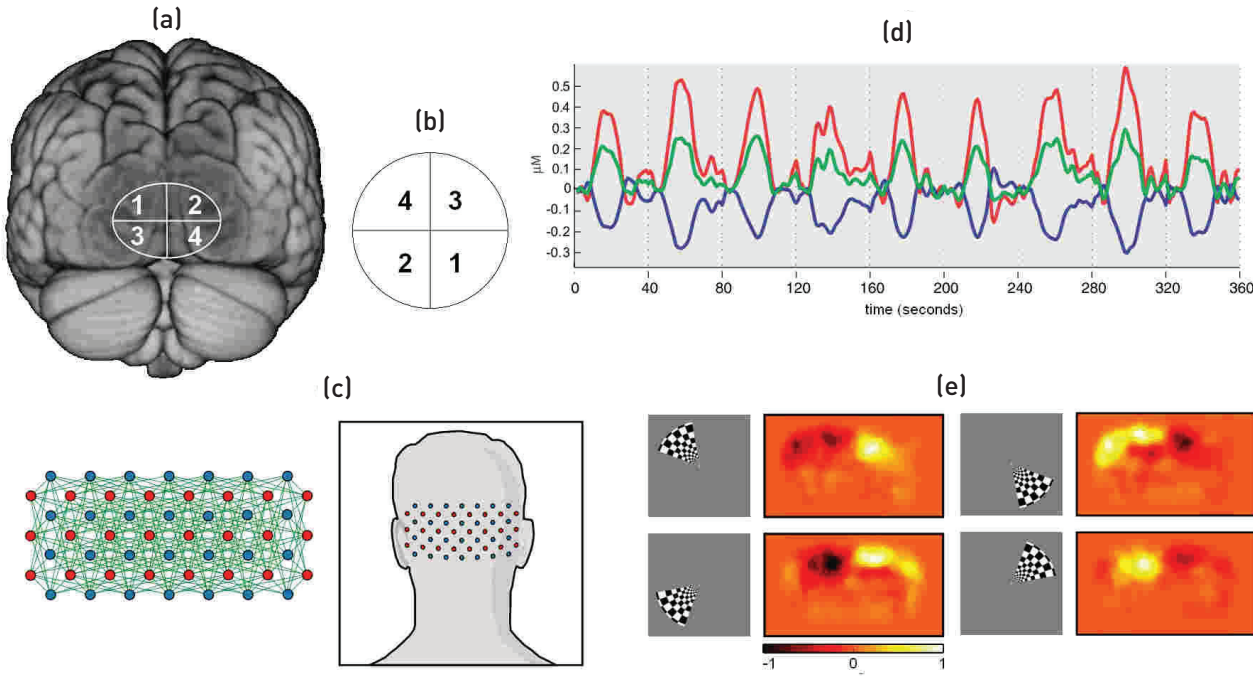

Figure 3. (a) A template brain with superimposed visual quadrants (numbered from 1 to 4). (b) Schematic illustration of the visual field: by comparing the organisation of the visual field with that of the visual cortex, it can be observed that visual quadrants are contralaterally organised and reversed on the vertical dimension (numbers from 1 to 4 refer to the same visual quadrant). (c) Illustration of the dense imaging array (sources: red; detectors: blue; channels: green) and its placement in correspondence of the visual cortex. (d) Single subject functional activity in correspondence of nine individual visual stimuli (*x*-axis: time in seconds; *y*-axis: concentration change): the first stimulus appears at time equal to 0 and then stimulation is repeated every 40 s, as indicated by dotted lines. The haemodynamic response profiles of the different concentrations are shown (HbO: red; HbR: blue; HbT: green). (e) Single-subject optical maps derived from functional responses to a rotating grid (speed of 10° of polar angles per second); the retinotopic organisation of the visual cortex is highlighted by the four optical maps recorded in different positions of the rotating grid. Copyright (2007) National Academy of Sciences, USA. Figures 3(c)–(e) are adapted from Reference 60.

rant, see Figures 3(a) and (b)]. Previous fNIR spectroscopy studies on visual cortex activity focused on discriminating contralateral activations,[59] mainly because the spatial resolution required to correctly identify retinotopic maps (< 1 cm) was inaccessible until recently. This relevant step forward with optical imaging was accomplished in an influential diffuse optical tomography (DOT) investigation of the visual cortex.[60] Using a high-density optode arrangement with 24 sources and 28 detectors [Figure 3(c)], with different source–detector separation distances that contributed to provide a haemodynamic signal [see Figure 3(d)] characterised by a remarkably high signal-to-noise ratio (SNR), the authors described individual retinotopic maps within the visual fields quadrant and angular maps of the visual cortex [Figure 3(e)], being able to detect shifts of activity of less than 1 cm. These robust intra-individual results showed that DOT has the potential to be used effectively in single-subject investigations. The features of the retinal maps found in the DOT investigation were consistent with previous results, suggesting that high-density DOT might be an efficient method for detailed mapping of cortical activity (see the somatosensory section for another high-resolution DOT study[61]). This impressive result was further extended by another DOT study:[62] using visual stimuli designed to generate a travelling wave of activation in the visual cortex, the authors were able to perform a detailed phase-encoded mapping of the retinotopic organisation of the visual cortex, as well as the representations of multiple visual angles and eccentricities within an individual hemisphere. These results testified to an important improvement in spatial resolution and SNR, confirming the significant progress at the level of detail that can be obtained from non-invasive optical imaging of functional brain responses.

Finally, it is worth noting that the difference between visual stimulation and mental imagery has been investigated with fNIR spectroscopy: a different involvement of parietal and occipital areas has been found in perception and imagery of affective pictures, demonstrating that different emotional stimuli modulate the visual cortex activation during mental imagery.[63]

Somatosensory activity

The somatosensory cortex (SI) receives sensory input from the body and converts it in a fuller sensory perception. The SI provides a cortical representation of the body (based on the degree of sensory innervation): for instance, it allows the source of a sensory input to be localised and its level of intensity assessed. The SI is located in the post-central gyrus and it has been widely investigated in optical imaging.

In an influential fNIR spectroscopy study,[64] the haemodynamic activity of SI has been measured during (i) unilateral finger opposition task, (ii) finger tactile stimulation and (iii) electrical median nerve stimulation of the left and right hands. The authors observed a systematic HbO increase/HbR decrease (i.e. a typical haemodynamic response) located contralaterally to the stimulated hand and a larger response to the unilateral finger opposition task with respect to the other two conditions. Notably, under median nerve stimulation, a standard haemodynamic response was observed contralaterally, while the ipsilateral side showed a haemodynamic inversion (i.e. HbO decrease/HbR increase).

A more recent fNIR spectroscopy study[65] checked for the presence of an objective haemodynamic signature of pain perception. The authors administered innocuous and noxious thermal stimuli to participants while recording their haemodynamic activity in the SI. Interestingly, the findings suggested that thermal innocuous and noxious stimuli can be distinguished on a temporal basis of the response in the SI: innocuous stimuli elicited a monophasic response on the contralateral side with a weak ipsilateral response, whereas the noxious stimulation caused a biphasic response with comparable amplitudes in the two hemispheres. These results strongly suggest that fNIR spectroscopy can be used effectively to assess acute pain in an objective way.

A recent DOT investigation[61] monitored haemodynamic activity of the SI during a finger tapping task and vibrotactile stimulation of the little finger and the thumb, using a methodological approach comparable to that exhibited in the pioneering investigation of retinotopic maps.[60] Using a multi-distance high-density optical imaging sensing array in conjunction with optical tomographic reconstruction, the authors were able to detect three dissociable functional patterns of activity: the finger tapping task recruited part of the pre-central gyrus (motor cortex), while vibrotactile stimulation of the thumb and the little finger engaged two distinct activation foci in the SI.

The anatomical reliability of the resulting optical maps was evaluated by comparing each individual optical map with the co-registered brain anatomy [obtained with magnetic resonance imaging (MRI)] of the correspondent participant; such comparison confirmed the localisation of the activation foci in the expected cortical regions on a single-subject basis. These results confirmed the potential of high-density DOT, showing that a dense arrangement of optodes may provide a dramatic increase in spatial sensitivity.

Motor activity

The primary motor cortex is located in the pre-central gyrus and it is one of the most investigated regions (for more details, see a recent review[66]) in optical imaging, mainly because of its strong and reliable activation during motor tasks.[67] Simple motor tasks, such as finger tapping, hand grasping and finger-to-thumb opposition have been employed by researchers to study the pattern of response of the motor cortex. As expected, knowing the data that come from fMRI,[68,69] the typical pattern of response elicited by a simple motor task is observed as rapid increases in HbO and HbT concentrations and a decrease in HbR concentration[70–72] which are spatially localised on the contralateral motor cortex.

For instance, a recent fNIR spectroscopy study[73] used a finger tapping task to investigate the pattern and the time course variations of brain activity across the task periods. During haemodynamic recording of frontal, temporal and parietal areas, participants were required to lean their thumb sequentially (i.e. from the index finger to the little finger and then in reversed order) on each finger as fast as possible while respecting the sequence order. Generally, finger tapping caused a higher haemodynamic response in the contralateral hemisphere, with HbO increase in a broad area surrounding the motor cortex and a HbR decrease in a more restricted area. Furthermore, the authors attempted to perform a functional segregation of the different brain regions based also on the time course variation across the task: according to them, it was possible to observe three partially overlapping anatomical clusters related to execution, sensory monitoring and maintenance of finger tapping.

Another fNIR spectroscopy study[74] investigated the influence of motor task complexity on the cortical activity. Participants were asked to perform different finger tapping tasks: unimanual simple and complex tasks and bimanual tasks. Simple and complex right hand tasks caused the largest HbO increase, followed by bimanual and left hand tasks, thus showing a significant task influence on motor cortex activity. Note also that other optical investigations revealed that the haemodynamic response in the motor cortex is strongly modulated by tapping frequency[75] and intensity.[76]

Memory and attention

The activation of the PFC in memory tasks has been widely examined with fNIR spectroscopy. For instance, a typical pattern characterised by an increase in HbO and a decrease in HbR was observed during a word memory task.[77] A sophisticated fNIR spectroscopy study[78] investigated the haemodynamic activity during the execution of a visual *n*-back task. This paradigm recruits both memory and selective attention: while observing a sequence of stimuli, the participant has to indicate whether the current stimulus matches the one presented from *n* steps earlier in the sequence (task difficulty can be manipulated by changing the value of *n*). In this optical study, the activity of the PFC was investigated while performing the aforementioned *n*-back task, with sequentially presented task-relevant and task-irrelevant faces. Participants were instructed to press a response button whenever a presented face of the relevant category (i.e. a white-bordered face) matched the previously presented face of the same category (pointed out by the black arrow above one picture). Relevant stimuli activated the middle frontal/pre-central cortices bilaterally and the left post-central cortex, probably in relation to a verbal rehearsal strategy to maintain the features of the relevant stimuli. Conversely, irrelevant stimuli activated superior, middle and inferior parts of the right PFC, consistently with the selective inhibition needed to properly perform the task. Thus, the results indicated that the prefrontal activity during working memory tasks reflected processes of maintenance, selection and inhibition of information, as well as attentional monitoring.

The PFC has also been studied in relation to information encoding and retrieval, which are known to involve partially overlapping neural circuits.[79] The results of a recent fNIR spectroscopy investigation on taste encoding and retrieval[80] indicated that haemodynamic activity during taste retrieval was significantly stronger than that observed during encoding in the bilateral frontopolar and dorsolateral prefrontal regions, particularly in the right hemisphere. These results are broadly consistent with the hemispheric encoding/retrieval asymmetry theory.[81] In parallel to memory, attention has been extensively investigated with fNIR spectroscopy. An optical investigation[82] measured the haemodynamic changes of the PFC during a continuous performance test. Participants were asked to react to infrequent letters appearing on a screen but not to frequent distractors. An increase in HbO and HbR was found in the DLPFC, but the lack of a suitable control task limited the interpretation of the results. Although the neural substrates of visuo-spatial attention have been widely investigated, it is not clear whether the attentional resources required for each visual hemifield are functionally separated between the cerebral hemispheres. An fNIR spectroscopy investigation[83] recorded brain activity during a visuo-spatial task. Interestingly, an increase in attentional load produced a greater increase in brain activity in the case of the left visual hemifield than in the case of the right visual hemifield. This asymmetry was observed in all the examined brain areas, including the bilateral occipital and parietal cortices; the strongest activations were seen in posterior parietal cortex, including the intraparietal sulcus. Those results have been interpreted as an effect of the asymmetry of inhibitory interactions between the hemispheres.

Interestingly, the same regions are involved in specific memory tasks. Indeed, a recent fNIR spectroscopy study[84] investigated the neural correlates of visual short-term memory; previous neuroimaging studies attempting to isolate the neural substrate of visual short-term memory in humans have concentrated on the posterior parietal cortex; in particular, classical fMRI studies have revealed that the activity recorded in posterior parietal regions increases with the number of objects encoded in visual short-term memory,[85] but only up to its capacity limits, levelling off thereafter. In the optical investigation, the authors adopted a spatially cued variant of the change–detection task to record haemodynamic responses to unilaterally encoded objects; participants were shown an arrow head pointing to the left or to the right side of the screen. The offset of the arrow was followed by a memory array, which was composed of either four or eight coloured squares, evenly distributed to the left/right of fixation (i.e. either two on each side, or four on each side). Participants were instructed to maintain their gaze at fixation and memorise the colour of the squares on the side of the memory array cued by the arrow head. Following the memory array offset, participants were shown another array of coloured squares in the same positions as occupied by the squares of

the memory array. Participants had to indicate (with button press) whether a change in colour had occurred or not. This task provides very different results for EEG and fMRI: whereas electrophysiological data[86] show that maintenance of unilaterally encoded objects elicits a contralateral negative activity (proportional to the number of objects retained in visual short-term memory), fMRI results indicate a modulation of the BOLD response in relation to the number of memorised elements in the parietal lobes of both hemispheres.[87] Similarly to fMRI results, the optical imaging investigation revealed a memory-related increase in HbO concentration located bilaterally in the posterior parietal cortex, even though objects had to be encoded unilaterally in the absence of eye movements. Interestingly, the high similarity of such results with those obtained with fMRI[87] suggests that EEG and fMRI/fNIR spectroscopy techniques might reveal partially distinct neural signatures of the mechanisms supporting visual short-term memory.

Language production

Language has been extensively investigated with optical imaging, thus this section and the following one are meant to provide general information on the use of fNIR spectroscopy in the language field (for a more extensive description of the literature, see a recent review[88]). Many fNIR spectroscopy studies are focused on the neural correlates of language during the generation of words beginning with a certain letter, in the letter version, or including the same category, in the semantic version. An optical study[89] investigated the effects of age and gender on brain activation during a letter verbal fluency task (VFT). The results indicated an effect of age: elderly participants showed less activity in the left DLPFC than younger ones and no lateralisation was seen in these participants; on the other hand, there was no effect of gender (although a previous study[90] found a higher frontal and temporal activity in males than in females).

In another study,[91] the short- and long-term reliability of brain activity was evaluated with a test–retest phonological VFT. The participants were asked to repeat the same task after 3 and 53 weeks from the first and second data collection, respectively. In both sessions, increases in HbO and decreases in HbR were observed in the inferior DLPFC and in part of temporal cortex; nevertheless, the authors observed a smaller haemodynamic response in the second session. Analysis of the brain activation in the time course revealed an adequate reliability of fNIR spectroscopy for repeated measurements of the cortical activity at group level, even though a weak retest reliability was found at single subject and single channel levels. The fNIR spectroscopy was employed in another study[92] to investigate the lateralisation and the functional connectivity of the frontal cortex in response to a VFT and jaw movement. First, the results demonstrated a significant difference in the activation between VFT and jaw movement in the PFC. Furthermore, a bilateral activation and a symmetrical connectivity of PFC were present in both tasks, although the laterality index calculated on the anterior frontal cortex showed a left hemispheric predominance; likewise, the connectivity analysis showed an asymmetrical neural recruitment of the same region during the VFT.

Other fNIR spectroscopy studies used word generation tasks in the determination of language hemispheric dominance as an alternative to the invasive Wada test[93–95] revealing the fNIR spectroscopy potential in the presurgical exploration of language. In order to investigate brain activity during a language-related task, the authors of an fNIR spectroscopy investigation[96] compared a covert visual object naming task (which required subjects to name pictures without oro-facial movements) to two motor tasks: finger opposition and tongue movement. Although the HbO increase was similar in the three tasks, HbR changes were larger in the anterior inferior frontal area during covert visual object naming tasks with respect to tongue movement. Moreover, a greater decrease in HbR in the posterior frontal regions during finger opposition was observed in comparison to the other two tasks.

Overt picture naming has been used in an fNIR spectroscopy experiment on bilinguals[97] to investigate the brain mechanisms that allow them to correctly use two languages without confusion. The authors compared the use of signed and spoken language in rapid alternation from bilingual to monolingual mode during an overt picture naming task; although bilinguals showed an accurate performance in both conditions, a greater activation of left posterior temporal regions was observed when bilinguals executed the task in bilingual mode than in monolingual mode, indicating a role of these areas in the bilingual language switching ability. Effects of the use of a second language were evaluated in an fNIR spectroscopy study[98] on sentence generation in native Dutch individuals who were proficient in English. The protocol required an overt translation of visually presented sentences; the sentences could have been presented in either of the two languages separately or alternately. The involvement of the left frontal cortex, which includes the Broca's area, was evidenced by an increase in HbO and a smaller decrease in HbR in all conditions although no differences were detected when subjects translated the sentences separately or in alternation.

Language representation has been investigated by fNIR spectroscopy during speech production to understand brain activity during social interactions;[99] the authors monitored an ordinary face-to-face conversation, assuming that autistic traits in typically developed participants were correlated to the amplitude of haemodynamic signals. Interestingly, the results indicated a negative correlation between autistic traits and the activity of the left superior temporal sulcus region of males (but no correlation was found for the PFC).

Language comprehension

Language processing has been investigated in a fNIR spectroscopy study[100] on syntactic and semantic decision tasks. Participants were asked to identify the presence of

semantic or syntactic errors contained in sentences. Although similar performances or reaction times were performed in the two conditions, the left inferior gyrus was more activated in the syntactic processing in contrast to the semantic processing.

Language comprehension has been studied through the discrimination of phonems, words or speeches in many fNIR spectroscopy studies. In a recent investigation,[101] the implicit processing of phonotactic cues was studied by co-registering fNIR spectroscopy and EEG. Monosyllabic pseudo-words, that were defined as phonotactically legals when the first consonant was equal to the onset of a German word, or illegals when it was not with respect to German, were presented to native German speakers. The hypothesis associated with the task was that pre-lexical cues processing in the spoken word recognition might modulate the lexical activation processes in the auditory speech. The fNIR spectroscopy results demonstrated a significant HbR decrease in the left fronto-temporal hemisphere for phonotactically legal pseudo-words with respect to that observed for illegal pseudo-words. These findings were confirmed by a larger response for phonotactically legal pseudo-words in EEG parameters, providing evidence that processing of legal phonotactic components contributes to language comprehension.

In an optical study on bilingualism,[102] Japanese long- and short-vowel contrasts were investigated in native Japanese speakers and in Korean subjects who spoke fluent Japanese as a second language. The results showed different cortical patterns of response in the two groups. Independently, by short- or long-vowel contrast, native Japanese speakers demonstrated a greater left activation in correspondence of Wernicke's area. On the other hand, fNIR spectroscopy results did not show a different neural recruitment or left predominance when phonemic differences were presented in speakers learning Japanese, despite behavioural results indicated that these participants were able to discriminate between long/short vowels. These findings suggested that, on some occasions, behavioural performance is not representative of the underlying haemodynamic activity.

Resting state functional connectivity

The study of resting state functional connectivity deserves to be briefly mentioned because of its potential. Resting state functional connectivity investigates the spontaneous cerebral haemodynamic fluctuations that reflect neuronal activity at rest. A recent study[103] investigated the spatio–temporal correlation of haemoglobin concentration signals over the whole head during resting state. Similar to previous fMRI investigations,[104] the authors found consistent regional interactions across participants. In particular, sensorimotor and visual cortices exhibited a strong interhemispheric correlation, while the PFC was subjected to higher variability. Importantly, the high definition of the maps obtained with HbT suggests that it could be useful to localise with precision the functional connectivity. Taken together, these findings confirm that resting state functional connectivity can be effectively investigated with whole head fNIR spectroscopy recording. Another recent optical investigation[105] verified the test–retest reliability of fNIR spectroscopy-based resting state functional connectivity in sensorimotor regions. Brain activity of participants was recorded during two resting state sessions separated by one week and independent component analysis was used to extract resting state functional connectivity in the somatosensory areas. The authors found an excellent reliability at group level, a reasonable reliability at individual level but a weaker reliability at a channel-wise level. Although these results confirm the high reliability of the fNIR spectroscopy-based resting state measurement, the authors conclude that a stringent probe placement method is required to increase channel-wise reliability in fNIR spectroscopy recording. Some probe placement methods[106–108] can provide consistent positioning of optodes across participants and/or sessions without the need of individual MRI scans. For instance, a method[107] designed for DOT measurements allows the focus of cortical activity to be reconstructed with reasonable precision. Another probe placement method[106] is based on the use of a physical model of the ICBM152 template (i.e. the current standard brain template in fMRI, which was obtained by averaging the MRI scans of 152 subjects) head surface as a reference scalp, and its validity is supported by previous investigations of cranio-cerebral correlation.[109] Notably, the latter approach offers a reproducible and straightforward method to place the optodes on the head surface, according to the stereotaxic coordinates of the regions of interest. This aspect is critical, because it ensures a ready comparison of fNIR spectroscopy results within the neuroimaging community, both across studies and techniques. Note that the use of those methods should be strongly encouraged within the community of fNIR spectroscopy users, since almost all types of fNIR spectroscopy investigations might benefit greatly from the adoption of a rigorous probe placement method.

Brain–computer interface

The brain–computer interface (BCI) is a research field that might dramatically benefit from the use of fNIR spectroscopy technology in the coming years. BCI consists of a system that allows a direct link between the brain and an external device. The main objective of BCI is to assist or substitute cognitive or motor functions in humans. BCI can represent an effective way to communicate and interact with the environment for the disabled, such as patients suffering from amyotrophic lateral sclerosis, brainstem stroke and spinal cord injury.[110]

Although one of the main obstacles to a proficient use of fNIR spectroscopy in BCI is related to signal processing difficulties, it is encouraging to note that there are already some valuable publications in this field. For instance, a recent work[111] proposed an fNIR spectroscopy-BCI paradigm based

on the decoding of subjective preference (i.e. the preferred drink). Nine participants were asked to mentally evaluate two possible drinks and decide which they preferred. The fNIR spectroscopy was used to monitor the PFC during the task; using mean linear discriminant analysis with signal amplitudes as input features, the accuracy in guessing the preferred drink on a single-trial basis was well above the chance level (around 80%).

Another study,[110] conducted to test the feasibility of using multichannel NIR spectroscopy in the development of a reliable BCI, provided excellent results. The motor cortex of five healthy participants was monitored during left-hand and right-hand motor imagery. The results indicated that there were two distinct patterns of haemodynamic responses which could be used in a pattern classifier oriented to the realisation of a BCI. Hidden Markov models classified left-hand imagery and right-hand imagery with an average accuracy of 89%. These impressive results confirmed the great potential of fNIR spectroscopy in BCI applications.

Co-registration studies

A promising use of fNIR spectroscopy concerns co-registration studies: fNIR spectroscopy signals can be easily recorded in combination with other imaging techniques to provide simultaneous information, as with the aforementioned investigation[47] on emotions. A recent fNIR spectroscopy–fMRI combined study[112] compared optical and BOLD responses in frontal and parietal brain regions across a wide variety of cognitive tasks. An extensive comparison of the two signals across spatial and temporal domains revealed a high correlation between optical and BOLD signals, although optical signals have significantly lower SNR; indeed, both cortical depth (i.e. the distance between the scalp and the cerebral cortex) and SNR influenced the strength of correlation between the two signals. The authors concluded that fNIR spectroscopy can be used effectively in cognitive neuroscience, provided that its weaknesses are taken into account when designing the experiment. This important investigation confirms the validity of fNIR spectroscopy as an instrument to investigate the neural correlates of cognitive processing.

As a further example, another fNIR spectroscopy–EEG combined study[113] investigated the cortical correlates of auditory sensory gating using a dual-click paradigm; typically, when two identical auditory stimuli are separated by a short temporal interval, the response to the second stimulus is reduced. In this study, participants listened to two different types of stimulation: a one-click condition (two clicks with no temporal delay) and a dual-click condition (two clicks separated by 500 ms). The fNIR spectroscopy results showed an increased activity of prefrontal and temporo-parietal cortices during increased sensory gating (dual-click condition), whereas the EEG results indicated that the P50 component (the electrophysiological response to an auditory stimulus) was significantly reduced after the second stimulus as compared to the first one. Furthermore, haemodynamic activity in the left prefrontal and temporal cortices was positively correlated with the strength of sensory gating (measured by means of an electrophysiological index), suggesting that the PFC might actively inhibit the activity of the primary auditory cortex. Two other remarkable fNIR spectroscopy–EEG combined studies reported a strong connection between electrophysiological signal and haemodynamic activity: the recent investigation by Koch *et al.*[114] revealed that EEG-measured gamma activity (~40 Hz) induced by stimulation or attentive state was strongly related to the haemodynamic response in visual cortex; their earlier fNIR spectroscopy–EEG combined study[115] showed that the individual alpha-frequency value at rest was predictive of the amplitude of both visually evoked potential and haemodynamic response in the visual cortex.

Other research topics

Optical imaging has also been used to investigate the neural correlates of numerical cognition: during the execution of arithmetical tasks, haemodynamic activity increases in superior and inferior parietal areas, as pointed out by many fMRI studies.[116,117] While some fNIR spectroscopy studies on arithmetical tasks revealed the involvement of the prefrontal regions,[16,118] a recent fNIR spectroscopy investigation[119] confirmed the fMRI findings, suggesting that both left and right parietal lobes play a crucial role in the processing and solving of arithmetic problems.

A recent optical investigation on dental phobia[120] can be regarded as proof of the fact that fNIR spectroscopy can be effectively adopted in environmental conditions that might be difficult to assess with fMRI. The study included two groups: one group of patients with dental phobia and a control group (healthy participants). The authors presented both groups with three different sounds: a dental drill (a sound feared by patients with dental phobia), a pleasant and a neutral sound. When listening to the dental drill, phobic patients exhibited increased activity in the supplementary motor area (probably reflecting a covert response of flight behaviour) with respect to controls, whereas there was no significant difference between groups for the other sounds.

Another intriguing use of fNIR spectroscopy concerns the hyperscanning (i.e. simultaneous brain activity recording of more than one participant). A recent study[121] adopted fNIR spectroscopy hyperscanning to measure brain activity coherence between two participants during a social game (with two main conditions: cooperation and competition). The study provided two interesting results: first, inter-brain coherence increased in the right superior frontal cortex only during cooperation (but not in competition); second, higher performance during cooperation was associated with increased inter-brain coherence. Notably, fNIR spectroscopy can be used in hyperscanning with no particular disadvantages, while hyperscanning with fMRI is expensive and technically challenging.

Finally, fNIR spectroscopy can also be used effectively in imaging genetics, a discipline that investigates the impact of genes on brain functioning (by conjunctively using neuroimaging and genotyping techniques). For instance, a recent fNIR spectroscopy investigation[122] revealed that a gene variant of cyclooxygenase-1 influences the neurovascular coupling in the visual cortex: the authors found that the cyclooxygenase-1 genotype-dependent enzymatic function was associated with a strongly reduced amplitude of the haemodynamic response. As well as the implications of this study, it should be noted that the advantage of using fNIR spectroscopy in imaging genetics is its low-cost application (a large sample size of subjects is vital for imaging genetics studies).

Conclusions

Functional near infrared optical imaging has some relevant disadvantages compared with other neuroimaging techniques: for instance, it is blind to subcortical activity and anatomical information must be obtained with other techniques or inferred with specific methods, while fMRI can measure haemodynamic activity of the entire brain and detailed anatomical information can be obtained within the same session of functional recording with MRI.

On the other hand, fNIR spectroscopy has also some undeniable advantages: unlike fMRI, it can be used with no problem on infants; similarly, it does not produce instrumental noise, allowing the execution of linguistic tasks that require subtle acoustic features of words or conversations to be distinguished.[123] Furthermore, fNIR spectroscopy has been promoted in a number of fields in which fMRI is limited due to the constraints induced by the scanning environment. In addition, the experimental measurements may be recorded in a more comfortable and natural environment,[124] providing a marked advantage when testing groups of clinical populations (which might not be conveniently examined with other techniques).

Nevertheless, even without taking into consideration such advantages, it appears clear that fNIR spectroscopy is often used even in those research fields where it does not immediately provide an apparent advantage over other techniques. Indeed, the heterogeneity of the researches mentioned in the present review testifies to the fact that fNIR spectroscopy can be successfully applied in almost all cognitive neuroscience issues. In some cases, it can provide converging evidence in regard to a specific cognitive theory, by confirming previous results obtained with different brain imaging techniques. Most importantly, in some other cases, the information obtained with fNIR spectroscopy can provide novel findings that could hardly be obtained with other brain imaging techniques. Thus, the use of fNIR spectroscopy in cognitive neuroscience should be directed towards those topics that allow a full capitalisation of the peculiar characteristics of optical imaging (for example, the simultaneous recording of HbO, HbR and HbT with high temporal resolution).

Finally, it is evident that functional near infrared optical imaging is constantly evolving from a technical point of view: the main proof of such progress is the fact that optical data are beginning to become meaningful at a single subject level,[60] although further development is needed to allow reliable single case studies in most of the research fields. Nevertheless, the high SNR and the spatial resolution that can be achieved with recent optical imaging methods,[60,61] the successful test–retest assessments of reliability[50,105] and the advanced probe placement techniques[106,107] should be viewed as encouraging elements that might be able to trigger the progress in single subject studies in the next few years. When considering the additional advantages of fNIR spectroscopy in testing clinical populations, it is reasonable to hypothesise that the biomedical field might radically benefit from the progress of fNIR spectroscopy towards its applicability in single case studies of clinical patients.

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