The good placement

Doctoral thesis

The Good Placement:

Information-driven choice of fNIRS optode location and its impact on brain-computer interface performance

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2021

Production: Ipskamp printing

Cover: Amaia Benitez-Andonegui

ISBN: 978-94-6423-145-8

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Information-driven choice of fNIRS optode location and its impact on brain-computer interface performance

Dissertation

to obtain the degree of Doctor at Maastricht University,
on the authority of the Rector Magnificus Prof. dr. Rianne M. Letschert
in accordance with the decision of the Board of Deans,
to be defended in public on Monday 1st of March 2021, at 16.00 hours

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The projects presented in this thesis were co-funded by Maastricht University through Luik 3 initiative (Funding for Strategic Innovation).

Amari, Aitari eta Anderri

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General Introduction

1 Prologue

Nearly a century ago, in the late 1920s, Hans Berger successfully demonstrated that brain activity can be recorded using electrodes placed on a participant's head (Berger, 1929). In the decades that followed, the idea emerged that recorded brain activity could be used as a communication channel or for controlling the environment without the need to engage the normal intermediaries of peripheral nerves and muscles. In his seminal paper, Vidal (1973) detailed a comprehensive theoretical and technical plan for direct brain-computer communication. In this work, he coined the term "brain-computer interface" (BCI) and described that "*to provide a direct link between the inductive mental processes used in solving problem and the symbol-manipulating, deductive capabilities of the computer, is, in a sense, the ultimate goal in man-machine communication"* and envisioned that BCIs *"would indeed elevate the computer to a genuine prosthetic extension of the brain*". He also predicted that "t*o achieve that goal with adequate generality is a formidable task that will require considerable advances in neurophysiology, in signal analysis, and in computer science."* While Vidal's vision influenced the development of BCIs, it would take several decades and technological advancements for that vision to materialize.

A BCI may be defined as a system that measures and converts brain activity into artificial output. This output replaces, restores or enhances outputs produced by the central nervous system, thereby enabling interactions with the external environment in the absence of motor output (Wolpaw et al., 2002; Wolpaw and Wolpaw, 2012). Since BCI technology augments human capabilities by providing a new motor-independent interactive link with the outside world, it constitutes a particularly relevant tool for patients suffering from neuronal damage such as brainstem stroke (Bauer et al., 1979), traumatic brain injury (Carrai et al., 2009), central pontine myelinolysis or end-stage amyotrophic lateral sclerosis (Birbaumer et al., 1999; León-Carrión et al., 2002; Bruno et al., 2008). These conditions can result in a so-called 'locked-in' state, which lacks voluntary muscle control abilities. For patients with such conditions, replacing (lost) motor functions through communication BCIs (Birbaumer et al., 1999; Nijboer et al., 2008; Sellers et al., 2010) and control systems such as wheelchairs, robotic body-parts or robotic agents (Galan et al., 2008; Muller-Putz and Pfurtscheller, 2008; Iturrate et al., 2009; Rebsamen et al., 2011; Tumanov et al., 2015; Murphy et al., 2017) are specially relevant.

BCIs have also been applied to a wide range of other applications: changing brain activation and associated behavior voluntarily through neurofeedback (Subramanian et al., 2011; Scharnowski et al., 2012; Shereena et al., 2018); mental state monitoring, namely alertness, workload and pain (Gagnon et al., 2012a; Shibata et al., 2014; Afergan et al., 2015; Khan and Hong, 2015; Myrden and Chau, 2015; Hu et al., 2019); entertainment purposes such as gaming (Tangermann et al., 2008; Congedo et al., 2011; Coyle et al., 2011; Maby et al., 2012; Vourvopoulos et al., 2016) and for artistic expression such as Multimodal Brain Orchestra (Le Groux et al., 2010) or Brain Painting (Kübler and Botrel, 2019).

With technological development, the number of BCI-related publications has increased almost exponentially. However, the number of real-life applications benefiting potential end-users has not grown as quickly (Shih et al., 2012). This could be due to substantial challenges associated with using BCIs in everyday situations, namely home-use or hospital settings. This ultimate goal of improving the lives of patients is a demanding endeavor since a BCI should be efficient, accurate and reliable but also easy to use, intuitive, and simple to set up. In this dissertation, we identify and address key factors hindering the translational potential of BCIs.

2 Components of brain-computer interfaces

BCIs aim to detect and extract meaningful information from brain signals that indicate what the user wants the BCI to do. BCIs then translate this information in real-time to an appropriate form for device control while providing feedback to the user about the intended act.

2.1 Measuring brain signals

Several functional neuroimaging modalities exist to measure brain activity for BCI applications. They can be divided into two categories: electrophysiological methods, which measure electrical potentials arising from neural activity directly, and hemodynamic (or metabolic) methods, which measure the vascular or metabolic response to neural activity and thus constitute an indirect measure of neural activity (see Figure 1.1).

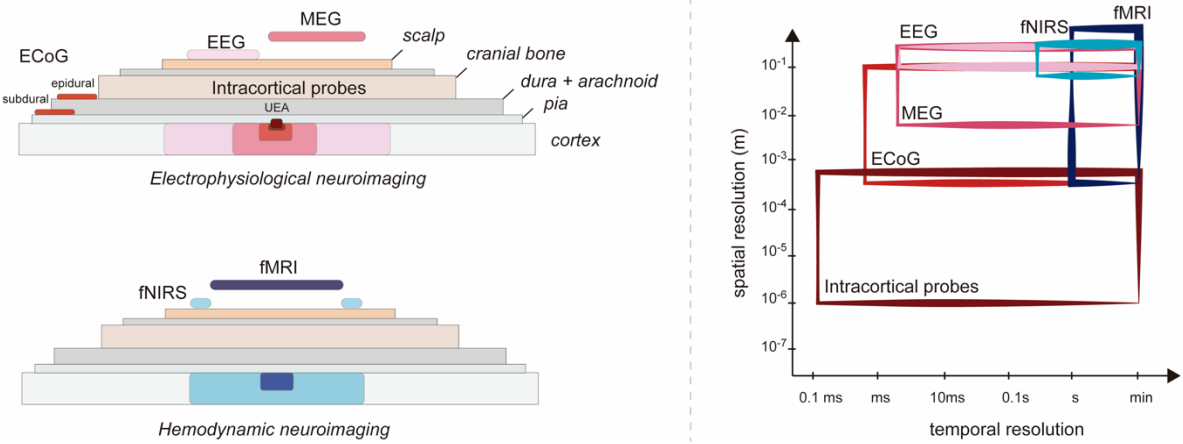

Figure 1.1. Summary of functional neuroimaging modalities used for BCI purposes. Electrophysiological methods (top, left) include electroencephalography (EEG), magnetoencephalography (MEG) and invasive electrocorticography (ECoG) and intracortical recordings (Utah electrode arrays, UAE). Hemodynamic imaging methods (bottom, left) include functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS). The size of the rectangles in the cortex provide a qualitative reference for the relative spatial resolutions of the various imaging technologies. Figure adapted with permission from (Sitaram et al., 2017). **Right**. Temporal (x-axis) and spatial resolution (y-axis) of the different functional neuroimaging methods. Figure adapted with permission from Hong and Lieber (2019).

2.1.1 Electrophysiological methods

The billions of neurons in the brain communicate with each other by transmitting neural signal across their synapses (Herculano-Houzel, 2009; Rothwell, 2009). Electroencephalography (**EEG**) measures ensembles of neurons that generate measurable potentials at the scalp surface when transmitting such signals synchronously (Min et al., 2010; Jackson and Bolger, 2014). The generated electric potentials in the brain are conducted through the cerebrospinal fluid, skull and scalp. Conductance through these tissues smears the electrical potentials recorded in the scalp, making the localization of brain activity in EEG challenging (Jackson and Bolger, 2014; Herff, 2016). Additionally, EEG is very susceptible to motion artifacts, particularly from head movements since EEG is very sensitive electrical activity from muscle movement (Yilmaz et al., 2014). Modern EEG devices are very easy to set up and can be used out of the lab easily (Debener et al., 2015). The only cumbersome aspect of an EEG setup is the electrode gel which is required to lower impedance between scalp and electrodes (Herff, 2016). Nonetheless, EEG is the most widely used functional neuroimaging method for BCI purposes due to its excellent temporal

resolution (milliseconds or below), good portability and cost-effectiveness (Min et al., 2010).

Electrocorticography (**ECoG**) measures the same neural signals as EEG, but records them using grid electrodes placed above (epidural) or below (subdural) the dura mater (Schalk and Leuthardt, 2011; Buzsáki et al., 2012). ECoG enjoys higher spatial resolution than EEG because it does not suffer the same volume conduction effects (Chauveau et al., 2004). ECoG measures neural ensemble activity directly below each electrode, effectively combining the advantageous temporal resolution of EEG with improved spatial resolution. However, ECoG is an invasive technique that requires a craniotomy (or at least minimally invasive procedures, depending on the size of the grid) to implant electrodes, limiting its usage to clinical populations (Schalk and Leuthardt, 2011).

Intracortical measurements use penetrating electrode arrays to record action potentials from a small population of neurons in close proximity to the electrode tip (Brandman et al., 2017). While there are multiple intracortical recording devices available, the Utah electrode array (Maynard et al., 1997) is the only intracortical electrode array with FDA approval for long-term human (clinical) studies. It consists of 100 silicon micro-needles (1.5mm long) arranged on a square grid (Fernández et al., 2014). Despite its high temporal resolution and spatial specificity, the Utah electrode array is limited by its ability to target deep neural structures (Choi et al., 2018) and can lead to surgical complications due to the craniotomy required for microarray placement (Szostak et al., 2017; Herff et al., 2020).

The neuronal activity measured by the abovementioned methods also induces magnetic field changes that can be detected by magnetometers placed around the head. Magnetic fields are less affected by the conductance properties of the skull and scalp than electric fields (Min et al., 2010). This gives Magnetoencephalography (**MEG**) better spatial resolution than EEG while remaining non-invasive (Hari et al., 2010; Sitaram et al., 2017). However, magnetic-field changes induced by neuronal activity are very weak (Hari et al., 2010; Singh, 2014) and thus require very sensitive and costly magnetometers to measure such signal (Min et al., 2010). Further, magnetometers require dedicated shielding from electromagnetic interference (Kobayashi et al., 2017), making the method less portable and less affordable than EEG. Finally, similar to EEG, MEG is also sensitive to strong contamination by motion artifacts (Muthukumaraswamy, 2013).

2.1.2 Hemodynamic methods

Oxygen is transported in the blood via hemoglobin. Based on its saturation state, hemoglobin can be oxygenated (i.e., HbO) or deoxygenated (i.e., deoxyhemoglobin, HbR). Neuronal activity increases oxygen metabolism, resulting in decreases in oxygen concentration in local capillary beds (Uludağ et al., 2015). This process triggers an increase in local cerebral blood flow and blood volume, which in turn supplies more oxygen than consumed to the area. This temporary oversupply of oxygen in regional cerebral blood flow results in relative increases in HbO concentration and a concurrent relative decrease in HbR.

HbO and HbR have different magnetic properties and functional magnetic resonance imaging (**fMRI)** utilizes this local blood oxygenation level dependency (termed the BOLD effect) to non-invasively measure neuronal activation (Ogawa et al., 1990; Bandettini et al., 1992; Kwong et al., 1992; Ogawa et al., 1992). Using fMRI, neuronal signals across the entire brain can be measured with relatively high spatial resolution (see Figure 1.1). However, hemodynamic responses build up much slower than electrical or magnetic changes caused by neuronal activity, which results in lower effective temporal resolution than all electrophysiological methods. Additionally, there are several practical constraints that limit the ecological validity of fMRI as a method for BCI applications. These include an unnatural supine subject position, noise produced by the scanner, contraindications to being in a magnetic field and potential patient claustrophobia. fMRI can also be strongly affected by motion artifacts. Thus, participants' movements are highly restricted during measurements (Scarapicchia et al., 2017).

In addition to having different magnetic properties, HbO and HbR also differ in their optical properties in the near-infrared (NIR) range of the electromagnetic spectrum (~650–950 nm (Scholkmann et al., 2014)). Light in the NIR range can propagate relatively deep (a few centimeters) into most biological tissue but is absorbed predominantly by hemoglobin molecules. In functional near-infrared spectroscopy (**fNIRS**), optical sensors ('optodes') are placed on the scalp, which can be classified into sources (emitters) and detectors (receivers), depending on their function. Light emitted from a source is propagated through extracerebral and cerebral tissues up to a few centimeters, where some photons are scattered and absorbed before light reaches the detectors (Machado et al., 2014). Common fNIRS systems use at least two different wavelengths as to be sensitive to both HbO and HbR. The shorter

wavelength (650–700 nm) is predominantly absorbed by HbR, while the longer wavelength (800–850 nm) is predominantly absorbed by HbO (Nishiyori, 2016). By emitting NIR light at different wavelengths and measuring absorption at detector sites, fNIRS can detect changes in concentrations of both HbO and HbR (here on referred to as Δ[HbO] and Δ[HbR], respectively) caused by neuronal activation.

Modern fNIRS systems are compact, portable, cost-effective, safe, user friendly and more robust against motion artifacts than most of other functional neuroimaging modalities (Boas et al., 2004; Lloyd-Fox et al., 2010; Pinti et al., 2018). These features make fNIRS a powerful technique for use in BCIs aimed at communication and control. In many ways, fNIRS can be regarded as an effective compromise between the high temporal resolution of EEG (Irani et al., 2007) and the robustness of the hemodynamic response in fMRI. Its mobility and cost are comparable to EEG, which is currently the most widely used modality for BCIs. FNIRS, however, has higher spatial resolution than EEG (although lower than fMRI (Lloyd-Fox et al., 2010). Penetration depth is shallow, similar to EEG, but this does not impose a limiting factor for BCI applications since measurable brain signals can be acquired from superficial cortical areas (Naseer and Hong, 2015a).

The work presented in this dissertation focuses on fNIRS-based BCIs due to the abovementioned features of fNIRS, which offer distinct advantages for developing practical, portable and robust BCIs. The remainder of this section describes the components constituting a BCI with an emphasis on fNIRS.

2.2 Encoding user intentions

Brain signals used in fNIRS (and fMRI) BCIs can be generated by moving a body part to activate the motor cortex, i.e., by performing a motor-execution task, or by covertly performing a task (Naseer and Hong, 2015a). Examples of covert tasks include:

- Motor imagery - imagining one’s own body part moving without muscular activity
- Mental calculation/arithmetic - performing calculations in one’s head
- Mental singing - reproducing a song in one’s head without any external music input

- Mental talking or inner speech - reciting a text or having a monologue in one's head
- Object rotation - imagining a rotating object
- Spatial navigation –imagining walking through and visualizing a (changing) three-dimensional scene

Covert tasks hold potential in BCI applications since they act as a non-muscular communication channel for generating commands. Further, these covert tasks engage superficial cortical areas, such as the prefrontal or motor cortices (Naseer and Hong, 2015a), which are easily measured using fNIRS.

2.3 Detecting and extracting relevant information

Regardless of the employed functional neuroimaging modality, measured brain signals are often weak, containing physiological and instrumental noise, and motion artifacts (Krusienski et al., 2012; Naseer and Hong, 2015a). The aim of data preprocessing pipelines is to correct or remove these noise sources. Next, information present in the preprocessed time-series is summarized in trials, blocks or epochs using a summary measure or feature. For fNIRS-BCIs, examples include temporal averages, slope or peak value in a predefined window (Naseer and Hong, 2015a; Hong et al., 2018) or the resulting *beta* or *t*-value after fitting a General Linear Model on the time points associated with a given trial (Valente et al., 2019).

2.4 Translating information and providing feedback to the user

User's intentions are indirectly measured by recording brain activity and must be translated into appropriate device commands to convey user intent. A model known as classifier must be trained to translate features of brain activity to one of a pre-defined set of user intentions (McFarland and Krusienski, 2012). Importantly, as BCIs preferably operate in real-time, this translation must occur as new observations come in, thus requiring generalization to new, unseen data.

The translated output of BCI applications serves a dual purpose. First, it serves as a command for the control device or communication system. For example, if the goal of the BCI is to establish a communication channel for the user, then the model would map brain activity onto a word or an answer to a question (see Figure 1.2). Alternatively, if the goal is

to control a robotic arm so that the user can, e.g., grab a coffee mug, then the brain activity would be mapped to joint movements of the robotic arm to accomplish the user's intents. Second, the translated output serves as feedback to the user about the success or failure of the intended act (Leeb et al., 2007). fNIRS-based BCI systems that rely on computer screens/displays for proving the output, most commonly use 2D visual displays/interfaces, such as pictures (Luu and Chau, 2009), geometrical figures (Coyle et al., 2004; Weyand and Chau, 2015), cartoon-like stimuli (Power et al., 2012) or auditory stimuli such as questions in communication paradigms (Naito et al., 2007; Gallegos-Ayala et al., 2014; Abdalmalak et al., 2017; Nagels-Coune et al., 2017; Abdalmalak et al., 2020; Nagels-Coune et al., 2020). In recent years, Augmented and Virtual Reality (AR/VR) technology has matured to enable complex and immersive interfaces (Putze, 2019; Putze et al., 2020). Virtual reality is an immersive system that provides users with a sense of presence through potential interactions with a simulated virtual world, rendered in real-time (Lécuyer et al., 2008). Augmented reality enhances the user's perception by overlaying virtual objects onto the user's environment (Si-Mohammed et al., 2017). These technologies enable multisensory display integration and have the potential to increase engagement and motivation in users (Chin et al., 2010).

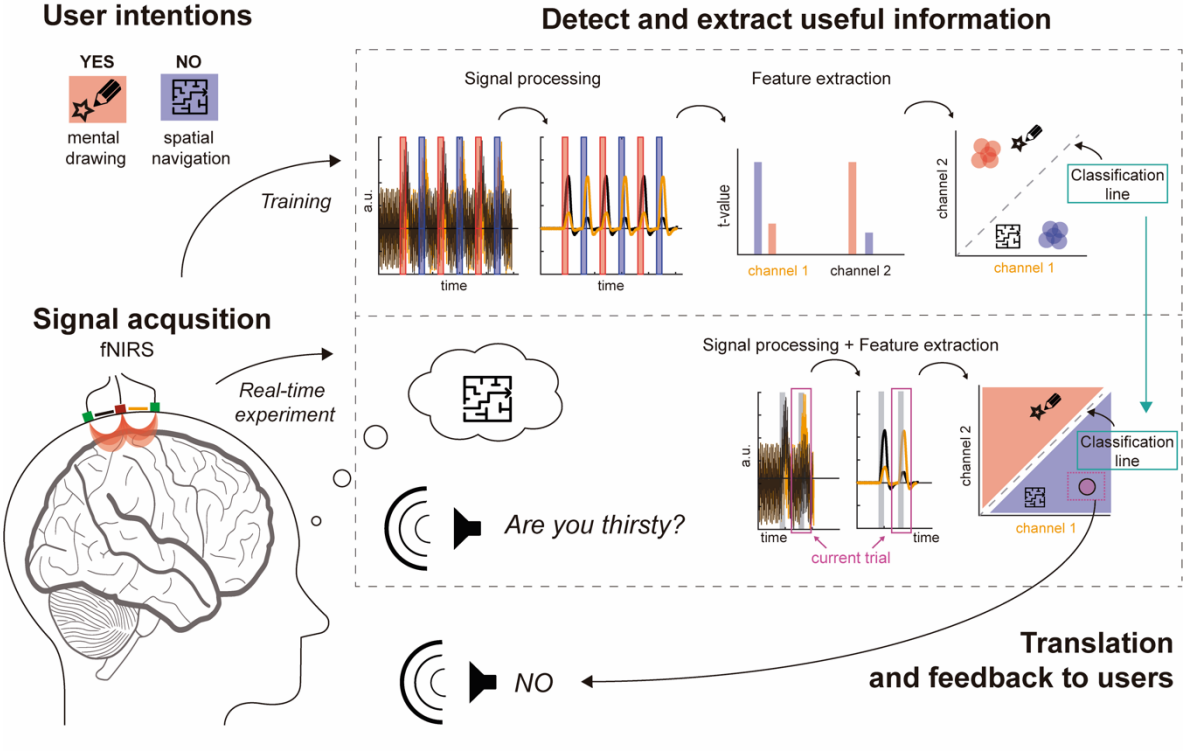

Figure 1.2. Schematic representation of an fNIRS-BCI system for communication. In this example, the participant is asked different sets of questions and encodes the answer YES via mental drawing (symbolized in red), where the participant imagines drawing simple geometric figures such as a star, while (s)he encodes the answer NO using spatial navigation (depicted in blue), which involves to imagine walking through and visualizing a (changing) three-dimensional scene. The neural activity is recorded through fNIRS channels (black and yellow lines) located on the motor and parietal cortex. The recorded noisy signal is processed before a general linear model is fitted onto the time points, after which t-values are estimated per channel. Here, channel 1 (yellow) is more sensitive to the spatial navigation task, while channel 2 (black) is more sensitive to mental drawing. A classification line that best distinguishes the two tasks is defined based on the training data across channels. During the real-time experiment, the participant's intention is decoded based on which side of the line in the feature space the current trial falls. For the current trial, the participant performed the spatial navigation task to indicate (s)he was not thirsty.

3 Challenges associated with fNIRS BCIs

The complex, interconnected processes that constitute a BCI pose numerous challenges to establishing communication and control interfaces using brain signals. While some obstacles are independent of the chosen functional brain-imaging modality, others are modality-specific. Here, we describe a number of challenges facing fNIRS-based BCIs.

3.1 Measuring brain signals: the problem of optode layout design

The spatial resolution of fNIRS depends on how source-detector pairs (or 'channels') are arranged on the scalp (Culver et al., 2001). The distance between a source and detector pair, along with the anatomical tissues between them, determines how deep light will travel and the sensitivity to underlying cortex physiology (Brigadoi et al., 2018). Therefore, fNIRS signal quality can differ dramatically between optode layouts.

Researchers often define a region of interest (ROI) in line with their research question and consequently design an optode layout in a grid-like fashion to target that ROI (Brigadoi et al., 2018). The simplest and most common optode layout design assigns source and detector locations on the scalp to cover a given cortical ROI according to the standardized 10-20 EEG system or its extended versions (Oostenveld and Praamstra, 2001). These locations can relate to underlying assumed cortical structure (Koessler et al., 2009; Giacometti et al., 2014) to standard Montreal Neurological Institute (MNI) stereotactic coordinates (Okamoto et al., 2004; Jurcak et al., 2007; Tsuzuki et al., 2007; Tsuzuki and Dan, 2014). Sometimes this approach results in a setup consisting of many optodes, resulting in increasing user discomfort over time. This approach may also lead to a suboptimal sampling of the active area. This is because fNIRS interrogates tissue located between a given source-detector pair and thus regions between a source-source and a detector-detector cannot be sampled or are not sampled optimally (see Figure 1.3).

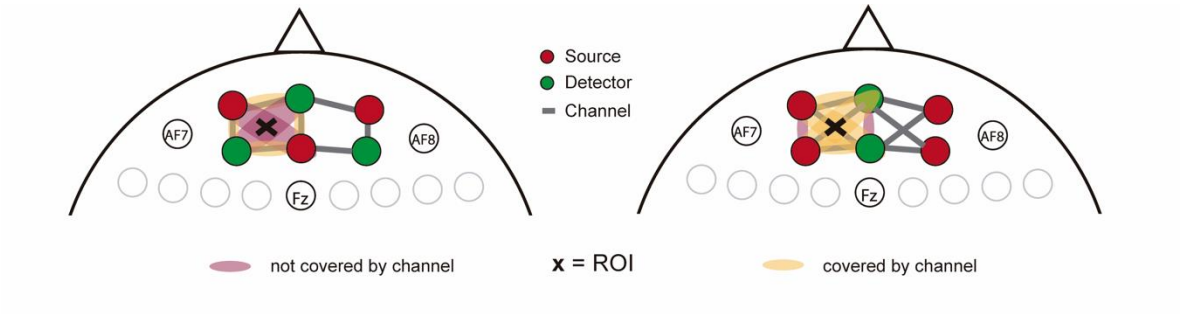

Figure 1.3. Schematic representation of the influence of optode placement on the coverage of the target ROI. This figure shows the top view of the international 10-5 EEG layout and an optode setup that covers the frontal cortex. The arrangement on the left does not properly cover the target ROI, but as indicated in the arrangement on the right, swapping optodes in the second row solves the issue.

To overcome this problem, one could design a given optode layout based on the approach described above, perform fNIRS measurements on a real subject and subsequently assess the quality of measured signals. This layout could then be iteratively modified until the researcher identifies the channels that best capture the signal of the target ROI. However, this is an unfeasible procedure that would require lengthy measurements.

Instead, models can describe the probability that a given photon transmitted from a source to a detector has traveled through a given tissue (Aasted et al., 2015). These models, also called light-sensitivity profiles, require the diffusion approximation of the radiative transport equation to be solved (Boas et al., 2002). However, finding an analytical solution is difficult because light propagation through scattering media with heterogeneous structure (such as the head) is inherently complex (Boas et al., 2002; Strangman et al., 2013). In the absence of analytical solutions, sensitivity-profile computations rely on numerical approaches, such as Monte Carlo Simulations (Strangman et al., 2013). Light-sensitivity profiles computed with Monte Carlo Simulations have been used by the fNIRS community as an objective measure to assess optode layout designs and a number of toolboxes, software and pipelines have been developed specifically for that purpose (Tadel et al., 2011; Machado et al., 2014; Aasted et al., 2015; Wijeakumar et al., 2015; Brigadoi et al., 2018; Zimeo Morais et al., 2018).

Monte Carlo simulations of photon migration use a set of rules to describe consecutive absorption and scattering events that the photons experience when traveling through the head. Simulations require three-dimensional tissue geometry (an anatomical MRI image), segmented into voxels of different tissue types. A common head model consists of five tissues – white matter, gray matter, cerebrospinal fluid, skull and scalp. Every voxel is assigned a set of optical properties (absorption and scattering coefficients, among others) depending on the tissue type they belong to. To begin, an initial position (source location) and direction of the photon is defined, together with an initial surviving weight set to 1. A scattering length L is probabilistically calculated from an exponential distribution, and the photon is moved through the voxels by this length. The photon's weight is incrementally decreased by an exponential factor that takes into account the length L and the absorption coefficient assigned to the voxel the photon had landed. A scattering angle is then calculated using a probability distribution and a new scattering length is determined from an

exponential distribution. The photon is moved the new distance in the updated direction defined by the scattering angle. This process continues until the photon exits the medium or has traveled longer than a predefined period of time, after which a new photon is launched. Millions of photons are typically launched in this process.

One of the outputs of the simulations is the accumulation of all photon weights within each voxel in the tissue, also known as the 2-point Green's function. The light sensitivity can be computed by multiplying the 2-point function obtained from the source location by the 2-point function from the detector location, voxel by voxel (Strangman et al., 2013)[1]. Although Monte Carlo simulations are computationally intensive, the resulting sensitivity profiles offer a way to design optode layouts that maximize sensitivity for an ROI prior to any experiment, thus promising increased signal quality and coverage. This becomes particularly relevant for fNIRS-based BCIs, where developing robust systems that use limited number of optodes is crucial to remain practical and comfortable for clinical applications.

Although Monte Carlo simulations follow a clearly predefined set of rules, approaches to optode layout design that use them allow for certain degree of individualization in their input parameters, such as the type of anatomical head model used (atlas based MRI vs. subject-specific models) or how the target ROIs are defined (anatomically or functionally). Importantly, the final choice will often depend on the temporal/monetary/material resources available to the researcher since collecting additional individualized data has always an associated cost. Therefore, it is important to elucidate the amount of individual MRI-derived information worth to include for designing optode layouts, more so when these resources are limited.

[1] This is true in continuous-wave fNIRS measurements. There are three types of fNIRS systems, namely continuous-wave, frequency-domain and time-domain instruments. The continuous-wave (cw) fNIRS systems emit light at a constant intensity and then only measure the changes in the intensity of the light that passed through the tissue at the detector site. Meanwhile, frequency- and time-domain systems, besides the change in light intensity, they measure the arrival times of the photons that emerge from the tissue (Scholkmann et al., 2014). In this dissertation, a cw-fNIRS system was used.

3.2 Detecting and extracting meaningful information: the presence of physiological noise

The fNIRS signal is susceptible to physiological fNIRS noise originating from global systemic and local regulatory processes of intra- and extra-cerebral origins (Kirilina et al., 2013). These noise sources can compromise sensitivity to brain activation measured by fNIRS BCIs, particularly when insufficiently preprocessed single-trial data feeds back noise instead of brain activity (Klein and Kranczioch, 2019).The main sources of physiological noise are heart rate (~1 Hz), respiration (~0.3 Hz) and blood pressure-related variations. These variations mainly come from so-called Mayer waves (~0.1 Hz) and very low frequency oscillations (<0.04 Hz), as outlined in Figure 1.4 (Boas et al., 2004; Scholkmann et al., 2014; Tachtsidis and Scholkmann, 2016; Tong et al., 2019). Mayer waves occur spontaneously in conscious subjects and are thought to be tightly coupled with synchronous oscillations of sympathetic nervous activity (Julien, 2006; Sassaroli et al., 2012). Very low-frequency oscillations are thought to be related to neurogenic activity of vessels and with vascular endothelial function (Stefanovska, 2007).

The most common approach to reduce the impact of these noise components is to remove specific frequency bands in fNIRS signals by means of digital filters (low-, high- or band-pass filters). The frequency of heart rate is relatively high with respect to the typical fNIRS responses and thus can be can be easily and effectively removed by low-pass filtering. However, the remaining noise sources are more difficult to remove due to their spectral proximity and potential for synchronization with BCI-task activity. If not correctly accounted for, these noise sources can be falsely interpreted as functional brain activity (Tachtsidis and Scholkmann, 2016) or can hinder the recovery of hemodynamic responses from the brain signal of interest (Yücel et al., 2016).

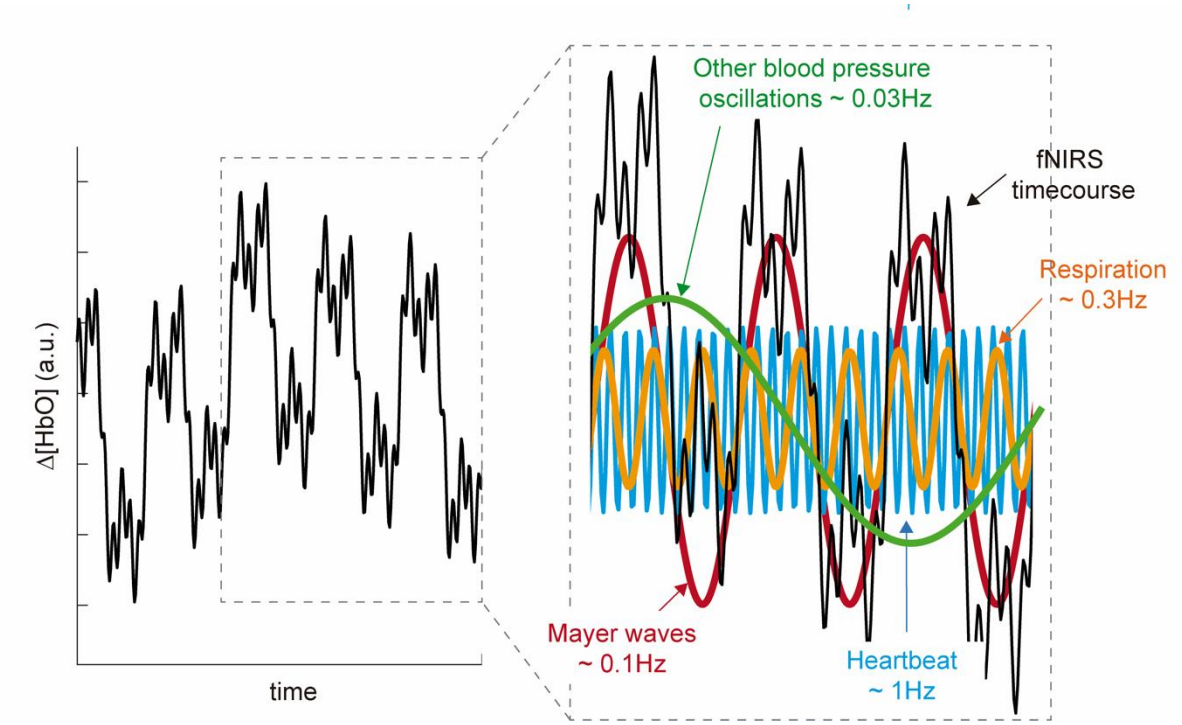

Figure 1.4. Schematic representation of physiological fluctuations present in the fNIRS signal (in black). Physiological processes, which contribute to the physiological noise in fNIRS, operate at different time scales: heartbeat (~1 Hz) in blue, respiration (~0.3 Hz) in orange, Mayer waves (~0.1 Hz) in red, and very low frequency oscillations (usually under 0.04 Hz and in this example depicted at ~0.003 Hz), in green.

A number of methods have been proposed for separating physiological noise from cerebral activation other than digital filtering. Some methods assume that systemic physiology is globally (spatially) uniform and thus aim to remove global covariance from the signal with multivariate techniques such as principal component analysis (Zhang et al., 2005), independent component analysis (Satoru et al., 2007) or global averaging (Batula et al., 2017). Others use auxiliary physiological measurements such as blood-pressure monitors, pulse oximeters, electrocardiograms, chest-band respirometers, spirometers or capnographs (Diamond et al., 2006; Kirilina et al., 2013; Scholkmann et al., 2013) to filter the fNIRS time course. State-space models based on Kalman filters have also been used (Kolehmainen et al., 2003; Prince et al., 2003; Diamond et al., 2006).

Another approach that is particularly powerful for real-time BCI applications relies on the idea that systemic physiological noise present in extracerebral regions can be locally measured using channels with short source-detector separations (<1 cm usually, here on

referred to as short-distance channels or SDCs). Since this approach assumes that the same systemic physiological noise present in the longer distance channels dominates the signal acquired with SDCs (Saager and Berger, 2005; Saager et al., 2011), they can be used to minimize/reduce unwanted physiological noise from the longer distance channels (usually >2.5 cm). SDCs constitute a versatile approach to account for the influence of physiological noise. Among others, they have been used as regressors using a general linear model (Saager et al., 2011; Goodwin et al., 2014; Sato et al., 2016) and in combination with state-space modeling (Gagnon et al., 2011; Gagnon et al., 2012b; Gagnon et al., 2014).

Although systemic interference is thought to be a global process, previous work reported a non-homogeneous distribution of physiological noise components present in fNIRS channels (Kirilina et al., 2012; Yücel et al., 2016). Further, it has been suggested that the contribution of certain components, such as Mayer's waves, may be different at measurements collected at different sites because of heterogeneity in blood vessel sizes, location, or geometry (Zhang et al., 2009; Gagnon et al., 2011). Therefore, understanding whether fNIRS channels capture physiological noise differently depending on their location is crucial to design physiological noise correction strategies.

3.3 Translating information: low information transfer rate

Information transfer rate (ITR) shows the amount of information transmitted per unit of time. ITR is measured in bits per second (or minute) and is a standard measure of BCIs systems that takes into account the number of possible selections, accuracy and the trial duration (McFarland et al., 2003; Allison et al., 2012):

$$ITR = \left(log_2 N + P * log_2 P + (1 - P) * log_2 \left(\frac{1 - P}{N - 1} \right) \right) * \frac{60}{\tau} \qquad (1.1)$$

where N is the number of classes, P is the classification accuracy and τ is the duration of the trial period, in seconds.

The performance of fMRI-BCIs using motor/mental imagery tasks ranges between 0.463 and 2.30 bits/min (Lee et al., 2009a; Sorger et al., 2009; Bardin et al., 2011; Sorger et al., 2012) in healthy participants, while reaching 0.07 bits/min in the patient with traumatic brain

injury (Patient 23, reported in Monti et al. (2010)). fNIRS-BCI applications that use motor/mental imagery tasks range between 0.02 and 1.5 bits/min in healthy participants (Sitaram et al., 2007; Batula et al., 2014; Naseer et al., 2014; Hong et al., 2015; Weyand and Chau, 2015; Naseer and Hong, 2015b; Nagels-Coune et al., 2017; Sereshkeh et al., 2018; Nagels-Coune et al., 2020) while reaching 0.47 bits/min in a case studies with an ALS patient (Gallegos-Ayala et al., 2014) and 0.18 bits/min in a patient with Guillain–Barré syndrome (Abdalmalak et al., 2017). Given the immobility of fMRI hardware, the studies mentioned above show great potential of mobile setups employing fNIRS, thereby enabling ecological BCI applications. To put this into perspective, normal speech rate ranges between 110 and 175 words per minute (Tikofsky, 2000) or 550 to 875 bits/min[2]. Keyboard typing rates range between 20.9 and 89.5 words per minute (Dhakal et al., 2018) or 104.5 to 447.8 bits/min[1]. Clearly, current hemodynamic-BCI systems convey considerably less information in healthy and clinical populations. However, it is important to note that even low ITR values have the potential to improve significantly the quality of life of someone who relies on these systems for communicating with the outer world.

A number of interconnected factors influence information rates for hemodynamic BCI systems. Shorter trials (τ) can increase performance of the BCI by allowing a greater number of selections per unit time. However, performance may decrease due to less information, thereby decreasing the information transfer of the system. The number of selections per unit time is dependent on the temporal resolution of the brain imaging method used. Unlike electrophysiological recordings, the lower temporal resolution of fNIRS constitutes a major limiting factor when used for BCI applications. The hemodynamic response to neuronal activation shows a small initial dip, followed by a tall peak around 5-10s after neuronal activation, subsequently followed by a variable post-stimulus undershoot. The total duration of a hemodynamic response is between 20 and 30s. For this reason, the biggest body of hemodynamic BCI applications has used a trial duration of 10s (Herff et al., 2013; Naseer and Hong, 2013; 2015b; Hong and Santosa, 2016; Nagels-Coune et al., 2017; Shin et al., 2017). Only a few studies have used trial durations under 10s. For example, Lee et al. (2009b) used a task duration of 5s and Shin and Jeong (2014) and Sorger et al. (2009) used

[2] Considering that the average English word is 5 characters long (Norvig, 2012) and that Shannon determined that the information content of typical written English was around 1.0 bit per letter (Shannon, 1951).

variable task durations of 6/8/10/15 s and 5/10/15 s, respectively. In addition, effort has been made reduce trial length and cope with the sluggishness of the hemodynamic response by focusing on the detection of the initial-dip (Zafar and Hong, 2016; Zafar et al., 2018).

The performance of a BCI (P) also depends on how well a classifier can discriminate the user's intentions. This in turn depends on the quantity and quality of data used for model training and the type of classification algorithm used to translate user's intention to output commands. The hemodynamic BCI community has adopted a number of multivariate classification techniques, including Linear Discriminant Analysis, Support Vector Machines and Artificial Neural Networks. All of these algorithms exploit the spatial features of fNIRS signals evoked by performing different mental-imagery tasks (Naseer and Hong, 2015a; Hong et al., 2018). In addition to training data, which may require several acquisition sessions to collect, multivariate approaches require multiple channels, which may increase optode setup time. Alternatively, BCI commands can be generated (encoded) and translated (decoded) by exploiting the temporal (onset, offset and/or duration) as well as spatial aspects of a set of mental tasks (Sorger et al., 2009; Bardin et al., 2011; Sorger et al., 2012; Nagels-Coune et al., 2017; Nagels-Coune et al., 2020). For example, up to four commands can be generated by assigning a unique encoding time for each command, e.g., commands would be generated in 0-10, 10-20, 20-30 and 30-40s time windows within a particular information-encoding trial. This temporal information approach is serial in nature, so it will have longer trial durations than multivariate approaches. Advantageously though, the temporal information approach can be implemented in a single measurement channel if only temporal encoding is pursued. It can also be combined with spatial encoding using two channels, each coding for a distinct mental imagery task, thus minimizing setup time and while increasing user comfort.

A greater number of possible selections or targets (N) could increase performance of a BCI system, since more targets convey more information. The majority of hemodynamic studies using motor/mental imagery tasks have focused on binary classification (Sitaram et al., 2007; Monti et al., 2010; Naseer and Hong, 2013; Stangl et al., 2013; Gallegos-Ayala et al., 2014; Naseer et al., 2016; Abdalmalak et al., 2017; Nagels-Coune et al., 2017; Abdalmalak et al., 2020; Nagels-Coune et al., 2020) and to a lower extent in multi-class problems. Studies on multi-class BCI applications have used three (Power et al., 2012; Hong et al.,

2015; Weyand and Chau, 2015; Sereshkeh et al., 2018; Shin et al., 2018), four (Sorger et al., 2009; Bardin et al., 2011; Batula et al., 2014; Weyand and Chau, 2015; Naseer and Hong, 2015b), five (Weyand and Chau, 2015), twenty-seven (Sorger et al., 2012) or thirty (Borgheai et al., 2019) targets. The primary reason why multi-class fNIRS-BCIs have not been elaborately studied relative to binary BCIs is that more targets will make trials longer when using (spatio)temporal encoding paradigms and may require longer training sessions or complex channel configurations for multivariate classification procedures. However, efficient stimulation paradigms design (as in Sorger et al. (2012) and Borgheai et al. (2019)) show the utility of using a high number of possible targets.

Improving ITR is important for hemodynamic BCIs, particularly for fNIRS-BCIs. Improvements have the potential to enable convenient BCI-based communication and control functionalities of patients in ecological settings. Thus, working towards lowering trial durations, increasing the number of targets while simultaneously maximizing classification accuracy is crucial to reach this goal.

3.4 Providing feedback to users: unnatural interfaces for communication and control

The interaction between the user and the BCI systems need to be simple and meaningful in clinical settings. In communication BCIs, letters or answer options to be encoded can be presented acoustically or visually. The output is usually a word or answer option recited out loud by the computer program or by the experimenter and no other sophisticated forms of output are necessary. In control BCIs, the interaction between the patient and the BCI system should result in a visible change in their environment. Thus, an ideal interface should be embedded in the environment itself. Interfaces such as robots and wheelchairs are a clear example of that. Importantly, other interfaces, such as the ones based on AR, allow for such scenarios too, since AR technology enables projecting virtual objects, such as control menus, as overlays into the real world.

4 Outline of this thesis

The principal rationale for BCI development has been that such systems could ultimately restore communication and control in the absence of words/gestures to people with severe neuromuscular disabilities (Shih et al., 2012). Although the number of BCI-related publications has increased almost exponentially, there have been fewer applications including end-users affected by disease, despite historically being the primary target population for BCI systems (Kübler, 2020). This dissertation addresses the limitations described above to ultimately reduce the translational challenges that fNIRS-BCIs face.

In **Chapter 2**, we aim to develop an fNIRS-BCI for communication and control purposes that is more integrated in the environment. To do so, 12 healthy participants used AR technology, a single mental task and fNIRS channel to communicate their intentions by navigating through an adaptive, six-choice menu. This work conveys fundamental steps toward developing fNIRS-based AR-BCI systems for bedside applications.

Designing optode layouts is an essential step when preparing an fNIRS-BCI setup as the quality of the measured signal and the sensitivity to cortical regions of interest depend on how sources and detectors are arranged on the scalp. Different amount of MRI-derived individualized data can be used for designing optode layouts and available resources often dictate the approach researchers will use. In **Chapter 3**, we investigate whether guiding layout design using different amounts of individual (f)MRI data affects the fNIRS signal quality and sensitivity to brain activation when healthy participants perform mental-imagery tasks typically used in fNIRS-BCI experiments. Based on insights gained as part of this work, we give preliminary advice to efficiently using resources for developing robust and convenient optode layouts for fNIRS-based communication/control and neurofeedback applications.

fNIRS is susceptible to extra-cerebral physiological noise, potentially compromising its sensitivity to detect task-related brain activation. Several studies have speculated that the presence of some physiological noise components in the fNIRS signal may be related to the position of optodes relative to the location, size and geometry of blood vessels. In **Chapter 4**, we first verify that physiological noise amplitude varies across channels in our optode layout. We then investigate whether fNIRS channels capture physiological noise differently

depending on their proximity to vessels in the scalp and brain and how this dependency affects physiological noise correction approaches. This chapter thus extends our understanding of the relationship between vasculature features, the fNIRS signal quality and methods designed to increase its applicability of fNIRS (and BCIs) for accurately detect brain activity.

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In the above reference list, 79.75% of first authors were male (vs. 20.25% that were female), while 86.08% of last authors were male (vs. 13.92 % that were female).

2

An Augmented-Reality fNIRS-Based Brain-Computer Interface: A Proof-of-Concept Study

Abstract

Augmented reality (AR) enhances the user's environment by projecting virtual objects into the real world in real-time. Brain-computer interfaces (BCIs) are systems that enable users to control external devices with their brain signals. BCIs can exploit AR technology to interact with the physical and virtual world and to explore new ways of displaying feedback. This is important for users to perceive and regulate their brain activity or shape their communication intentions while operating in the physical world. In this study, twelve healthy participants were introduced to and asked to choose between two motor-imagery tasks: mental drawing and interacting with a virtual cube. Participants first performed a functional localizer run, which was used to select a single fNIRS channel for decoding their intentions in eight subsequent choice-encoding runs. In each run participants were asked to select one choice of a six-item list. A rotating AR cube was displayed on a computer screen as the main stimulus, where each face of the cube was presented for 6 s and represented one choice of the six-item list. For five consecutive trials, participants were instructed to perform the motor-imagery task when the face of the cube that represented their choice was facing them (therewith temporally encoding the selected choice). In the end of each run, participants were provided with the decoded choice based on a joint analysis of all five trials. If the decoded choice was incorrect, an active error-correction procedure was applied by the participant. The choice list provided in each run was based on the decoded choice of the previous run. The experimental design allowed participants to navigate twice through a virtual menu that consisted of four levels if all choices were correctly decoded. Here we demonstrate for the first time that by using AR feedback and flexible choice encoding in form of search trees, we can increase the degrees of freedom of a BCI system. We also show that participants can successfully navigate through a nested menu and achieve a mean accuracy of 74% using a single motor-imagery task and a single fNIRS channel.

Based on: A. Benitez-Andonegui, R. Burden, R. Benning, R. Möckel, M. Lührs, B. Sorger (2020). An Augmented-Reality fNIRS-Based Brain-Computer Interface: A Proof-of-Concept Study. *Frontiers in Neuroscience*

1 Introduction

A brain-computer interface (BCI) is a system that enables users to send commands to the external world through brain signals in the absence of motor output (Wolpaw et al., 2002). BCI research has mainly focused on developing applications for (1) changing brain activation and associated behavior voluntarily through neurofeedback (Subramanian et al., 2011; Scharnowski et al., 2012; Shereena et al., 2018) and for (2) replacing (lost) motor functions through communication BCIs (Birbaumer et al., 1999; Nijboer et al., 2008; Sellers et al., 2010) and (e.g., wheelchair/robotic body-part) control systems (Galan et al., 2008; Muller-Putz and Pfurtscheller, 2008; Iturrate et al., 2009; Rebsamen et al., 2011; Murphy et al., 2017). Independent of the application, information is fed back to users about the success or failure of the intended act (Leeb et al., 2007). In communication and control BCIs, feedback may allow the BCI user to adapt the communication content (of a next encoding trial) in a sense of "back-and-forth communication", which enables users to communicate with or control a specific component of the external world.

The most common approach to provide feedback to users is through simplified unimodal (visual or auditory) representations of brain activation, such as bars or single tones (Sulzer et al., 2013). Alternative ways have emerged in the past years due to new technological developments in the areas of multimedia and entertainment, such as virtual reality (VR). VR is an immersive system that provides users with a sense of presence through potential interactions with a simulated virtual world rendered in real-time (Lécuyer et al., 2008). It has been suggested that VR environments can improve the BCI experience as it offers a richer and potentially more motivating feedback (Chin et al., 2010; Allison et al., 2012). Recent advances in VR research enabled the development of augmented reality (AR) systems. Unlike VR systems, AR enhances the environment the user is in by projecting virtual objects as overlays into the real world. This projection is called registration and it can be carried out using a camera that detects a number of fiducial markers placed in the real environment (Si-Mohammed et al., 2017). AR can be displayed using systems worn on the head (also known as head mounted displays, HMD) or visualized through a dedicated screen that the participant is not wearing (phone, computer screen, etc.). Depending on the augmentation type, AR systems can be divided into visual see-through (VST) and optical see-through (OST) systems. In VST-AR, real images are recorded in real-time by the camera of a device (tablet, phone, etc.) before being visualized through a screen, augmented with

virtual information. In OST-AR, the virtual content is directly displayed in front of the user's eyes onto a semi-transparent screen.

The number of studies exploring the use of BCIs in AR applications remains relatively small (Si-Mohammed et al., 2017). Up until now, the majority of the AR-BCI literature has focused on electroencephalography (EEG)-based evoked potentials applied to a wide range of fields, namely robotics (Lenhardt and Ritter, 2010), medicine (Blum et al., 2012), home automation (Takano et al., 2011; Park et al., 2019), navigation (Faller et al., 2010), and neurofeedback (Chin et al., 2010; Mercier-Ganady et al., 2014). Importantly, some of these studies have assessed the impact of AR feedback in mental workload and engagement compared to traditional forms of feedback. For example, Chin et al. (2010) compared 3D-AR displays vs. traditional 2D feedback (both displayed on a computer screen) and found that despite the higher mental load experienced by the participants during the 3D-AR feedback, participants reported the 3D-AR feedback being more engaging and motivating.

AR-BCIs based on hemodynamic signals have also been explored, but to a smaller extent (Si-Mohammed et al., 2017). One way of measuring hemodynamic signals is using functional near-infrared spectroscopy (fNIRS), a portable, silent, and affordable counterpart to functional magnetic resonance imaging (fMRI) (Scarapicchia et al., 2017). Both EEG and fNIRS make use of sensors [electrodes and optode pairs (sources and detectors), respectively] placed on the scalp to measure signals which correlate with neural activity (Allison et al., 2012). While EEG measures the postsynaptic potentials of ensembles of neurons, fNIRS is based on the optical measurement of the hemodynamic response of both oxy- and deoxyhemoglobin (Δ[HbO] and Δ[HbR], respectively) to neural activity (Lloyd-Fox et al., 2010). Although EEG offers a higher temporal resolution than fNIRS, the latter represents an interesting option as it provides higher spatial resolution and is less vulnerable to motion artifacts (Lloyd-Fox et al., 2010).

To our knowledge, only three fNIRS-based AR-BCIs have been reported. Hu et al. (2019) used an fNIRS-based AR-BCI in a simulated real-time environment aimed at clinicians to measure and visualize in real-time the ongoing cortical activity to determine when and where the patients were suffering from pain. For that, they placed fNIRS optodes over the patients' bilateral prefrontal cortex and primary somatosensory area and monitored brain activity while volunteers with hypersensitive teeth underwent a thermal stimulation session.

The cortical activity was superimposed onto a participant's head in the real world in real-time through an OST-HMD (HoloLens) device the clinician was wearing. Afergan et al. (2015) developed an fNIRS-based BCI using OST-HMD called Phylter. They developed a control system connected to Google Glass that helped preventing the user from getting flooded by notifications. By monitoring users' mental workload in real-time with an fNIRS device, their system would only show notifications to the user if the mental workload was low enough. In the context of mental workload monitoring, McKendrick et al. (2016) assessed the cognitive differences between a wearable AR display (Google Glass) and a handheld display (smartphone) using a mobile fNIRS system covering the lateral PFC during an outdoor navigation task. They complimented it with two separate secondary tasks to assess differences in mental workload and situation awareness during navigation. They concluded that navigating with an AR wearable display produced the least workload during one of the working-memory task, and reported a trend for improved situational awareness in their measures of prefrontal hemodynamics. In this proof-of-concept study we tested whether healthy participants can use an AR fNIRS-based BCI paradigm motivated by the successful implementation in fNIRS-based BCIs, the increased engagement associated to the use of AR reported in previous studies (Chin et al., 2010) and its ability to preserve the real world while blending digital components to it.

Generally speaking, the hemodynamic response to a given task execution/stimulus shows a specific and reproducible temporal behavior (Menon and Kim, 1999). Previous fMRI-based BCI work exploited this property and demonstrated that up to four distinctive BCI commands could be encoded/decoded by varying the temporal aspects (onset, offset and/or duration) of a (set of) mental task(s) (Sorger et al., 2009; Bardin et al., 2011; Sorger et al., 2012). Despite its simplicity, so far no fNIRS-based BCI has implemented this temporal information encoding approach. This is probably because the temporal encoding approach is serial in its nature, which can make the encoding process lengthy depending on the experimental design. In addition, it has been used in combination with univariate information decoding approaches, while the hemodynamic BCI community has mostly adopted multivariate classification techniques such as Linear Discriminant Analysis, Support Vector Machines or Artificial Neural Networks that have been used to exploit the spatial features of fNIRS signals evoked by performing different mental-imagery tasks (Naseer and Hong, 2015a; Hong et al., 2018). However, with appropriate experimental

designs, the temporal encoding approach offers a way to increase the degrees of freedom of a BCI using a single mental task. With this in mind, the present study aimed at transferring the fMRI-based temporal encoding approach mentioned above to fNIRS. For that, we used a selection paradigm where participants had to sift through a multi-leveled menu using a motor-imagery task. This menu consisted of four levels, in such a way that the choice options provided in each level (always six) were based on the decoded choice of the previous level. Thus, here we expanded the traditional four-choice temporal information encoding approach to include six options for choice selection in each of the levels comprising the menu, where an AR object guided the temporal encoding approach. We then used a univariate procedure for decoding participants' intention and used the same AR object to back-communicate the decoded answer. Additionally, to account for potential mistakes during the decoding process, we implemented an active error-correction procedure to be applied by the participants. Importantly, this specific combination of temporal encoding and univariate decoding approaches allows participants' intentions to be decoded based on the information recorded from even a single fNIRS channel provided that this channel has enough signal quality. With this in mind, in the present study we used a single channel for decoding participants' choices.

Although the application of BCIs has been limited primarily to a laboratory setting, some of the studies mentioned above have examined the possibility of using BCIs in everyday-life settings in different contexts (Takano et al., 2011; Blum et al., 2012; Afergan et al., 2015; Hu et al., 2019; Park et al., 2019). However, ecologically valid approaches are challenging to develop as, among other reasons, they should be as efficient, accurate and reliable as possible, but also easy to use, intuitive, and simple to (dis)assemble. This is probably the reason why most BCI research has focused predominantly on improving the technology (Liberati et al., 2015). There is a relevant body of work addressing that BCI design and development should become more user-centered in order to achieve successful everyday-life applications (Kübler et al., 2014; Liberati et al., 2015; Nijboer, 2015). Effort has been made to incorporate this aspect into various applications (Weyand and Chau, 2015; Weyand et al., 2015; Nagels-Coune et al., 2017; Weyand and Chau, 2017; Si-Mohammed et al., 2018). While still in a laboratory setting, in the present study we worked toward a user-centered communication system by letting participants choose their preferred motor-imagery task and by selecting participant-specific (single) most-informative fNIRS channel

for decoding their choices. Using a single channel constitutes the simplest setup to (dis)assemble. In addition, it should make the setup comfortable and thus prevent participants from withdrawing from fNIRS recordings due to setup-related discomfort (Suzuki et al., 2010; Cui et al., 2011; Rezazadeh Sereshkeh et al., 2018).

It is important to note that fNIRS measurements are contaminated by systemic interference of especially (but not limited to) extracerebral regions, which is mainly caused by cardiac pulsations, respiration, and blood-pressure variations (Boas et al., 2004; Tachtsidis and Scholkmann, 2016). Several approaches have been reported in the literature to reduce these noises: conventional band-pass filtering (Hocke et al., 2018; Pinti et al., 2019); modeling physiological noises as a sum of sinusoidal functions with known frequencies where their amplitudes are estimated by using the extended Kalman filter and regressed out using a general linear model (Prince et al., 2003); global signal-covariance removal by either principal/independent component analysis (Zhang et al., 2005; Aarabi and Huppert, 2016) or global average procedures (Batula et al., 2017); adaptive filters that use recursive least-squares estimation methods (Nguyen et al., 2018) or short-distance channel (SDC) regression (Saager and Berger, 2005; Saager et al., 2011; Goodwin et al., 2014). In fNIRS measurements these SDCs are channels that have reduced inter-optode separations such that the interrogated volume is confined primarily to extracerebral regions (Goodwin et al., 2014). The main assumption underlying their usability is that the same systemic physiological noise present in the normal-distance channels (NDCs) dominates the signal acquired with SDCs (Gagnon et al., 2012). Intuitively, SDCs can then be used to minimize/reduce unwanted physiological noise from the normal-distance channels. So far, not many fNIRS-based BCIs have employed them (but see (Shin et al., 2017)). This is partially because fNIRS equipment that allows such measurements has only recently become widely available. Here, SDC correction was used for the selection of the most-informative fNIRS channel as well as during the decoding process.

In this preliminary study participants achieved mean accuracy level of 74% (with a chance-level of 37.5% for six answer options), which shows that the temporal features of the fNIRS signal can be exploited in a temporal encoding paradigm to increase the degrees of freedom of a BCI using a single mental task. These accuracies also indicate that the proposed fNIRS-based AR-BCI setup can be successfully controlled, on average, by participants.

Importantly, this work conveys the fundamental steps toward developing the first fNIRS-based AR-BCI system to be used as a communication device for bedside applications in a clinical setting.

2 Materials and Methods

2.1 Participants

Twelve healthy volunteers [five males; mean age (SD) = 27.1 years (3.2 years)] with varying previous BCI/fNIRS/task experience participated in this study (see Table 2.1). Participants did not have a history of neurological disease and had a normal or corrected-to-normal vision. The experiment conformed to the Declaration of Helsinki and was approved by the ethics committee of the Faculty of Psychology and Neuroscience, Maastricht University. Informed consent was obtained from each participant before starting the measurements. Participants received financial compensation after the session.

Table 2.1. Participant characteristics

	Age range	fNIRS Cap Size (cm)	Previous experience			
			BCI	fNIRS	Task	
					Mental drawing	Interacting with cube
P01	20-25	56	First time	< 5 times	< 5 times	First time
P02	20-25	56	< 5 times	5 to 10 times	5 to 10 times	First time
P03	20-25	56	< 5 times	< 5 times	< 5 times	First time
P04	25-30	56	> 10 times	> 10 times	> 10 times	First time
P05	35-40	58	First time	First time	First time	First time
P06	25-30	56	< 5 times	< 5 times	5 to 10 times	First time
P07	25-30	58	< 5 times	5 to 10 times	< 5 times	First time
P08	25-30	58	First time	First time	First time	First time
P09	25-30	56	< 5 times	< 5 times	< 5 times	First time
P10	25-30	56	5 to 10 times	5 to 10 times	5 to 10 times	First time
P11	25-30	56	> 10 times	> 10 times	> 10 times	First time
P12	25-30	58	First time	< 5 times	< 5 times	First time

2.2 Experimental Design and Stimulus Display

2.2.1 General Structure

The experiment consisted of a training session and an immediately following experimental fNIRS session. The training session was self-paced and ranged between 15 and 35 min across participants: we only switched to the experimental fNIRS session when participants felt comfortable with the stimuli and the motor-task performance.

In an attempt to follow a user-centered approach, participants were introduced to two motor imagery tasks during the training session and asked to choose between them: (option 1) mental drawing [of small geometrical figures (a square, circle, etc.) or contour drawings (a star, flower, boat, etc.) and (option 2) imagine to interact with the virtually presented AR cube (by, e.g., to imagine to hit/squeeze it)]. Participants were asked to choose the mental task (mental drawing or imagining interacting with the cube), the specific strategy (drawing a square or imagining hitting the cube) they expected would work best and would interfere the least with the stimuli and to perform the motor-imagery task with their right hands. They were instructed to keep their eyes open throughout the experiment and to look at the computer screen while staying as still as possible during the runs.

The experimental fNIRS session lasted around 1.5 h. Participants first performed a functional localizer run, during which the participants were presented with a gray AR cube that contained specific symbols (5/6 = crosses, 1/6 = checkmark). For twelve consecutive times, they performed the selected motor imagery task when the checkmark was facing them (for 6 s) and had to rest for the remaining faces (for 30 s, see Figure 2.1). There was an initial baseline period of 36 s indicated by a blue rotating cube, in which participants rested. We chose a baseline period of 36 s to guarantee a stable baseline measure for real-time conversion of raw data into hemoglobin (Hb) concentration changes. After the twelve trials, the cube stopped rotating and became blue again, indicating the end of the run. This run was used to select a user-specific most-informative (“best”) fNIRS channel to decode participants’ choices in the eight subsequent choice-encoding runs (here on referred to as choice runs).

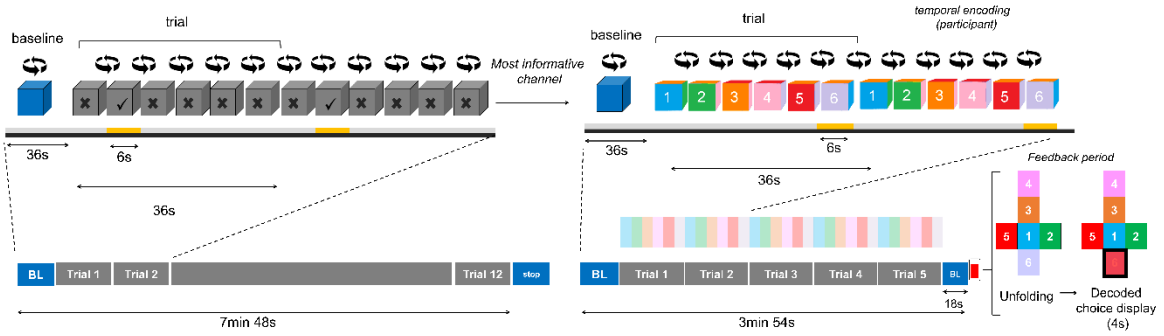


Figure 2.1. Experimental design. During the training session participants chose between two motor imagery tasks. Then, during the functional localizer run, participants performed the chosen task for twelve consecutive trials when the checkmark was facing them (indicated in yellow, below the face showing a checkmark) and had to rest for the remaining faces. There was an initial baseline (BL) period indicated by a blue rotating cube, in which participants rested. After the twelve trials the cube stopped rotating and became blue again, signaling the end of the run (indicated with the word stop in the figure). The user-specific most-informative channel from this run was used to decode participants' choices during the choice runs. Participants were asked to perform the mental task when the number corresponding to their choice was facing them (temporal information encoding), for five consecutive trials (in this example it corresponded to choice number 6, again underlined in yellow). After each run the feedback period started (indicated by the red square), during which the cube unfolded and the decoded choice was highlighted in red (for visualization purposes, we added a black thick square in this schematic representation). After the choice runs, participants were asked to fill in several questionnaires.

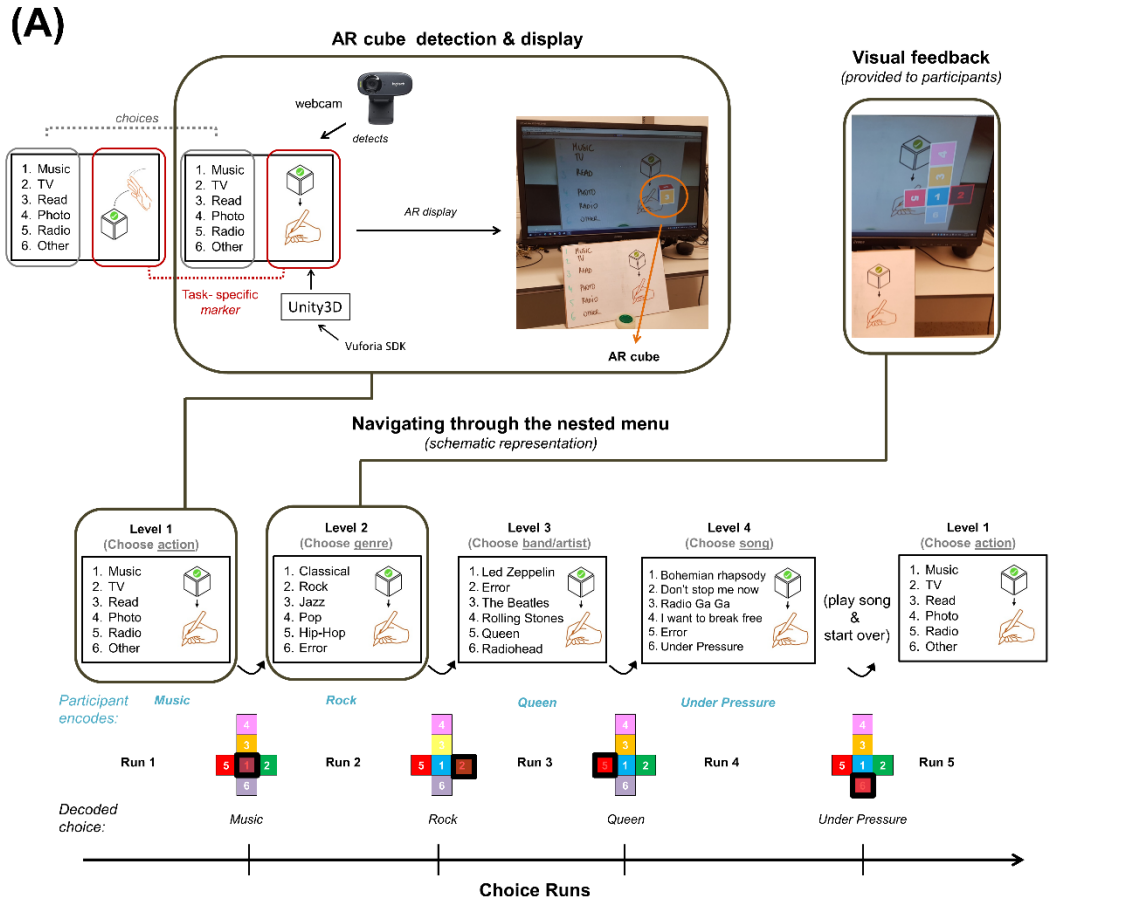
Each choice run aimed at selecting one option from a six-item list (menu). These runs differed from the functional localizer run in (1) the number of active motor imagery trials [five trials (choice runs) vs. twelve (functional localizer run)] and (2) the fact that the AR cube was color-coded and numbered (choice runs) vs. the AR cube was gray and contained geometrical shapes (functional localizer run). Importantly, the task duration remained at 6 s during the choice runs. During each choice run, participants selected one choice from a six-item list provided before the start of the run and performed the motor imagery task only when the number corresponding to their choice was facing them (temporal information encoding), for five consecutive times. There was an additional baseline period of 18 s after the last trial to ensure that the hemodynamic response goes back to baseline. After the run, the cube unfolded and the decoded choice (based on real-time analysis of the fNIRS data) was highlighted in red (see Figure 2.1).

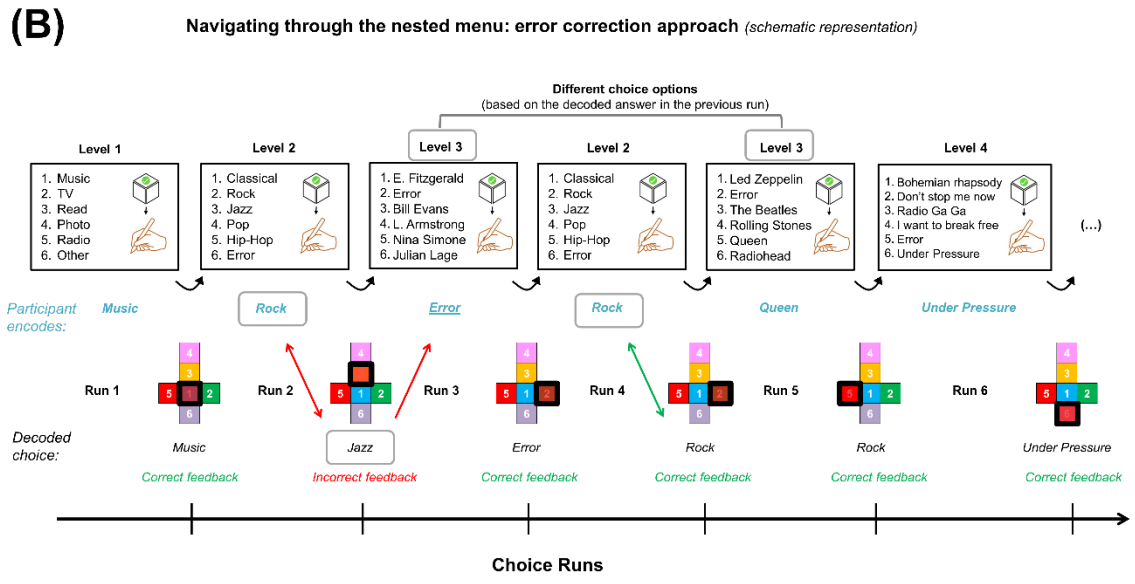
2.2.2 AR Stimulus Display

In this experiment, we used a variation of a VST-AR system, where a rotating AR cube

displayed on a computer screen embodied the menu and each face of the cube represented one choice of the list (see Figure 2.2A for an example of a user's view). In the presented AR system, a white A4 cardboard was used to represent the real-world stimulus that also served as a spatial point of reference necessary for the visualization of the AR cube. The A4 cardboard was placed on the desk, between the computer screen and the participants. The left half of the board was wrapped in transparent wrapping paper and served as a whiteboard, where choice options were handwritten (and modified after each run). The right half of the board contained a marker (a 2D-image, see hand-icon in top-left image of Figure 2.2A) that, when detected by the HD webcam (Logitech C270 HD, which was fixated on the participant's forehead using an elastic band and recording the cardboard), triggered the visualization of the AR cube on a standard computer screen. The AR cube was placed relative to the marker as seen in the camera image (see top-left image in Figure 2.2A) with the help of Vuforia (v7.1.34), an AR software development kit (SDK) that was running in Unity3D. This SDK makes it possible to detect the marker and to place the virtual cube on it, creating the effect of augmented reality. The marker was motor imagery task-specific and reminded participants of the task to be performed (mental drawing or virtual interaction with the cube). After each run, an unfolded AR cube was displayed on the computer screen highlighting the decoded choice of the participant (see top-right image, Figure 2.2A).

Figure 2.2. AR display and example of a full cycle of the nested menu (next page). (A) A task-specific marker in the right-side of the A4 cardboard served as the spatial point of reference necessary for the visualization of the AR cube. This cube was used to navigate through a four-level nested menu with six options in each level. The choice options encoded by the participant are written in blue, while the decoded answers are written in black and highlighted in red with a black thick square in the schematic representation of the unfolded cube. The choice options provided in each level were based on the decoded choice of the previous run. (B) If the decoded choice was incorrect, they were asked to choose the "Error" option in the next run. If "Error" was decoded, they were provided with the same option list they saw before the error occurred. In this example, the participant chose to perform a mental drawing task, as indicated by the markers under "Navigating through the nested menu". In the first level, we provided participants with keywords that responded to the question "What would you like to do?" Since the decoded choice [Listen to] Music (highlighted in red only in the actual run; highlighted in red and with a black thick square in the schematic view) was correct, the next run summarized music-genre options (Level 2). Here, the participant chose "Rock" [music] but the decoded choice was "Jazz". Thus, the participant was provided with Jazz-band options in the next run (Level 3), where (s)he encoded the "Error" option. Since the "Error" option was correctly decoded (see displayed choice after Run 3), the participant was provided again with Level 2 choice options. The procedure went on until the participant reached the last level of the nested menu. At the end of the run, we played the decoded song ("Under pressure" in this example) to the participant and (s)he was directed back to the first level of the menu.


(A)
AR cube detection & display
webcam
detects
choices
1. Music
2. TV
3. Read
4. Photo
5. Radio
6. Other
AR display
Task- specific marker
Unity3D
Vuforia SDK
AR cube
Visual feedback
(provided to participants)
Navigating through the nested menu
(schematic representation)
Level 1
(Choose action)
Level 2
(Choose genre)
1. Classical
2. Rock
3. Jazz
4. Pop
5. Hip-Hop
6. Error
Level 3
(Choose band/artist)
1. Led Zeppelin
2. Error
3. The Beatles
4. Rolling Stones
5. Queen
6. Radiohead
Level 4
(Choose song)
1. Bohemian rhapsody
2. Don't stop me now
3. Radio Ga Ga
4. I want to break free
5. Error
6. Under Pressure
(play song & start over)
Participant encodes:
Music
Rock
Queen
Under Pressure
Run 1
Run 2
Run 3
Run 4
Run 5
Decoded choice:
Choice Runs


(B)
Navigating through the nested menu: error correction approach (schematic representation)
Different choice options
(based on the decoded answer in the previous run)
Level 1
Level 2
Level 3
Level 4
1. Music
2. TV
3. Read
4. Photo
5. Radio
6. Other
1. Classical
2. Rock
3. Jazz
4. Pop
5. Hip-Hop
6. Error
1. E. Fitzgerald
2. Error
3. Bill Evans
4. L. Armstrong
5. Nina Simone
6. Julian Lage
1. Led Zeppelin
2. Error
3. The Beatles
4. Rolling Stones
5. Queen
6. Radiohead
1. Bohemian rhapsody
2. Don't stop me now
3. Radio Ga Ga
4. I want to break free
5. Error
6. Under Pressure
(...)
Participant encodes:
Music
Rock
Error
Rock
Queen
Under Pressure
Run 1
Run 2
Run 3
Run 4
Run 5
Run 6
Decoded choice:
Music
Jazz
Error
Rock
Rock
Under Pressure
Correct feedback
Incorrect feedback
Correct feedback
Correct feedback
Correct feedback
Correct feedback
Choice Runs

2.2.3 Nested Menu and Error-Correction Approach

The menu presented during choice runs consisted of four levels that were interconnected in such a way that the choice options provided in each level were based on the decoded choice of the previous run. The provided answer options became more specific throughout the levels. An example transition of provided options from level one to level four would be: listen to music > choose a genre > choose a band/artist > choose a song. Displaying the selected choice of the fourth level (a song, a picture, a movie, etc., depending on the choice in the first level) indicated the end of the navigation round, and participants were directed back to the first level of the menu (see Figure 2.2A). This structure allowed participants to go through a four-level nested menu twice if all choices were correctly decoded.

Importantly, it could be that the decoded choice of any given level of the nested menu did not match the encoded option by the participant. To account for such decoding mistakes and in a first attempt to correct for it, participants were instructed to choose the "Error" option in the next run. This "Error" option was part of the choice list in levels > 1 and the position this option appeared on the menu list was balanced across the different levels. If "Error" was decoded, they were provided with the same option lists they saw before the decoding mistake was made (see first Level 2 trial in Figure 2.2B).

2.3 fNIRS Data Acquisition

fNIRS data was recorded using a continuous-wave system (NIRScout-816, NIRx, Medizintechnik GmbH, Berlin, Germany). The optode setup consisted of nine sources and eight detectors which were placed on the left hemisphere that cover areas commonly associated with motor imagery, i.e., premotor cortex and part of the supplementary motor area, primary motor cortex, somatosensory motor cortex and part of the parietal cortex following the extended 10/10 EEG system (see Figure 2.3; (Sorger et al., 2012; Abdalmalak et al., 2016; Batula et al., 2017; Erdogan et al., 2019; Klein and Kranczioch, 2019). An in-house SDC was created by placing source S9 as close as the optodes would allow (∼13 mm away) to detector D5 on the same sagittal plane that connects D5 and source S6 (see Figure 2.3). The signal measured by the SDC should be influenced by the mid-sagittal sinus and other large vascular structures commonly found in this region (Duvernoy et al., 1981), which have been shown to be affected by low frequency oscillations and cardiac signals (Tong and Frederick, 2012). We used this information as a proxy to account for physiological noise in

the region covered by the optode setup.

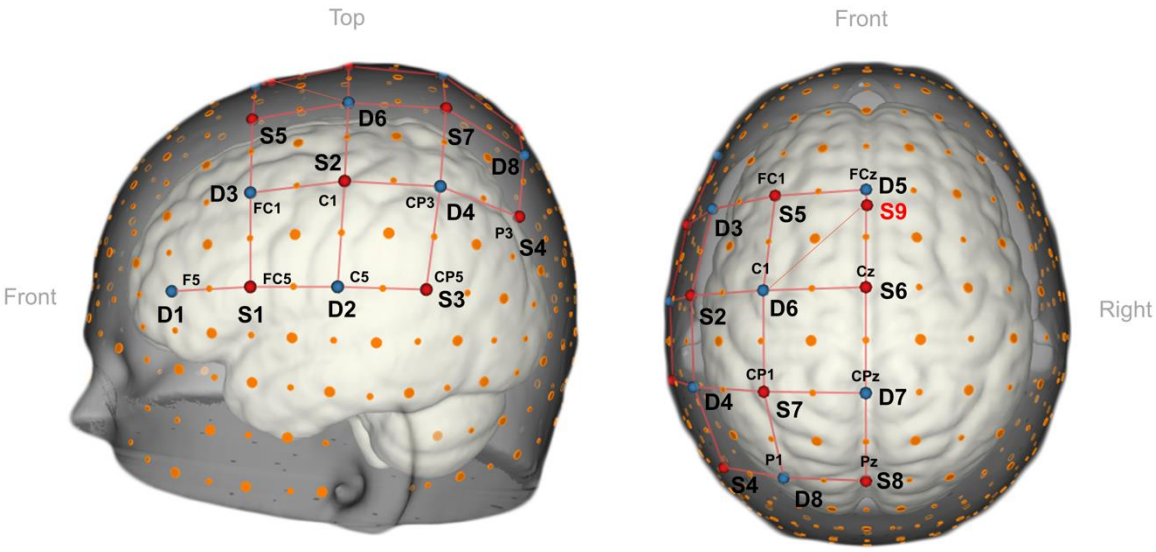


Figure 2.3. 3D view of the fNIRS-optode arrangement. The setup consisted of nine sources (in red), and eight detectors (in blue) placed over the left-hemipsheric motor and premotor regions. In total the setup contained one SDC (S9-D5) and 24 NDC. For the 3D representation we used NIRSite v1.0 software (NIRx Medizitechnik GmbH, Berlin, Germany; RRID: SCR_002491).

In total, the setup contained 24 NDCs and one SDC. The mean inter-optode distance of the standard channels spanned from 26.1 to 36.5 mm. Sources emitted light at wavelengths 760 and 850 nm, and the light intensity acquired at the detector side was sampled at 6.94 Hz. Besides the standard cap fixation (using the chin band), the fNIRS cap (EasyCap 128Ch ActiCap, EasyCap GmbH, Herrsching, Germany) was fixated onto the participants' head with three medical tape stripes (connecting the cap and the participant's forehead) to assure the cap would not shift during the measurements. In addition, a black, plastic overcap was placed on top of the fNIRS cap to additionally prevent the light in the room from reaching the optodes.

2.4 Apparatus

The session took place in a lab that consisted of two rooms, i.e., an inner and an outer room, where the hardware and materials comprising the setup were distributed (see Figure 2.4). We used NIRStar 15.2 (NIRx, Medizintechnik GmbH, Berlin, Germany) for recording the data and Turbo-Satori (TSI) 1.4.2 (BrainInnovation B.V., Maastricht, the

Netherlands;(Lührs and Goebel, 2017)) and Matlab 2017a (The MathWorks Inc., Natick, Massachusetts, United States) for real-time preprocessing and decoding the participants' choices, respectively (see Data Analysis section). The three programs ran on the data-recording and -analysis laptop (depicted with number 6 in Figure 2.4). NIRStar 15.2 was connected to the NIRScout system via USB and to TSI via Lab Streaming Layer (LSL). TSI and Matlab were connected via the TSI-Matlab interface, a self-designed network interface enabling real-time access to raw and preprocessed fNIRS data as well as protocol and statistical information (Lührs and Goebel (2017); BrainInnovationSupport, 2019). In addition, Matlab was used to log the different experimental conditions by sending triggers to the fNIRS system via LSL and to control the stimulus display that was running in Unity 3D software (v2018.3.2.f1, Unity Technologies, San Francisco, California, United States), which was running in the stimulus laptop (number 5 in Figure 2.4). During choice-encoding runs Matlab sent to Unity3D the following commands via TCP/IP: ("a") start of the run, which initiated the rotation of the inactive (blue) AR cube; ("b"), start of the encoding period, which turned the inactive cube into an active one by changing the blue-colored faces into color-coded faces; ("c") last rest period, which turned the face of the AR cube back to blue, indicating the last rest period of the run; ("1–6") decoded choice, which unfolded the cube and highlighted in red the decoded choice. All commands except for those pertaining to the decoded choice were used for the functional localizer run. The computer screen in the inner room was connected to the stimulus laptop through an HDMI cable. The HD webcam in the inner room (number 3 in Figure 2.4) was connected to the stimulus laptop via USB.

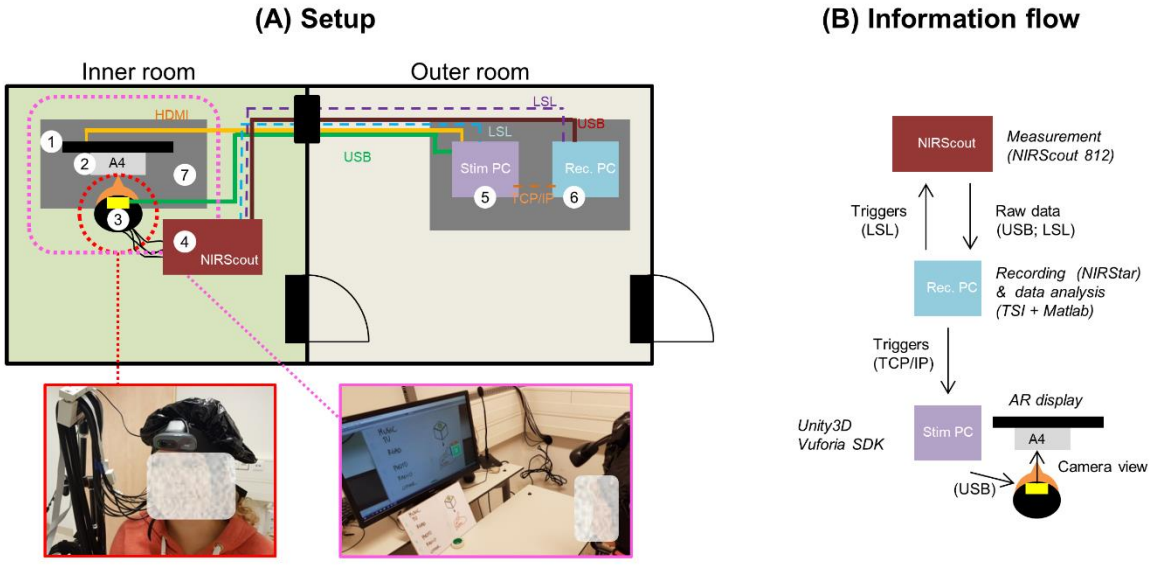


Figure 2.4. Summary of the technical setup and connections between its different components. (A) Setup. The inner room, where participants were measured while seated (see (3) and enlarged picture), contained the fNIRS system (4), a computer screen (1), an HD webcam (3), the A4 cardboard (2) and a desk (7). The outer room, where the experimenter was located, hosted the two laptops, i.e., the data-recording and -analysis laptop (6) and the stimulus laptop (5). Physical connections (wires) are depicted with continuous lines, while non-physical connections [Lab Stream Layer (LSL), TCP/IP] connections are depicted with dashed lines. (B) Information flow. NIRStar 15.2 was connected to the NIRScout system via USB and to Turbo-Satori (TSI) via LSL. TSI and Matlab were connected via the TSI-Matlab interface. Matlab was used to send triggers back to the fNIRS system via LSL and to control the stimulus display in Unity3D software (via TCP/IP).

2.5 Subjective Ratings and Previous Experience Report

After the completion of the experiment, participants first rated how comfortable the setup (optodes and webcam) felt throughout the session according to a Likert-scale ranging from 0 (extremely uncomfortable) to 10 (extremely comfortable). We predicted that comfortability ratings would decrease over time due to the presence of local pressure on the head surface caused by optodes (Nagels-Coune et al., 2017) and the webcam. Then participants rated the general easiness, pleasantness and vividness of the two motor imagery tasks they were trained on using another Likert-scale ranging from 0 (extremely difficult/unpleasant/not vivid at all) to 10 (extremely easy/pleasant/very vivid). In addition, participants were asked to report on their previous motor imagery task, fNIRS and BCI experience (first time, less than five, five to ten times or more than ten experiments).

2.6 Data Analysis

2.6.1 Real-Time Analysis

2.6.1.1 Data preprocessing

Raw fNIRS data were first converted into optical-density data and then into changes in Hb concentration through the modified Beer-Lambert law in real-time, using differential path-length factors of λ_{760} = 6.40 and λ_{850} = 5.85 (Essenpreis et al., 1993) and a baseline calculation period of 15 s (10–25 s after run onset). Data were filtered using a first-order moving-average high-pass filter with a cutoff of 0.01 Hz and a second-order moving-average low-pass filter with a cutoff of 0.25 Hz. No motion correction was applied.

2.6.1.2 Channel selection

The channel and Hb-type selection per participant was based on the result of the general linear model (GLM) analysis. Specifically, the selection was based on the chromophore and channel that led to the highest t-statistic of the task vs. rest contrast in the functional localizer run. The design matrix included one task predictor convolved with a standard hemodynamic response function (HRF). The default HRF from SPM12 was used (two Gamma HRF, the onset of response and undershoot 6 and 16 s, respectively, dispersion 1 s, response to undershot ratio 6) and the same amplitudes were used for the Δ[HbO] and Δ[HbR] task predictors. In addition, a constant term and the SDC time course were used as confound predictors should the latter satisfy the coefficient of variation criterion (CV < 7.5%, which was the case for all participants). The pre-whitening approach implemented in TSI was used to remove serial correlations (Lührs and Goebel, 2017).

2.6.1.3 Temporal decoding

During choice runs the time course of the selected channel was read in real-time in Matlab using the TSI-Matlab interface. Participants' choices were decoded by fitting a GLM in Matlab using glmfit to all five trials in each choice run (see Figure 2.5). The design matrix differed from the functional localizer run in that it included six task predictors (one for each choice option, i.e., choice period) instead of one convolved with the HRF. Importantly, the SDC time course was used as a confound predictor during choice runs only if it was used as a confound predictor during the channel selection process. No pre-whitening was applied. The condition that led to the highest t-estimate of the task vs. rest contrast was considered the selected choice (see Figure 2.5). It should be noted that this analysis was re-computed

offline using a simulated real-time approach for participants P01–P07 due to a technical mistake during these sessions.

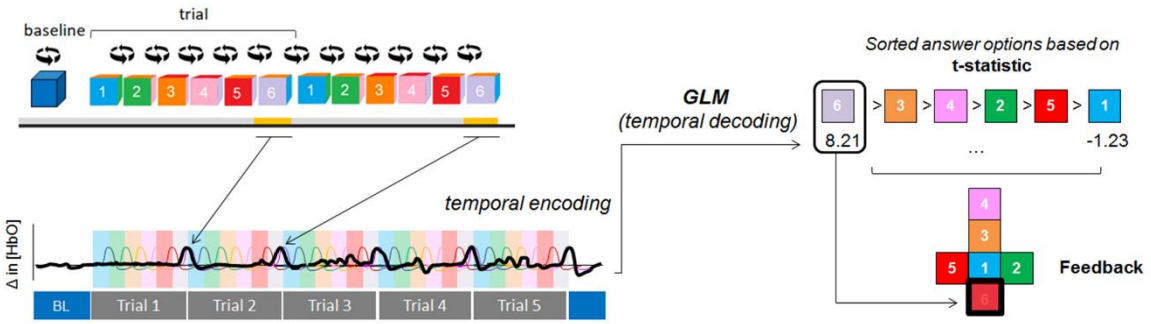


Figure 2.5. Temporal-decoding approach. A GLM was fitted to the Δ[HbX] data (from five repeated trials) to decode the participants' intentions. In this example, the participant encoded option #6 (represented by the black, thick line) and Δ[HbO] signal was used for decoding. Each colored area represents the encoding time (the period where participants were instructed to perform the mental task) for each of the cube faces. Each colored HRF represents the expected fNIRS response for each of the options. After the run the cube unfolded and feedback was provided by highlighting in red the decoded intention (which was the condition that led to the highest t-statistic [option 6, t-value = 8.21]). For visualization purposes, we added a black thick square in this schematic representation).

2.6.2 Offline Analysis

2.6.2.1 Channel-selection assessment

We evaluated the effect (on choice-decoding accuracies) of using a predefined Hb type for the channel selection vs. selecting the most informative Δ[HbX] channel (where Δ[HbX] ϵ{Δ[HbO], Δ[HbR]}). Importantly, and despite following a single-channel decoding approach, we kept all channels in place to carry out this assessment.

Besides, we evaluated the effect (on choice-decoding accuracies) of using the SDC as confound predictor in the channel-selection process. Differences across Hb-type and usage of SDC were tested for significance using a two-way ANOVA with factors SDC (with SDC, without SDC) × Hb-type (Δ[HbX], Δ[HbO], Δ[HbR]), followed by paired t-tests.

2.6.2.2 Effect of the number of trials in the decoding process

We used the same univariate choice-decoding approach as described in section *Temporal decoding* to evaluate the effect of the number of trials in a given run on decoding accuracies

(based on the most informative Δ[HbX] channel). For that, we computed the accuracies of all consecutive trial combinations for every trial number (1:n trials, where n={1,2,3,4,5}). For example, to compute the decoding accuracy of three trials, trial combinations 1-2-3, 2-3-4, and 3-4-5 were used. We then quantified the effect of the number of repetitions in the decoding accuracy at the group level using Spearman's rho correlation coefficient. The effect of number of trials was additionally evaluated using information transfer rate (ITR), defined as in (Allison et al., 2012):

$$ITR = \left(log_2 N + P * log_2 P + (1-P) * log_2 \left(\frac{1-P}{N-1} \right) \right) * \frac{60}{\tau} \qquad (2.1)$$

where N is the number of classes, P is the classification accuracy and τ is the duration of task and rest period, in seconds.

2.6.2.3 Decoding accuracy of error-correction trials

We incorporated an error-correction mechanism in our decoding process by including an "Error" option in levels > 1 of the menu. We assessed the accuracy of the error-correction approach with a confusion matrix. For that, we pooled all encoded answers across participants and divided them into "Error" and "Non-Error" instances, depending on whether the participant intended to encode "Error" or not, respectively. The encoded choices were then compared to the decoded ones. Four measures were extracted from the confusion matrix, namely accuracy, recall, precision and specificity, which were calculated as follows:

- Accuracy = (TP + TN)/(TP + TN + FP + FN)
- Recall = TP/(TP + FN)
- Precision = TP/(TP + FP)
- Specificity = TN/(TN + FP)

where TP = True positive or correctly detected "Error" trials; TN = True negative or correctly detected "Non-Error" trials; FP = False Positive or incorrectly detected "Error" trials; FN = False negative or incorrectly undetected "Error" trial.

2.6.2.4 Chance-level definition

A quantile function of a multinomial distribution was used to define the upper bound of the

chance-level (37.5% for N = eight runs, c = six classes and a $p < 0.05$).

2.6.2.5 Subjective ratings

Mean and SE of normalized subjective comfortability ratings was computed by calculating the mean (of eight runs) for each subject and subtracting the subject's mean to each item. The effect of the duration of the experiment (number of runs) on the comfortability score was quantified using Pearson's correlation. In addition, the relation between previous BCI/fNIRS/task experience on task accuracies reached by each participant was assessed using Spearman's correlation coefficient. Finally, to evaluate the perceptual differences the mental tasks elicit on each participant, normalized absolute mean differences between the preferred and non-preferred mental task ratings were assessed. First, each item was normalized following the same approach as for the comfortability ratings. Next, the three scores (easiness, pleasantness and vividness) were averaged for each mental task and participant. Then, absolute differences between mental tasks were computed and a right-tailed t-test was used in Matlab.

3 Results

3.1 Choice-Decoding Results Obtained in (Simulated) Real-Time

Figure 2.6 shows the individual and group accuracies achieved in the experiment. In addition, it shows that half of the participants chose to perform the mental-drawing task and that Δ[HbR] was selected for seven out of twelve participants. All participants but P04 exceeded the upper bound of the chance-level (37.50%, orange dashed line). It should be noted that accuracies from participants P01-P07 were computed offline using a simulated real-time approach due to a technical mistake during these sessions, while accuracies from participants P08-P12 were calculated online based on real-time results. On average, participants reached an accuracy of 73.96% (SD = 20.96), as depicted by the left-most gray bar of the group plots. Mean decoding accuracies with different grouping factors were also computed and descriptively did not differ substantially within each group (see Figure 2.6).

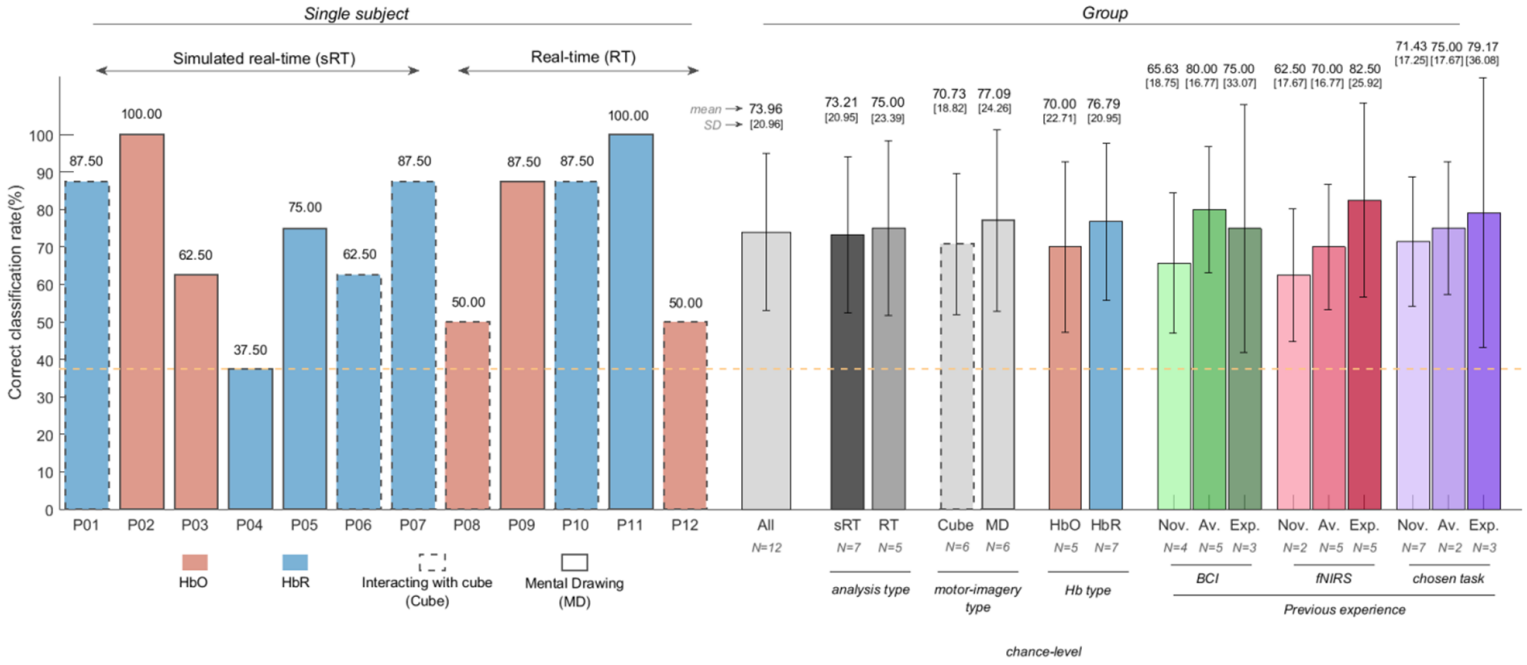


Figure 2.6. Choice-decoding accuracies obtained in (simulated) real-time (individual and group results) using Δ[HbX] channel selection and SDC correction. All participants but P04 reached accuracies higher than chance-level (orange, dashed line). The face colors and line pattern of the bar plots of each subject (left-half of the figure) represent the selected Hb-type and strategy participants chose to perform, respectively. Mean decoding accuracies and standard deviation of all participants and with different grouping factors can be found on the right-half of the figure. Groupings were based on the analysis type (simulated real-time vs. real-time), the motor imagery participants chose [interacting with the cube (cube) vs. mental drawing (MD)], the selected chromophore (Δ[HbO] vs. Δ[HbR]) and previous BCI experience (novices, average and experts). Participants with no previous BCI/fNIRS/task experience were considered novices; expert participants were those who had participated in more than five BCI experiments; the remaining participants were considered average (see Table 2.2). The integer after "N = " indicates the number of participants employed in each computation.

3.2 Evaluation of Error-Correction Procedure

In total, participants had to encode the "Error" option 22 times (see Figures 2.7A,B). Out of the 22 instances, the error option was correctly detected 14 times, missed eight times, and incorrectly labeled once, as indicated in the confusion matrix (Figure 2.7A). Overall, the accuracy of the error-correction trials was 90.6% (upper bound of the chance level was 58.88%, assessed by the quantile function of a multinomial distribution with n = 96 trials, c = 2 classes and alpha = 0.05).

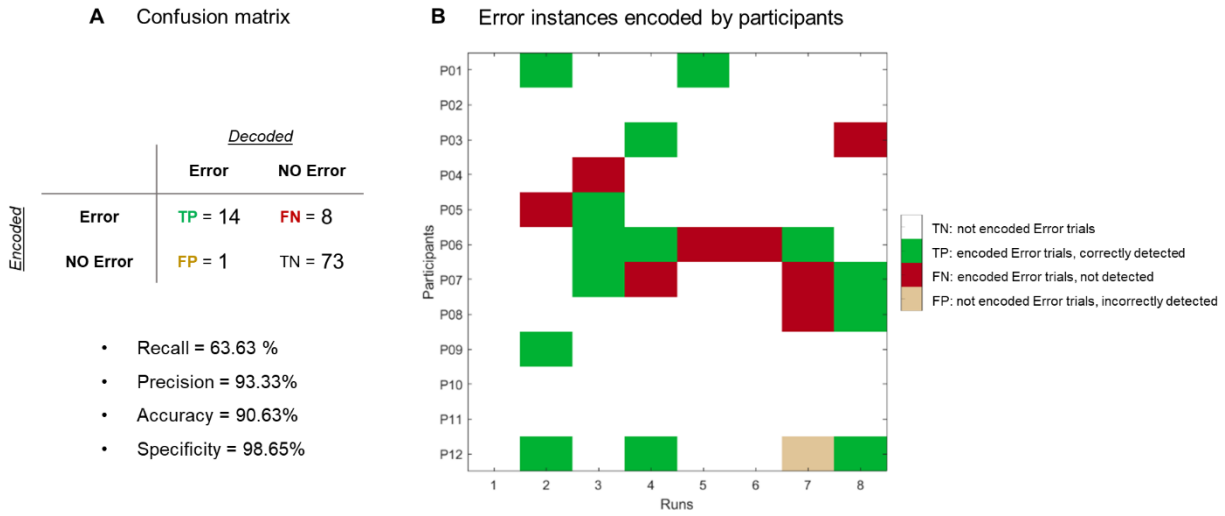


Figure 2.7. Evaluation of error-correction procedure. (A) Confusion matrix. Participants reached an accuracy of 90.62% (72/96 trials were correctly labeled as "Error" or "NoError") and a recall level of 65.22% (out of 22 error trials, 8 trials were missed). (B) Summary matrix of when participants encoded the "Error" option (marked in dark gray). Green (red) cells represent trials where the "Error" option was correctly (incorrectly) detected. The beige cell indicate a false positive trial.

3.3 Assessment of the Effect of Number of Trial Repetitions

To assess how the number of trial repetitions affects the decoding process, we sequentially reduced the number of trial repetitions we used for decoding. Table 2.2 summarizes the individual and group decoding accuracies for a decreasing number of repetitions and Figure 2.8A shows that the number of repetitions used to decode each run influences the decoding process. Specifically, we observed a significant negative correlation between the accuracies and the number of repetitions, as assessed by Spearman's rho correlation coefficient

($\rho = -0.639$, $p < 0.0001$). Importantly, mean- and several single-subject accuracies (7 out of 12 participants) remained above chance level even when using a single trial. As for the ITR computation, Figure 2.8B indicates that slightly higher ITR values can be reached, on average, when using four trials (0.34 bits/min) instead of five (0.29 bits/min).

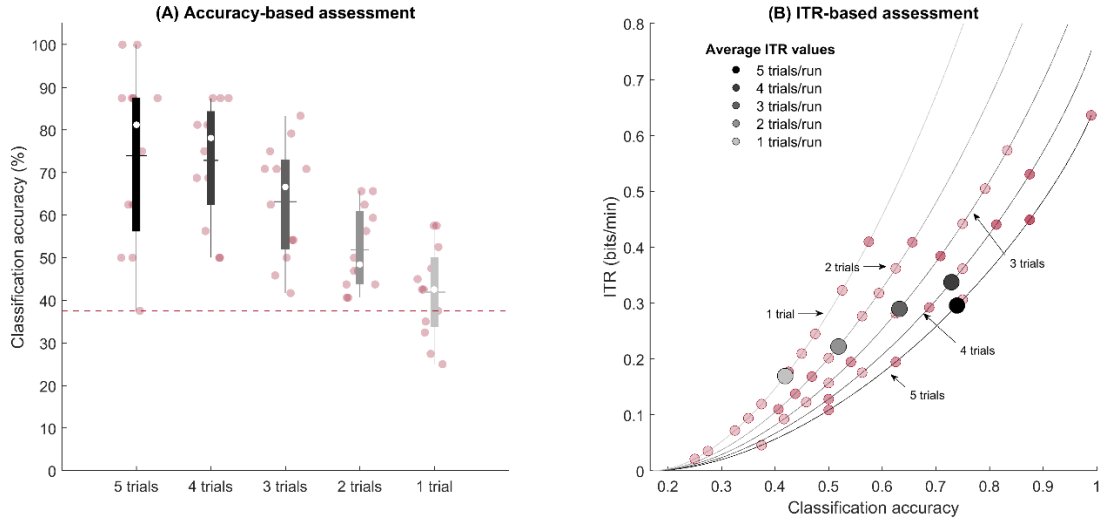


Figure 2.8. Effect of the number of trial repetitions on obtained decoding accuracy (individual and group results). (A) The box-plot shading depicts the number of repetitions used for decoding: from five trials (black) to a single trial (light gray). Median values are represented by the white circles, while the mean values are indicated with the horizontal lines. The y-axis represents the accuracy (%) achieved by the participant. The red, dashed line shows the chance-level defined by the cumulative multinomial distribution. The number of trials used to decode each run influences the decoding process, but mean- and several single-subject accuracies remain above chance level even with a single trial. (B) Average (gray-scale markers) and single-subject (red markers) ITR values (bits/min) for different number of trials as a function of achieved classification accuracies. Lines represent the theoretical values the ITR can take as a function of the number of classes, trial duration and accuracy.

Table 2.2. Individual and group decoding accuracies over decreasing number of repetitions

	Accuracies (%)				
	5 trials	**4 trials**	**3 trials**	**2 trials**	**1 trials**
P01	87.50	81.25	70.83	65.63	47.50
P02	100.00	81.25	70.83	59.38	57.50
P03	62.50	75.00	54.17	56.25	45.00
P04	37.50	50.00	54.17	43.75	37.50
P05	75.00	50.00	50.00	50.00	42.50
P06	62.50	68.75	41.67	46.88	27.50
P07	87.50	87.50	79.17	65.63	57.50
P08	50.00	56.25	45.83	40.63	32.50
P09	87.50	81.25	75.00	43.75	35.00
P10	87.50	87.50	83.33	62.50	52.50
P11	100.00	87.50	62.50	46.88	42.50
P12	50.00	68.75	70.83	40.63	25.00
Group [SD]	**73.96 [20.96]**	**72.92 [14.19]**	**63.19 [13.74]**	**51.82 [9.56]**	**41.88 [11.83]**

3.4 Assessment of Channel Selection

Although our channel selection approach was based on selecting the most informative Δ[HbX] channel for each participant, it is not uncommon to have a predefined Hb-type before the data acquisition (Naseer and Hong, 2015a). In this context, we looked at whether the selected channel would change had we decided to focus on only one chromophore. In addition, since we used the SDC time course as a confound predictor, we assessed whether applying SDC correction (or not) influences the channel selection. Table 2.3 shows that for some participants, the channel selection approach does not affect the selected channel (see P01, P02, P07 and P11 across all columns), while for other participants it does. Descriptively speaking, SDC correction slightly reduced the mean accuracy for the most-informative Δ[HbX]-channel approach. The reason behind this observation is that the increased accuracy for some participants (P03, P06, P09, P11, and P12) was smaller than the decrease in accuracies for other participants (P04, P05, P08, and P10). The mean decoding accuracy increased for the most-informative Δ[HbO] and Δ[HbR] channel approaches (although to a considerably lesser extent for the latter).

Table 2.3. Most informative channel for different channel selection approaches and (individual and mean) accuracies reached with each approach

	Accuracies (%)											
	Best Δ[HbX]				Best Δ[HbO]				Best Δ[HbR]			
	SDC		no SDC		SDC		no SDC		SDC		no SDC	
P01	S3-D2	87.5 (=)	S3-D2	87.5	S3-D2	75.0 (↑)	S3-D2	25.0	S3-D2	87.5 (=)	S3-D2	87.5
P02	S9-D6	100 (=)	S9-D6	100	S9-D6	100 (=)	S9-D6	100	S9-D6	87.5 (=)	S9-D6	87.5
P03	S6-D5	62.5 (↑)	S2-D6	37.5	S6-D5	62.5 (↑)	S9-D6	25.0	S2-D6	62.5 (↑)	S2-D6	37.5
P04	S1-D3	37.5 (↓)	S9-D6	100	S1-D3	25.0 (↓)	S9-D6	100	S1-D3	37.5 (↓)	S5-D6	75.0
P05	S2-D4	75.0 (↓)	S2-D4	87.5	S7-D8	25.0 (↑)	S6-D7	12.5	S2-D4	75.0 (↓)	S2-D4	87.5
P06	S2-D6	62.5 (↑)	S3-D2	25.0	S2-D6	62.5 (↑)	S2-D6	12.5	S2-D6	62.5 (↑)	S3-D2	25.0
P07	S2-D4	87.5 (=)	S2-D4	87.5	S2-D4	75.0 (↑)	S2-D4	37.5	S2-D4	87.5 (=)	S2-D4	87.5
P08	S1-D2	50.0 (↓)	S2-D2	100	S1-D2	50.0 (↓)	S1-D2	62.5	S2-D2	100 (=)	S2-D2	100
P09	S2-D3	87.5 (↑)	S2-D3	75.0	S2-D3	87.5 (↑)	S2-D3	75.0	S1-D3	75.0 (=)	S5-D6	75.0
P10	S1-D2	87.5 (↓)	S1-D2	100	S1-D2	87.5 (↑)	S3-D2	75.0	S1-D2	87.5 (↓)	S1-D2	100
P11	S1-D3	100 (↑)	S1-D3	62.5	S1-D3	50.0 (↑)	S1-D3	37.5	S1-D3	100 (↑)	S1-D3	62.5
P12	S5-D5	50.0 (↑)	S2-D4	37.5	S5-D5	50.0 (↑)	S2-D4	37.5	S2-D3	12.5 (↓)	S2-D4	37.5
Group (SD)		**73.96 (20.96) (↓)**		**75.00 (27.70)**		**62.50 (23.84) (↑)**		**50.00 (31.53)**		**72.92 (26.02) (↑)**		**71.88 (25.63)**

Note 1: Red (blue) cells indicate that the selected chromophore was Δ[HbO] (Δ[HbR])

Note 2: The different symbols summarize the effect in decoding accuracy (↑ [increased], ↓ [decreased], = [maintained]) when SDC was used as a confound predictor *vs. w*hen it was not

A repeated measures 2-way ANOVA with factors SDC (with SDC, without SDC) × Hb-type (Δ[HbX], Δ[HbO], Δ[HbR]) showed that the mean accuracies were different across Hb-types [main effect of Hb-types; $F(2,66) = 3.494$, $p = 0.036$; no significant interaction], but not across SDC. Subsequent paired t-tests showed that Δ[HbX] and Δ[HbR] performed better than Δ[HbO] [$t(23) = 3.83$; p(FDR [$q = 0.05$]) = 0.001, and $t(23) = 2.736$; p(FDR [$q = 0.05$]) = 0.008].

3.5 Previous Experience and Subjective Reports

Due to the (novel) AR component, the participants were enthusiastic about the research study. Independent of the achieved accuracies participants rated the setup positively and considered the experiment as "fun," "engaging," and "motivating." The setup became uncomfortable over the runs as indicated by a significant negative correlation ($r = -0.991$, p

< 0.0001). Participants reported the main source of discomfort to be the pressure caused by the webcam on their foreheads and to a lesser extent the optodes on the head surface. We observed that the preferred motor imagery task was rated significantly higher than the non-preferred task [$t(11) = 5.240$, $p < 0.001$]. In addition, we observed that previous BCI/fNIRS/task experience correlated positively with individual accuracies, but none of them reached significance ($\rho task = 0.429$, $\rho BCI = 0.360$, $\rho fNIRS = 0.566$, $p > 0.05$).

4 Discussion

The present proof-of-concept study combined AR technology and an fNIRS-based BCI to apply it in a communication context, where twelve healthy participants were asked to navigate in real-time through a nested six-choice menu while following a temporal information encoding approach. The decoded choice was defined for each participant based on the time course of the most-informative channel in the setup. In case the decoded choice was incorrect, an active error correction procedure was used. We achieved mean accuracy levels of 73.96% (with a chance-level of 37.5% for six answer options) and error detection accuracies of 90.6%. The following sections discuss the general implications of this study, together with its limitations and prospects for the future.

The Temporal Information Encoding Approach – A Powerful Paradigm for fNIRS-Based BCIs

In this experiment, we applied for the first time a temporal information encoding approach and a GLM-based decoding scheme previously reported in fMRI-based BCIs (Sorger et al., 2009; Bardin et al., 2011; Sorger et al., 2012) to an fNIRS-based BCI system to distinguish between six options using a single channel and mental task. An advantage of using this procedure is that a single channel may be sufficient for decoding participants' intentions without hampering our decoding ability. Intuitively, using a single channel should also make the setup more comfortable. It should be mentioned that although we assessed the feasibility of the single-channel approach and recorded participants' comfortability scores over time, we kept all channels in place for post hoc analyses. Another advantage is that, theoretically, this approach could allow including a considerably high number of conditions. In the present work we have further advanced previous applications by going from four (Sorger et al., 2009; Bardin et al., 2011) to now six temporally different but still differentiable encoding

phases. Importantly, future work should explore the upper limit of the included number of conditions that would yield a sufficiently high decoding accuracy. In any case, increasing the number of conditions would inevitably rise the duration of the run, but this could be solved by reducing the task duration to a certain extent. Until now the biggest body of hemodynamic BCI applications has used a task duration of 10 s (Herff et al., 2013; Naseer and Hong, 2013; Hong and Santosa, 2016; Nagels-Coune et al., 2017; Shin et al., 2017) or longer (Bardin et al., 2011; Bauernfeind et al., 2011; Batula et al., 2017), and very few studies have used task durations under 10 s: for example, (Sorger et al., 2009)and (Shin and Jeong, 2014) used variable task durations of 5/10/15 s and 6/8/10/15 s, respectively. To maintain the single-trial duration as low as possible without hindering the ability to distinguish between conditions, we opted to use 6 s task duration per condition for our experiment. However, the considerable inter-subject variability in accuracies suggests that user-tailored task durations should be considered in future studies.

Using a Single fNIRS Channel – A Promising Approach in the Context of Temporal Information Encoding

Selected Feature

Feature selection varies across studies, but in general, previous work has focused on either using only Δ[HbO] signal (Stangl et al., 2013; Erdoğan et al., 2014; Hong et al., 2015; Koo et al., 2015; Hong and Santosa, 2016; Lapborisuth et al., 2017; Noori et al., 2017; Liu et al., 2018) or the combination of different chromophores (computing the mean or the difference of Δ[HbO] and Δ[HbR], Naseer and Hong, 2015b). A few fNIRS-BCI applications have used/explored Δ[HbR] on its own (Cui et al., 2010; Naseer and Hong, 2015b; Hwang et al., 2016). The main reason is that Δ[HbO] is considered to exhibit larger and more pronounced concentration changes than Δ[HbR] in response to mental tasks (Stangl et al., 2013; Sato et al., 2016). Besides, it has been reported that Δ[HbO] signals are more discriminative and perform more robustly than Δ[HbR] signals (Mihara et al., 2012; Naseer and Hong, 2015b). However, Cui et al. (2010) and Hwang et al. (2016) found that Δ[HbO] and Δ[HbR] performed similarly in terms of accuracy. In the present work the channel selection approach led to selecting Δ[HbR] for 7/12 participants. In addition, our post hoc analysis revealed that at the group level channel selection using either Δ[HbX] approach or Δ[HbR] performed better than only Δ[HbO] channel selection. Despite having lower SNR, these results point at the usefulness of the Δ[HbR] signal for the classification of motor imagery (at least) in a

GLM-based decoding approach.

SDC Correction

SDCs are used to minimize/reduce unwanted physiological noise contained in NDCs (Goodwin et al., 2014). In the current work, a custom-built SDC was used as a GLM confound predictor during both, the selection of the most informative channel and the decoding process. Offline, we evaluated the effect of using SDC for channel selection and choice decoding. As derivable from Table 2.3, when using the Δ[HbX] approach, SDC correction did not affect the channel selection in seven out of twelve participants (P01, P02, P05, P07, P09, P10, and P11). The selected channels for the remaining participants differed either in location only (P06) or in location and Hb-type (P03, P04, P08, and P12). This suggests that the former group of participants had a relatively stable signal compared to the latter ones. Interestingly, the mean accuracies were higher for the former group, too [89.29% (SD = 8.63) vs. 58.33% (17.08)]. Although the accuracy did not significantly change on average when SDC correction was used vs. when it was not, a clear divergence between both approaches was observed in some participants. For example, the accuracy reached by P04 and P08 was considerably reduced after SDC correction (100–37.5% and 100–50%, respectively), while it improved for P06 and P11 (25–62.5% and 62.5–100%, respectively). It is not straightforward to attribute this opposing and seemingly irregular effect across participants to an isolated cause. Instead, it may be the result of an interaction between the spatial relation of the SDC and the selected channel, which suggests that the location of the SDC matters even in a relatively small setup. In addition, the selected chromophore (whether it is Δ[HbO] or Δ[HbR]) may influence the effect of SDC correction. Indeed, unlike for the Δ[HbX] (and the Δ[HbR]) approach, we observed a clear improvement before/after SDC correction when selecting channels based on Δ[HbO] (see Table 2.3, "Best Δ[HbO]"). Specifically, the mean decoded accuracy increased from 50 to 62.5% after SDC correction. This is expected, as Δ[HbO] signal is more affected by global systemic artifacts in both extracerebral and intracerebral compartments than Δ[HbR] (Kirilina et al., 2012).

t-Statistic for Channel Selection and Decoding

Different approaches for channel selection have been reported in the literature. Hu et al., (2013) compared the difference between the maximum value during the task and rest periods, and considered the channel to be active if the difference was positive. Hong and

Naseer (2016) and Khan and Hong (2017) suggested selecting channels where the initial dip could be reliably detected. For that, a vector-based phase analysis with a threshold circle as a decision criterion was employed. Previous fNIRS studies have also followed a t-value (Hong and Santosa, 2016; Nagels-Coune et al., 2017) or beta-value criterion (Klein and Kranczioch, 2019) between the measured and expected hemodynamic response by the given stimulation for channel selection.

In the present study we selected the most informative channel and Hb-type combination based on the highest t-statistic of the task vs. rest contrast of the functional localizer data. We ensured correct t-value estimation during channel selection by removing serial correlations generally present in the fNIRS data (Huppert, 2016). The decoded answer option was based on the choice that led to the highest t-statistic of the choice i vs. rest contrasts, where i = {1,2,3,4,5,6}. No pre-whitening was used during decoding since the ranking of the t-estimate should not change across choices. The reason for this is that, as a single channel was used for decoding, each t-estimate was affected by the same amount of serial correlations (Lührs et al., 2019).

Necessity of Trial Repetition

Sorger et al. (2009) and Bardin et al. (2011) used an fMRI-based temporal-encoding and decoding approach to carry out five and two communication runs (respectively) with four answer options; while Sorger et al. (2012) used it in a letter speller context with 27 letter options to encode words between 7 and 13 characters. They reached single-trial mean accuracies of 94.9% (Sorger et al., 2009), 100% (Bardin et al., 2011), and 82% (Sorger et al., 2012) in healthy participants. As for fNIRS-based BCIs, previous work has addressed classification problems using multivariate approaches that maximally distinguished between five mental tasks with an average single-trial accuracy of 37.2% (Weyand and Chau, 2015), or four commands involving motor-execution (Shin and Jeong, 2014) and motor imagery tasks(Batula et al., 2014; Weyand and Chau, 2015; Naseer and Hong, 2015b) that reached mean single-trial accuracies of 82.46, 45.6, 73.3, and 46.7%, respectively. In the present work, participants encoded the same choice five consecutive times in each of the eight choice runs, and we achieved mean (multi-trial/repetition) accuracy levels of 74%.

To assess whether five consecutive trials were actually necessary to successfully decode

their choice, the effect of reducing the repetitions on the decoding accuracy was evaluated post hoc. We observed a significant negative correlation between the accuracies and decreasing the number of repetitions ($\rho = -0.639$, $p < 0.0001$). Interestingly, encoding the same choice only once maintained the mean group accuracies above chance level although with considerably lower values than with five trials (73.96% vs. 41.88%). In line with the observed accuracies, the mean ITR value was considerably reduced when a single trial is used ($ITR_1 = 0.17$ bits/min) compared to when five trials were used ($ITR_5 = 0.30$ bits/min). In addition, we observed that reducing the number of repetitions to four slightly improves the mean ITR, with 0.34 bits/min. To put these values in a broader context, the average ITR of the studies mentioned above were calculated and can be compared to the present study in Figure 2.9. This figure shows that the ITR_1 is closely related to the ITR values from Batula et al. (2014) and Weyand and Chau (2015) and that with the approach employed in this study (ITR_5) considerably higher accuracies are reached, while maintaining the ITR value. This figure also depicts that ITR_5 is considerably lower than in Shin and Jeong (2014) and Naseer and Hong (2015b).

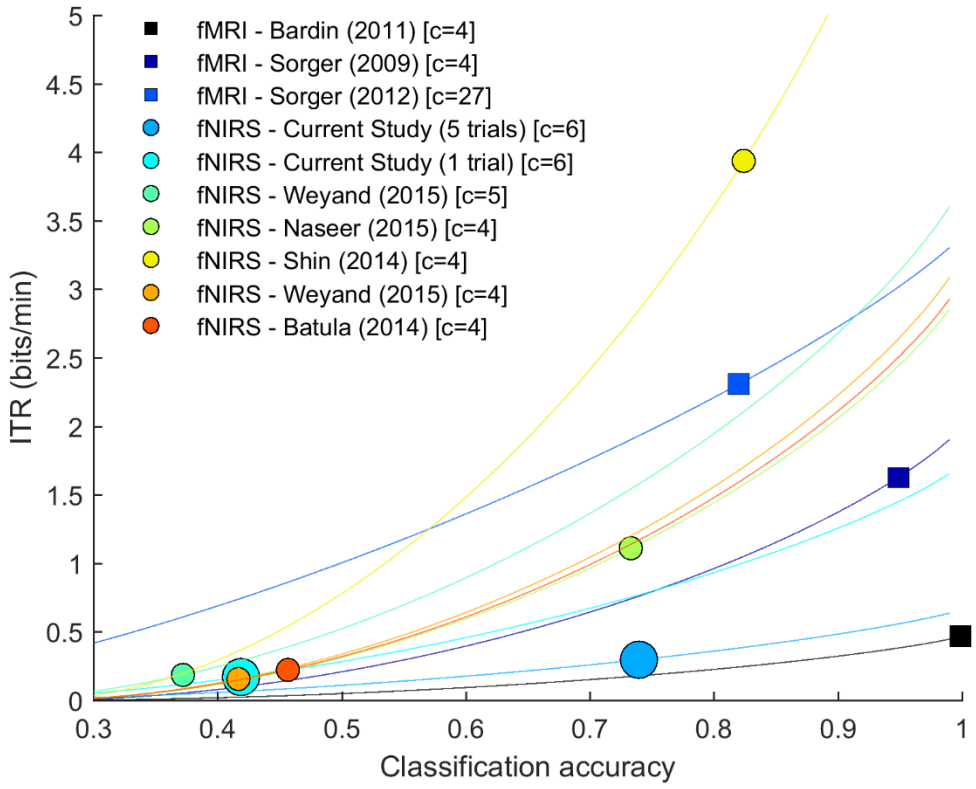


Figure 2.9. Average ITR values from relevant hemodynamic-BCI literature. Square markers represent fMRI-based BCIs, while circular markers represent fNIRS-based BCIs. Lines depict the theoretical values the ITR (bits/min) can take as a function of the number of classes (c), trial duration and accuracy.

Lower decoding accuracies compared to fMRI studies are expected since fMRI has a higher spatial resolution (Valente et al., 2019), fMRI signals have stronger signal-to-noise ratio (Cui et al., 2011) and because unlike fMRI, the brain signal measured with fNIRS also contains (unwanted) superficial scalp information (Erdoğan et al., 2014). This is because light traveling from a source to a detector to reach the brain must pass through scalp and skull tissues twice (Brigadoi and Cooper, 2015). Lower decoding accuracies compared to fNIRS-BCI studies employing multivariate approaches may require further explanation. Multivariate approaches are pattern-classification algorithms used to decode the information that is represented in a given pattern of activity (Norman et al., 2006). They integrate information of multiple voxels/electrodes/channels by optimizing their weights and theoretically should provide higher sensitivity to disentangle overlapping distributed activation patterns than univariate approaches (Valente et al., 2019). The fundamental steps

comprising multivariate approaches are, generally speaking, feature extraction, feature selection, model learning and validation (Norman et al., 2006). The available number of trials/examples for model learning and feature extraction influences the performance of multivariate approaches, as estimating a model based on few examples may not be sufficiently reliable or may not capture the differences between classes in a relatively high-dimensional space (Valente et al., 2019). Thus, it is expected that a model trained on a sufficient number of examples should be able to accurately classify examples never seen by the model. Naseer and Hong (2015b) and Shin and Jeong (2014) employed multivariate approaches and both used > 100 trials to train their models, collected over four separate sessions and a single session, respectively. In addition, their classification problem aimed at distinguishing between different task patterns, which we suspect may elicit more discernible patterns than classification problems aimed at detecting the presence or absence of a task-related information (i.e., task vs. rest scenario). It should be noted that Batula et al. (2014) and Weyand and Chau (2015) also applied multivariate approaches that aimed at distinguishing between different motor imagery tasks, but employed less total number of trials to address the classification problem, which can partially explain the lower accuracies reported in these studies. The temporal approach employed in this study did not require any model learning, but relied on a time course extracted from a single channel with certain degree of trial-to-trial variability that was not constant across participants. Indeed, in some participants (see P03, P04, P06, P08, or P12), we did not observe a linear decrease in the decoding performance with reducing the number of repetitions as in the group results, which suggests that for some participants the inter-trial variability is higher than for others. Altogether, we believe these are the main reasons that could explain the divergence in the mean single-trial accuracies observed in the present study and in the literature.

In the future, a multivariate temporal approach could be tested that would also only require a single localizer run. Specifically, instead of selecting and using a single (most-informative) channel for decoding participants' intentions, a task-specific activation pattern would be defined after the localizer session (based on a univariate approach over each channel comprising the setup), here called as "base-pattern." For each of the communication runs a new activation pattern for each condition would be calculated and compared to the base-pattern as in Monti et al. (2010). The answer option leading to the highest correlation or the smallest distance between the patterns would be the selected option. Importantly, the

number of optodes comprising the setup should be optimized to guarantee participants' comfort and a good accuracy level. In addition, due to the existing trial-to-trial variability within and across participants, a subject-specific number of trials could be considered instead of seeking a group-based criterion. This could be achieved, for example, by implementing an evidence accumulation process with a stopping criterion that trades speed and accuracy for each participant (Mattout et al., 2015).

Feasibility of Error-Correction Approach

Automatic recognition of error potentials has been successfully used in EEG-based BCIs that focus on sensorimotor rhythms and event-related potentials, since evoked responses by the feedback differ depending on whether the feedback is correct or not (Chavarriaga et al., 2014; Mattout et al., 2015). Hemodynamic signals do not show such distinct patterns, which makes direct forms of error-correction mechanisms more challenging to implement. Here we developed an active error-correction approach where participants were asked to indicate a decoding error by encoding the "Error" option in the next choice run if the decoded choice they received did not correspond to what they intended to encode. This approach assumes that we can correctly detect the "Error" option when participants encode it. We built a confusion matrix by pooling all encoded answers across participants to evaluate the performance of our proposed error detection approach. In an ideal scenario, the number of "Error" trials comprising this matrix should be zero or close to zero, which would indicate that no decoding mistakes were made. The fact that participants reached an average of ~74% accuracy indicates that participants had to encode "Error" several times, but importantly, this number differed across participants. Figure 2.7B shows that for example, P06 had to encode "Error" 5/8 times, while P02 did not have to encode any. The figure also indicates that the number of "Error" trials was lower than "not Error" trials (thus making the confusion matrix unbalanced). The confusion matrix shows that we reached an accuracy of 90.62% (72/96 trials were correctly labeled as "Error" or "not Error"). However, we only reached a recall level of 63.63% (out of 22 error trials, 8 trials were missed), which indicates that this approach did not always work.

It is also important to note that the number of encoded errors does not directly represent the accuracy of the BCI setup. This is due to three reasons: first of all, owing to a technical mistake, data from P01-P07 were reanalyzed offline. In turn, some trials that were

incorrectly decoded in real-time were correctly decoded offline (and vice versa), which misplaced the presence of "Error" encoding runs (and disrupted the semantic link between the encoded and decoded choices). This means that in the former case (after offline analysis the choice was correctly decoded), a subsequent error-encoding run became unnecessary, while for the latter case (after offline analysis the choice run was incorrectly decoded) a following "Error" encoding run should have occurred (see Supplementary Material). Second, our experimental design did not include an error option in the first level of the nested menu. This implies that if choices were wrongly decoded in the fourth level of the menu, participants were no longer able to encode the "Error" option in the next run. Third, and similarly, if a decoding error occurred in the last run of the experiment (run number eight), participants were no longer able to encode the "Error" option. These two scenarios could be addressed in the future by using additional short runs (under a minute) where the participant would verify if the decoded answer was correct or not. The run would consist of an initial and final baseline periods of 20 and 10 s, respectively, with a single full rotation of the AR cube presented in between. Specifically, the AR cube would show faces corresponding to yes/no answers, alternated with rest periods, i.e., YES-NO-REST-YES-NO-REST (6 s per face, 36 s in total). This would allow participants to encode twice whether the decoding option was correct or not in 66 s, while leaving enough time for the hemodynamic response to get back to baseline.

In this experiment participants navigated through a four-level, nested menu. After completing one full round (i.e., reaching level four), participants were directed back to the first level of the menu. Since participants performed eight choice runs, this structure allowed them to maximally go through the menu twice. Due to the technical mistake mentioned above, the following lines will only discuss results pertaining P08–P12: P11 completed two full rounds (100% accuracy), while P09 and P10 completed one full round (both participants reached a 87.5% accuracy); P08 and P12 did not manage to complete a single round (the decoding accuracy for both participants was 50%). These results clearly show that statistically significant accuracy is a necessary but not sufficient prerequisite to achieve a functionally significant accuracy. Indeed, the accuracy that would be necessary to use the system in a convenient way requires the accuracy to be much higher. Future work should include the "Error" option in each level of the nested menu. It should also consider an additional measure besides the magnitude of the t-statistic for decoding participants'

choices, such as a confidence measure based on the absolute differences in the t-estimate across conditions. We expect that a more informed decision helps improving the decoding and the error-detection processes.

Task Selection Based on Participants' Preference and Previous Experience

In the present study, we first trained participants to perform two different motor imagery tasks and subsequently let them choose their preferred option. However, unlike previous work, we did not test whether user preference leads to better performance compared to an experimenter-based task selection approach (Weyand and Chau, 2017).

Intuitively, experienced BCI users may have a more realistic idea of which mental strategy works best for them and thus choose the task that has worked well in the past. Although we asked participants to choose the task they felt most comfortable with in the given setup independent of their previous experience, P02, P04, P05, and P11 chose to use mental drawing for this very reason. In contrast, participants P07 and P10, who also reported being familiar with the mental drawing task (and unfamiliar to the interacting with the cube task), chose to use interacting with the cube as it felt more natural for them given the AR stimuli.

Previous experience with the mental task, BCI setups and fNIRS systems did not show significant correlation with obtained accuracies. However, differences in decoding accuracies between (1) novices and (2) average and more experienced BCI/fNIRS users were considerably high [65.63% vs. 80% (average) and 75% (more experienced) for BCI and 62.5% vs. 70% (average) and 82.5% (more experienced) for fNIRS]. Similarly, we observed differences between the same groups but to a lower extent regarding previous task experience. Specifically, novices reached a mean accuracy of 71.73%, while average and more experienced users reached 75 and 79.17%, respectively. These observations suggest that participants with a certain level of experience with a BCI/fNIRS system or a given mental task may have enough introspective information to make an adequate and informed decision on their preferred task after a single training session.

Using AR in BCIs Offers a Great Flexibility

Recent work has shown that EEG-based BCIs can successfully be used in combination with new technological developments such as AR to improve real-world practicality by offering

a richer, more direct, and intuitive interface (Kansaku et al., 2010; Takano et al., 2011; Borges et al., 2016; Faller et al., 2017). However, very few fNIRS applications have explored this option (Afergan et al., 2015; McKendrick et al., 2016; Si-Mohammed et al., 2018; Hu et al., 2019). In the present study, we employed an AR cube to guide the temporal-encoding approach and to display the decoded answer of participants' intentions. For that, we used a relatively simple and flexible setup from the hardware point of view: we made use of two laptops, one additional computer screen, an HD webcam, and home-made A4 cardboards. The home-made A4 cardboards served as whiteboards and triggered the display of the AR cube in Unity3D on an additional computer screen. Importantly, a whiteboard offers a high degree of flexibility and individuality as anyone (a caretaker, family member, experimenter, etc.) could write potential choice options based on previous knowledge of the user and/or the social context (although we used the same choice options for all participants in this experiment, see Supplementary Material). Also, a whiteboard provides a degree of proximity to the setup and interaction between the user and the experimenter as new choice options need to be written down after each run. Besides, handwriting may offer a sense of familiarity to the user. It is important to note that participants were instructed to look at the computer screen at all times throughout the runs, which makes the chosen location of the cardboard (on the desk, between the computer screen and the participant) not intuitive from a pure AR setup perspective. Indeed, the cardboard could have been placed in a different location (behind the screen, for example) as long as the webcam's placement would change accordingly. However, we chose consciously to place the cardboard between the screen and the participants exclusively to exploit the cardboards' interactive and proximity features mentioned above.

Altogether, this relatively simple setup has the potential to be successfully implemented in a more ecologically valid environment such as a hospital room or a rehab center. From the setup point of view, we picture a situation where the user would be placed comfortably in a Fowler's position (head is placed at a 45-degree angle), while wearing the optodes, fNIRS cap and overcap. The fNIRS system would be located next to the bed. A removable desk would be attached to the structure of the bed, above the user's thighs, slightly tilted toward the user's head. A tablet fixated almost perpendicular to the desk could be used instead of the additional computer screen to display the AR cube. To maximize comfort, the rotation of the desk would be adjusted to ensure the tablet was placed at the same height as the user's

eye gaze. The webcam would be integrated into the tablet or a separate camera would be placed on a stable structure such as a tripod located right next to the participant and it would be recording the contents of the whiteboard. Alternatively, smart glasses with an integrated camera could be used. These glasses would then also replace the tablet and could display the cube directly on the glasses.

From the data analysis point of view, the current decoding process could be improved to increase the performance of the BCI (as discussed in previous sections). Importantly, as the majority of the analysis steps have been streamlined (through scripts written in Matlab and Unity3D), a single BCI operator would be sufficient to perform the measurements. However, to assure that the channel selection procedure is properly done (i.e., the selected channel is sufficiently informative and not corrupted extensively by noise), an experienced researcher or a trained medical professional in understanding the fNIRS signal would be necessary. Of course, caretakers and family members should be encouraged at all times to assist the experimenter in selecting the most appropriate options to be presented to the user through the whiteboard.

5 Conclusions

In the present study, we showed that fNIRS-based BCIs can be successfully combined with AR technology to address a six-class problem using a single mental task and fNIRS channel. AR technology allows for a seamless real-world interaction that future studies should explore in more detail. The high inter-subject variability observed in this study not only in achieved accuracies but also in task preference and channel selection, points at the need of shifting the BCI field toward a true user-centered approach. Future studies should consider pursuing individualized approaches to bridge the gap from research to real-world applications.

6 Supplementary Material

6.1 Encoded and decoded answers

This section compiles all encoded (by participants) and decoded choices (based on the temporal decoding approach) for each participant. It is important to note that, the data from P01 to P07 were reanalyzed offline due to a technical mistake. Thus, some trials that were incorrectly decoded in real time were correctly decoded offline (and vice versa), which misplaced the presence of "Error" encoding runs (and disrupted the semantic link between the encoded and decoded choices). This is clearly observed in participants P03 (Table S2.3) to P07 (Table S2.7). Choices in **green** indicate a *successful* completion of the (four-level) navigation round, while choices in **red** indicate an *unsuccessful* completion of the navigation round.

Table S2.1. Encoded and decoded choices for P01

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	Music	1	Photo	4
Run 2	Error	1	Error	1
Run 3	Music	1	Music	1
Run 4	Jazz	3	Classical	1
Run 5	Error	2	Error	2
Run 6	Jazz	3	Jazz	3
Run 7	Nina Simone	4	Nina Simone	4
Run 8	I put a spell on you	1	**I put a spell on you**	1

Note: due to a technical mistake, the choice order of Jazz artists presented to P01 was different than for the rest of the participants

Table S2.2. Encoded and decoded choices for P02

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	Photo	4	Photo	4
Run 2	Pets	6	Pets	6
Run 3	Album 1	3	Album 1	3
Run 4	Picture 5	1	**Picture 5**	1
Run 5	Other	6	Other	6
Run 6	Room Control	1	Room Control	1
Run 7	Bed	6	Bed	6
Run 8	Move Up	2	**Move Up**	2

Table S2.3. Encoded and decoded choices for P03

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	TV	2	TV	2
Run 2	Movie	1	Movie	1
Run 3	Action	4	Error	1
Run 4	Error	4	Series/News	4
Run 5	Action	4	Game Show	4
Run 6	Terminator	5	**First Date**	5
Run 7	Read	3	Other	6
Run 8	Error	2	Internet	5

Table S2.4. Encoded and decoded choices for P04

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	TV	2	TV	2
Run 2	Series/News	4	Movies	1
Run 3	Error	1	Sci-Fi	2
Run 4	Series/News	4	**The martian**	5
Run 5	Comedy	3	Read	3
Run 6	The good place	6	Comic	1
Run 7	Music	1	Superhero	1
Run 8	Rock	2	**Capt. America**	5

Table S2.5. Encoded and decoded choices for P05

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	Photo	4	Photo	4
Run 2	Error	6	Error	1
Run 3	Error	2	Music	1
Run 4	Albeniz	1	Classical	1
Run 5	Cordoba	3	Mozart	3
Run 6	TV	2	**Magic Flute**	2
Run 7	Series	4	Photo	4
Run 8	Children	6	Pets	6

Table S2.6. Encoded and decoded choices for P06

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	Music	1	Music	1
Run 2	Hip-Hop	5	Hip-hop	5
Run 3	Error	2	Error	2
Run 4	Error	5	Hip-hop	5
Run 5	Error	2	Jay-Z	3
Run 6	Error	5	**King´s Dead**	6
Run 7	Error	2	TV	2
Run 8	Hip-Hop	5	Documentaries	2

Table S2.7. Encoded and decoded choices for P07

	Encoded *(based on real-time experiment)*		**Decoded** *(based on offline analysis)*	
	Name	*choice #*	*Name*	*choice #*
Run 1	Radio	5	Radio	5
Run 2	Spain	2	Spain	2
Run 3	Error	4	Error	4
Run 4	Error	6	Germany	6
Run 5	Music	1	**FM1**	1
Run 6	Rock	2	Program 5	5
Run 7	Error	2	TV	2
Run 8	Error	5	Shows/News	5

Table S2.8. Encoded and decoded choices for P08

	Encoded		Decoded	
	Name	*choice #*	*Name*	*choice #*
Run 1	Music	1	Music	1
Run 2	Jazz	3	Jazz	3
Run 3	Louis Armstrong	4	Louis Armstrong	4
Run 4	Let´s do it	3	**Blue Skies**	1
Run 5	Read	3	Read	3
Run 6	Magazine	5	Poetry	3
Run 7	Error	5	Emily Dickinson	3
Run 8	Error	3	Error	1

Table S2.9. Encoded and decoded choices for P09

	Encoded		Decoded	
	Name	*choice #*	*Name*	*choice #*
Run 1	TV	2	Radio	5
Run 2	Error	5	Error	5
Run 3	TV	2	TV	2
Run 4	Movies	1	Movies	1
Run 5	Sci-Fi	2	Sci-Fi	2
Run 6	Star Wars	3	**Star Wars**	3
Run 7	Photo	4	Photo	4
Run 8	Pets	6	Pets	6

Table S2.10. Encoded and decoded choices for P10

	Encoded		Decoded	
	Name	*choice #*	*Name*	*choice #*
Run 1	Music	1	Music	1
Run 2	Classical	1	Classical	1
Run 3	Chopin	6	Chopin	6
Run 4	Requiem	1	**Requiem**	1
Run 5	TV	2	TV	2
Run 6	Movies	1	Movies	1
Run 7	Sci-Fi	2	Sci-Fi	2
Run 8	The martian	5	Interstellar	1

Table S2.11. Encoded and decoded choices for P11

	Encoded		Decoded	
	Name	*choice #*	*Name*	*choice #*
Run 1	Photo	4	Photo	4
Run 2	Pets	6	Pets	6
Run 3	Album 2	2	Album 2	2
Run 4	Picture 1	1	**Picture 1**	1
Run 5	Read	3	Read	3
Run 6	Poetry	3	Poetry	3
Run 7	Pablo Neruda	1	Pablo Neruda	1
Run 8	Die Slowly	5	**Die Slowly**	5

Table S2.12. Encoded and decoded choices for P12

	Encoded		Decoded	
	Name	*choice #*	*Name*	*choice #*
Run 1	Photo	4	Other	6
Run 2	Error	2	Error	2
Run 3	Photo	4	Music	1
Run 4	Error	6	Error	6
Run 5	Photo	4	Photo	4
Run 6	Pets	6	Pets	6
Run 7	Album 3	3	Error	6
Run 8	Error	1	Trips I	2

6.2 Choices presented to participants

Participants were presented with the same set of choices, which can be viewed here (select Data Sheet 2).

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In the above reference list, 76.00% of first authors were male (vs. 24.00% that were female), while 81.00% of last authors were male (vs. 19.00% that were female).

8 Data Availability Statement

The raw data supporting the conclusions of this article is readily available on https://dataverse.nl/dataset.xhtml?persistentId=doi:10.34894/DF83FF and the code will be made available by the authors, without undue reservation, to any qualified researcher.

9 Author Contributions

RBu, AB-A, and BS conceived the idea and designed the experiment. RBe and RBu prepared the Unity3D environment. RBe developed the dynamic object control functions. RBu, ML, and AB-A optimized the hardware setup. RBu and AB-A measured pilot participants. BS and AB-A adapted the design based on pilot measurements. AB-A carried out the fNIRS measurements, analyzed the data, and wrote the manuscript. BS, ML, and RM assisted on the interpretation of results and data analysis. AB-A, BS, and ML structured the manuscript. RBu, BS, RM, ML, RM, and RBe revised the manuscript critically.

10 Funding

This research was supported by The Luik 3 grant for joint research between Cognitive Neuroscience and Knowledge Engineering Departments, Maastricht University, on advanced brain-robot interfaces, 2015-2019 (to RM and BS).

11 Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

12 Acknowledgments

We would like to thank Giancarlo Valente and Andrew Morgan for their advice on data analysis; to Anita Tursic and Laurien Nagels-Coune for their advice on the experimental setup; the Instrumentation department for their timely assistance; and to all the participants for their time and effort.

This chapter is embargoed at request

3

Guiding functional near-infrared spectroscopy optode-layout design using individual (f)MRI data: Effects on signal quality and sensitivity

This chapter is embargoed at request

4

The influence of extra-cerebral vasculature on the efficacy of the short-separation regression approach applied to fNIRS data

5

General Discussion

The principal rationale for the development of BCIs has been to ultimately restore communication and control in the absence of words/gestures/other motor actions to people with severe neuromuscular disabilities (Shih et al., 2012). Despite being the historically main target, the body of literature involving end-users with disease has lagged behind the nearly exponentially growth of general BCI-related literature (Kübler, 2020). fNIRS is a promising neuroimaging modality to measure brain signals for controlling BCIs. However, fNIRS-BCI systems suffer from a number of limitations that has hindered its translational potential. This dissertation aimed to address some of these limitations. In **Chapter 2**, we evaluated factors that could improve the feasibility of ecologically-friendly fNIRS-based BCIs, namely short task duration periods, the usage of single optode pairs and the use of augmented-reality (AR) technology for a more immersive experience. In **Chapter 3**, we investigated the effect of different strategies for optode placement on the fNIRS signal quality and sensitivity to detect brain activation. Finally, in **Chapter 4**, we assessed if the amount of unwanted physiological noise present in the fNIRS signal depends on the proximity and density of vascular structures around the optodes.

After summarizing the results from each study, we will discuss the implications of the work presented in this dissertation. Subsequently, we describe the limitations and challenges of the current work and suggest the directions research should take to assure the realization of the translational potential of fNIRS-based BCIs.

1 Summary

In **Chapter 2**, we aimed to improve the feasibility of ecologically-friendly fNIRS-based BCIs for communication and control purposes in healthy participants. We tested the feasibility of using AR technology to navigate a through a virtual control menu that consisted of four levels and six options in each level. Additionally, we evaluated the feasibility of using a single mental-imagery task and fNIRS channel to select an option in each level. This was possible by using a temporal en- and decoding approach, previously implemented in fMRI-BCIs but never tested in fNIRS. Participants could successfully navigate through the nested control menu and achieved a mean accuracy of 74%. With this work, we showed that fNIRS-based BCIs can be successfully combined with AR technology and flexible choice encoding in form of search trees, to increase the degrees of freedom of a BCI system using a single mental task and fNIRS channel.

In **Chapter 3**, we aimed to answer the following questions: does additional individual (f)MRI data help optimizing the proper placement of fNIRS sensors? If so, how much individual data is needed? To do so, we selected and compared four approaches that incrementally incorporated individual (f)MRI information. The first approach was the literature-based approach (LIT), which uses a literature review to guide the optode layout design. The second approach, the probabilistic approach (PROB), employed individual anatomical data and probabilistic maps of functional MRI (fMRI)-activation derived from an independent dataset. The third approach used individual anatomical and fMRI data (iFMRI approach) and, the fourth approach used individual anatomical, functional and vascular information of the same subject (fVASC). We observed that the four approaches produced different optode layouts and that the more informed approaches (PROB, iFMRI, and fVASC) outperformed the minimally informed LIT approach in terms of signal quality and sensitivity. Further, the three more informed approaches (PROB, iFMRI and fVASC) resulted in similar outcome. We thus conclude that acquiring additional individual MRI data leads to a better signal quality, but that not all the modalities tested are required to achieve a robust setup.

In **Chapter 4**, we investigated whether fNIRS channels capture physiological noise differently and whether potential differences depend on the density and proximity of vessels in the vicinity of channels. We looked into three physiological noise types: Mayer waves, respiration and heartbeat. Our analyses showed variability in the amount of noise captured by fNIRS channels, but no relation between the amplitude of physiological noise and vascular proximity/density in normal-distance channels (NDCs). One way for correcting physiological noise in NDCs is to use short-distance channels (SDCs) that record exclusively from extra-cerebral regions. This method assumes that the systemic physiological noise present in the NDCs is present in SDC signals as well (Gagnon et al., 2012) but that SDCs do not have the penetration power to access brain activity. Our analyses indicated that the Mayer-wave amplitude captured by SDCs was related to the presence and density of vascular structures in their vicinity, but only for Δ[HbO]. Since the Short-separation regression (SSR) approach reduces the presence of physiological noise in NDCs data, we investigated whether this reduction depended on the presence of vascular structures. If that were the case, it would help researchers to shape the physiological noise correction approaches. However, we did not find any evidence for this dependence.

Nevertheless, this chapter extends considerably our understanding of the relationship between the vasculature features and the presence of physiological noise in fNIRS channels.

Taken together, the empirical studies presented as part of this dissertation address a number of challenges affecting different stages of and fNIRS-BCI setup. The studies describe a temporal en-/decoding paradigm previously used in fMRI-BCIs and successfully transferred to fNIRS-BCI research, offer guidance to efficiently using resources for developing robust and convenient optode layouts and provide insights on a number of factors affecting the presence of physiological noise in the fNIRS signal. The knowledge gained in these studies can therefore improve data-acquisition and analysis strategies in fNIRS-BCI research.

2 Implications and challenges of the presented work, and the way forward

2.1 Optode-layout design

How many optodes should the optode layout contain? How should they be arranged? These are important questions impacting fNIRS signal quality and sensitivity to cortical regions of interest (Culver et al., 2001). Additionally, the coverage and number of optodes in a layout affect the comfort of the participant. The fNIRS community has developed several tools and pipelines that aim to optimize solutions to this problem. Using 3D visualization tools, researchers have proposed methods to design optode layouts "manually" and interactively that target specific cortical regions based on light sensitivity profiles (Aasted et al., 2015; Wijeakumar et al., 2015). Machado et al. (2014) proposed a mathematical optimization strategy to address the problem and combined it with light-sensitivity profiles from individual anatomical head models. In 2018 they improved their work by allowing optodes to take any position along the scalp surface (using water-resistant adhesive [e.g., collodion] to glue the optodes on the scalp), instead of using fixed discrete positions along an EEG cap (Machado et al., 2018). The same year, two toolboxes were published to automatically design optimized fNIRS arrays given a user-defined ROI, FOLD (Zimeo Morais et al., 2018) and Array Designer (Brigadoi et al., 2018). Each of the above-mentioned approaches allows for variable user-defined and system-tailored restrictions. These include the maximum channels/optodes comprising the layout and the coverage and solution space of the layout, to name just a few.

Optimal solutions to the optode-layout-design problem depend on the restrictions the problem is subject to. This in turn depends on a number of factors, including the research question or application, the available technical and financial resources, as well as the researcher's available time. Data availability are included in these resources and the tools presented above, with the exception of the FOLD method, have partially considered them. This is because they all enable creating layouts based on individual subject MRI data or using an MRI atlas. In **Chapter 3**, we defined four scenarios by varying the available resources a researcher could have and assessed the potential gain of incorporating not only individual anatomical data, but also functional and vascular MRI data when optimizing optode-layout designs. Based on our results, we suggested that researchers should use individual functional and anatomical data for designing optode layouts when possible. When anatomical data are available and functional data are not, probabilistic functional maps are a promising alternative.

So far, existing tools for optode-layout design do not provide an option for defining target regions of interest based on individual or probabilistic functional activation maps derived from fMRI. In **Chapter 3** we observed that using these information sources can benefit the optode layout design process. We hope that future iterations of these tools will consider incorporating this functionality. One obvious challenge is acquiring such data. Fortunately, freely available (or available upon request) fMRI probabilistic maps constitute a feasible solution. However, we could not find any published work on probabilistic mental-imagery maps, which could be particularly beneficial for fNIRS-BCI research. We have attempted to improve this situation by making inner-speech, mental-calculation and mental-rotation probabilistic functional maps available to the fNIRS community. We hope that more research groups follow these efforts.

2.2 Physiological noise in fNIRS

Accounting for and removing physiological noise from the fNIRS signal is important for developing effective and efficient BCI applications. Physiological noise can compromise sensitivity to brain activation measured by fNIRS channels and can feed back noise to a participant instead of brain activity. Among the many choices for physiological noise correction, we opted for the short-separation regression (SSR) approach. Short-separation regression requires additional channels that are easily integrated in a real-time experiment,

making them suitable for fNIRS-BCI applications. In **Chapter 2**, we created an in house-made single SDC, while in **Chapters 3** and **4** we used short-distance bundles from a certified fNIRS provider. We did not actively assess the effect of SDC correction in **Chapter 3**, so the following discussion will focus on **Chapters 2** and **4**.

In **Chapter 2**, we observed that applying the SSR approach increases the accuracy of the BCI system more for Δ[HbO]than for Δ[HbR]. In **Chapter 4**, SSR improved sensitivity to brain activation, and again this was more for Δ[HbO]than for Δ[HbR]. These improvements were independent of the task employed, as we used a motor-imagery task in **Chapter 2** and an overt and inner-speech task in **Chapter 4**. It was also independent of the number of SDCs in the setup, as a single SDC was used for the whole setup in **Chapter 2** and one was used for each source in **Chapter 4**. Further, the improvements did not depend on the inter-optode distance constituting the SDC, as ~13mm for **Chapter 2** and 8mm for all SDCs in **Chapter 4** was used. An important outcome was that when SDC bundles are not available, the improved accuracies after SDC correction for Δ[HbO] (and to a lower extent for Δ[HbR]) suggest that using a single in house-made SDC located relatively close to its respective NDC is already beneficial.

In **Chapter 4** we observed that physiological noise amplitude is higher in Δ[HbO]channels than in Δ[HbR] channels, as previously reported (Lina et al., 2008; Gagnon et al., 2011; Kirilina et al., 2013). In BCI studies it is more common to use Δ[HbO]-based features, as Δ[HbO]usually exhibits larger and more pronounced concentration changes than Δ[HbR]in response to mental tasks (Stangl et al., 2013; Sato et al., 2016). Therefore, strategies accounting for physiological noise are particularly advisable.

2.3 Vasculature mapping

In this dissertation, subject-specific vasculature maps were used to study the potential impact on physiological noise (**Chapter 4**) and on optode layout design (**Chapter 3**), because, similar to fMRI signals, fNIRS signals are influenced by the underlying vasculature. In **Chapter 4**, we observed a positive, non-linear relation between most superficial vessels and the presence in Mayer waves in short distance channels. This finding suggests that adding vasculature information can be useful to design strategies to mitigate the effect of physiological noise in fNIRS signals. In **Chapter 3**, we concluded that,

although including individual vascular information improved signal quality and sensitivity to the brain, the experimental resources spent to include such information was not efficient. This is mainly because whole brain vascular segmentations can be tedious and time consuming. Further, it is not common practice for fNIRS-based BCI studies or fNIRS studies in general to acquire vascular data at the MRI scanner.

Similar to functional activation maps, probabilistic vascular atlases of individual arteries (Forkert et al., 2012; Viviani, 2016; Dunås et al., 2017), veins (Ward et al., 2018) or both (Bernier et al., 2018) have been reported. It should be noted even though there is considerable inter-subject variability especially in smaller vessels (Nowinski et al., 2011; Bernier et al., 2018), effort to minimize this variability using nonlinear registration has been made (Viviani, 2016; Dunås et al., 2017; Bernier et al., 2018; Ward et al., 2018). Incorporating probabilistic maps at different thresholds into the anatomical models for Monte Carlo simulations would help to have (even) more accurate models without the need of costly and lengthy acquisition and preprocessing times. However, the maps mentioned above are "limited" to the brain. Unlike fMRI, vessels located between the skin and CSF influence the fNIRS signal, because light traveling from a source to a detector needs to travel twice through superficial tissues (Brigadoi and Cooper, 2015). To our knowledge, no openly available superficial vascular atlas exists[10]. This is because these vessels are not as relevant to the fMRI community as cerebral vessels are. After all, non-cerebral signals are not expected to be associated with fMRI activation (Uludag et al., 2005). Additionally, these types of vessels are generally smaller and in our own experience, highly variable across participants. We believe a large-scale effort to map both, scalp and cerebral vasculature would be highly beneficial for fNIRS studies.

2.4 Comfort-performance tradeoff

In this dissertation, we successfully transferred the temporal information encoding approach and a GLM-based decoding scheme previously reported in fMRI-based BCIs (Sorger et al., 2009; Bardin et al., 2011; Sorger et al., 2012) to an fNIRS-based BCI system. Further, we advanced previous applications by extending the four-choice paradigm (Sorger et al., 2009;

[10] Technically speaking, an atlas that includes scalp/skull vessels exists (Nowinski, et al. 2011). However, this atlas is based on a single participant and according to the authors data cannot be exported in a way that could be incorporated into, among other applications, Monte Carlo simulations.

Bardin et al., 2011) to six temporally unique (yet still differentiable) encoding phases. An advantage of using this procedure is that a single channel may be sufficient for decoding participants' intentions without hampering our decoding ability. In **Chapter 2**, a joint analysis of five trials from a single channel showed promising results, as eleven of the twelve participants reached above-chance level (37.5%) accuracies, with an average accuracy of 74%. Even seven of the twelve participants reached above-chance level accuracy when the number of trials was reduced to one (average accuracy was 42%).

While temporal encoding/decoding approach may work well when combining multiple trials, decoding on a single trial basis needs to be improved for real-world BCI applications. One way forward is to include more channels, since in general, having more (informative) channels increases SNR, as task information is coupled in channels but noise is often independent between channels (Shlens, 2014), at least after accounting for physiological noise. However, increasing the number of channels will most likely affect the comfort of participants. Whether there is an optimum number of channels to ensure participant comfort *and* maximize the performance of a BCI system remains an open question. Despite its relevance for fNIRS-BCIs, to our knowledge no study has systematically investigated the tradeoff between BCI performance and participant comfort by varying the number of channels comprising the layout, while recording comfort scores.

2.5 The potential of augmented reality

Comfort is closely linked to participant motivation and engagement: an uncomfortable setup will hinder the engagement and motivation of the participant, which can lead to lower performance. On the other hand, a highly engaged and motivated participant will probably have more tolerance to less comfortable setups or longer measurements. The BCI paradigm and interface can affect the engagement and motivation of the participant. In **Chapter 2**, we utilized AR technology, as it allowed participants to act on the environment using the BCI system while still being present in it. While still in a laboratory setting and using a in house-made, simple setup, participants indicated that AR was engaging and motivating. Still, augmented reality technology requires additional elements to be incorporated into a BCI system and thus asks for careful consideration to ensure the system remains ergonomic and feasible. One possible modification to increase usability would be to incorporate smart glasses into the BCI design. Proof-of-concept fNIRS-based BCIs have assessed the potential

of smart glasses. These include *Phylter* (Afergan et al., 2015) and *Zero Shutter Camera* (Shibata et al., 2014), which adaptively determine whether a user can receive notifications or trigger a photo based on the cognitive load. Importantly, these applications rely on users' visual abilities to control BCI systems. However, some individuals such as those with acute motor disabilities may suffer from severe visual impairments and/or disability to control eye movements (Käthner et al., 2015). Thus, BCIs based on other sensory modalities such as auditory and tactile stimulation have been proposed (Riccio et al., 2012; Kaufmann et al., 2013). Most of the AR applications have focused on visually integrating virtual objects into real environments, including those in this dissertation. Instead, researchers could explore auditory AR, in which virtual acoustic objects are integrated into the real world. This approach has been proposed (in a non-BCI context) for visually impaired users (Ribeiro et al., 2012). Future work could therefore explore its feasibility for BCI applications using fNIRS measurements. Overall, these promising studies suggest that AR-based fNIRS-BCIs are worth further investigation to develop practical real-world applications.

2.6 Beyond the technical improvements of fNIRS BCIs

The work presented in this thesis examined a number of factors affecting fNIRS-BCI performance. These include optode placement, physiological noise and BCI-paradigm parameters such as encoding time and the nature of the interface. Importantly, we examined each of these elements in isolation to best determine their potential effects on BCI systems. Future work focusing on improving technological aspects of fNIRS-BCI systems should aim to validate these factors jointly in real-world experiments. All empirical chapters of this dissertation were limited to a well-controlled laboratory setting, in healthy young participants with differing acquaintance of and experience with neuroscience and/or BCI technology. However, in practice, BCIs for communication and control are used in hospital rooms or at home and the profiles of end-users are likely to differ compared to healthy young adults. Focus groups with end-users and other stakeholders such as their family members, caregivers, doctors and other professionals will provide BCI developers a more practical perspective of the needs and expectations of BCI systems. Additionally, understanding the technical limitations of user environments, such as available measurement space, whether there is internet connection, level of noise, *etc.*, would help to shape the design of BCI systems.

One key advantage of fNIRS is that combining it with other modalities such as EEG is relatively easy. Combined EEG and fNIRS BCI systems, also known as hybrid systems (hBCIs), consist a promising way forward. They have demonstrated higher performances compared to unimodal BCIs in terms of classification accuracy and information transfer rate (Fazli et al., 2011; Khan et al., 2014; Khan and Hong, 2017; Shin et al., 2018a; Rezazadeh Sereshkeh et al., 2019). These advantages are intuitive given their increase in available information for BCI use since there is no significant interference between the EEG and fNIRS signals (Shin et al., 2018a; Shin et al., 2018b). That said, future work using hybrid systems should balance setup size and user comfort, similar to the work in this dissertation.

3 Conclusion

The work presented in this dissertation focused on addressing some of the challenges faced by fNIRS-BCIs under well-controlled laboratory conditions. These examinations were able to advance our understanding of the fNIRS signal used in BCI applications. We hope that future communication and control fNIRS-BCI studies will be able to combine the novel BCI paradigm developed in **Chapter 2**, the improved optode-placement schemes introduced in **Chapter 3** and the better understanding of the role of physiological noise in fNIRS signal correction methods obtained in **Chapter 4**. We believe that the way forward not only involves technical advancements of BCIs but also requires active collaboration between BCI researchers and end-user groups. With this joint effort in place, we will be able to materialize the translational potential of fNIRS-BCI applications to improve the lives of patients that would benefit from computer assistance for communication or motor control.

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In the above reference list, 74.36% of first authors were male (vs. 25.64% that were female), while 89.74% of last authors were male (vs. 10.26 % that were female).

Summary

A brain-computer interface (BCI) is a system that measures and converts brain activity into artificial output that replaces, restores or enhances natural central nervous system output. Thus, BCIs have the potential to ultimately restore communication and control in the absence of words/gestures and other motor actions to people with severe neuromuscular disabilities. Functional near-infrared spectroscopy (fNIRS) is a promising functional-neuroimaging modality for this objective that has been used for BCIs in healthy participants and in few occasions, in clinical settings. This is because there are substantial challenges associated with fNIRS-based BCIs in everyday situations, such as home-use or hospital settings. This dissertation outlined progress to overcome some of these obstacles. In **Chapter 2**, we evaluated factors that can improve the feasibility of ecologically-friendly fNIRS-based BCIs. We evaluated short task-duration periods alongside augmented-reality (AR) technology that enables a more immersive setup. Further, we evaluated the feasibility of using a single mental-imagery task and fNIRS channel to select an option in each level. For that, we used a temporal en- and decoding approach. This proof-of-concept study revealed that participants can successfully control the BCI system with a single fNIRS channel and motor-imagery task when using a relatively short task duration (6s) while achieving a promising mean classification accuracy of 74%. Positive reports from study participants suggest that AR is a promising and feasible technology to enhance user experience for fNIRS-BCI applications. This work conveys fundamental steps towards developing fNIRS-based AR-BCI systems to be used as communication and control devices in a clinical setting or for home-use. In **Chapter 3**, we investigated how different quantities of individualized MRI-based data influence the optode placement and in turn, fNIRS signal quality and sensitivity to detect brain activation. This work revealed that acquiring additional individual MRI data leads to better outcomes and that not all the modalities tested are necessary to achieve a robust setup. Finally, in **Chapter 4** we assessed whether the quantity of unwanted physiological noise present in the fNIRS signal depends on the proximity and density of vascular structures around optodes. Further, we tested if this relationship affects one particular physiological noise-correction approach: short-separation regression (SSR). This approach uses short-distance fNIRS channels (SDCs) to regress out physiological noise from normal-distance channels (NDCs). We examined three sources of

physiological noise: Mayer waves, respiration and heartbeat. Our analyses indicated that the Mayer-wave amplitude captured by SDCs was related to the presence and density of vascular structures in their vicinity for oxyhemoglobin data only. We did not find any evidence that the reduction of physiological noise in NDCs after SSR is related to the presence of vascular structures. This chapter therefore extends our knowledge of the relationship between the vasculature features and the presence of physiological noise in fNIRS channels. Taken together, the three empirical studies provide insights that can contribute to the advancement of data acquisition and analysis strategies to improve the applicability of fNIRS-BCIs to everyday situations.

Knowledge Valorization

The principal motivation for the development of BCIs is to restore communication and control in the absence of words, gestures and other motor actions to people with severe neuromuscular disabilities (Shih et al., 2012). FNIRS is a promising functional-neuroimaging modality for this objective that has been used for BCIs in healthy participants (Naseer and Hong, 2013; Weyand and Chau, 2015; Batula et al., 2017; Nagels-Coune et al., 2017; Weyand and Chau, 2017; Sereshkeh et al., 2018; Rezazadeh Sereshkeh et al., 2019; Abdalmalak et al., 2020; Nagels-Coune et al., 2020) and in patients (Gallegos-Ayala et al., 2014; Abdalmalak et al., 2017). However, clinical applications of fNIRS-BCI systems suffer from a number of limitations that have slowed its translational potential. This dissertation outlined progress to overcome some of these limitations. First, we evaluated factors that could improve the feasibility of real-life fNIRS-based BCIs (**Chapter 2**). There we saw that participants can successfully control the BCI system by imagining doing a short task (mental imagery) and using a single pair of measurement sensors. Further, positive reports from participants suggest that augmented reality is a promising technology to enhance user experience for fNIRS-BCI applications. In the next chapters, we evaluated factors that can compromise fNIRS signal quality and its sensitivity to detect task-related brain activation, which is crucial to ensure a correct functioning of BCI systems. The way fNIRS sensors are arranged on the participant's head is one of such factors, and in this context, we investigated how different sensor placement strategies affect the fNIRS signal in **Chapter 3**. This study revealed that using gradually more individualized information obtained from the MRI scanner led to a better outcome, but that not all the information acquired at the scanner was required to achieve a robust setup. Another factor strongly influencing the fNIRS signal is the physiological noise such as heartbeat and breathing, to name a few. This physiological noise is measured at the same time as task-related brain signal by the fNIRS sensors, and it is not straightforward to tear them apart, which compromises our sensitivity to detect task-related brain activation. It has been suggested that the presence of vessels around fNIRS sensors can influence the amount of unwanted physiological noise, and in **Chapter 4**, we investigated precisely that. In addition, we tested whether the effectiveness of a physiological noise correction method named short-separation regression (SSR), which uses additional sensors placed on the participant's head, also depends on the proximity and

density of vessels. The study verified that SSR improves fNIRS-signal quality and the sensitivity to detect task-related brain activation considerably and shows that signals obtained via these additional channels are affected by close vascular structures.

Short- and long-term impact

Although the presented work was framed in a communication and control BCI context, the knowledge gained here can be extended to other BCI applications. As indicated in Figure KV1, the most immediate beneficiaries of the work presented in this dissertation are other research groups working directly on fNIRS-based BCI for communication and control as well as neurofeedback. This is because all empirical chapters addressed challenges shared amongst these applications. Moreover, the findings from **Chapters 3** and **4** are applicable to research that focuses on the study of other (if not all) neural processes using fNIRS. These chapters provide insight to factors influencing signal quality and sensitivity to brain activation which is relevant to any fNIRS study. Specifically, the knowledge gained in **Chapter 3** will help researchers to efficiently utilize resources when designing fNIRS experiments. Meanwhile, basic methodological investigations like the one presented in **Chapter 4** will form the basis of fNIRS physiological noise-removal strategies in the future. These two chapters are further relevant for those developing tools to optimize optode layout design and fNIRS data analyses. In addition, we have purposely made the dataset from **Chapter 2** and probabilistic maps from **Chapter 3** available to support this progress.

Within the realm of BCIs, our work contributes to ongoing development of brain-robot interfaces and their extended range of potential applications in the many domains where robots are used. Examples include disaster management (e.g. remote control of robots that inspect dangerous or contaminated areas), industrial manufacturing (e.g. training robots to determine what is defective on a conveyor belt and remove it automatically based on a human inspector's brain signals), entertainment (e.g. games with robotic agents) and healthcare (e.g. support for people with severe motor impairments completing daily-life activities or regaining functionality through neuroprosthetic devices).

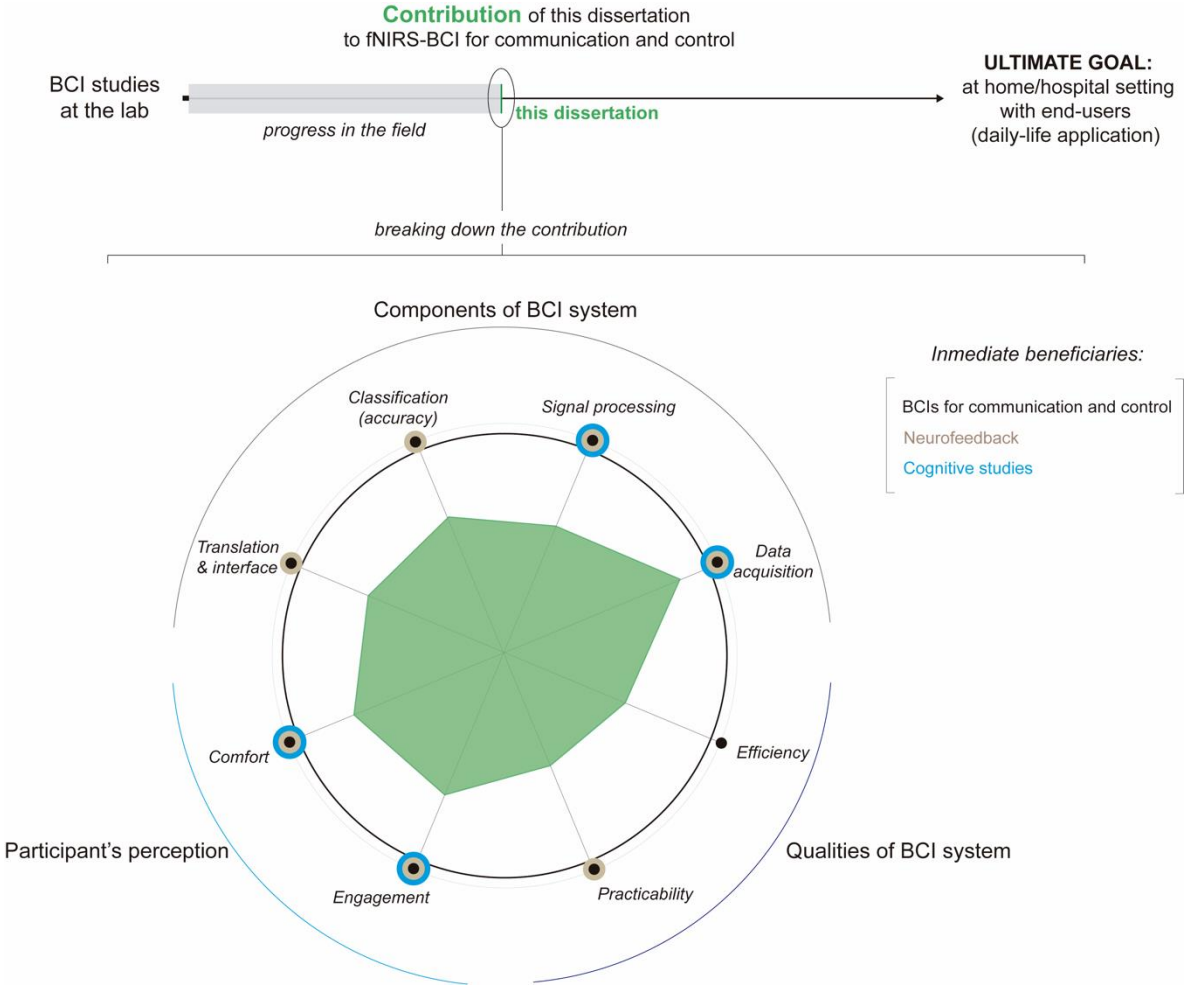

Figure KV1. Contribution of this dissertation and its immediate beneficiaries. The knowledge obtained in this thesis contributes to the advancement of data analysis and acquisition techniques to ultimately make fNIRS-BCIs applicable to everyday situations. The main contributions were divided into three categories, namely components constituting a BCI system, qualities of a BCI system and participant's perception. The polar diagram illustrates the contribution of this work regarding each subcategory. The concentric circles represent the immediate beneficiaries of this thesis: other fNIRS-based BCI researchers focusing on communication and control applications (in black), fNIRS-based neurofeedback applications (in beige) and other fNIRS-based cognitive studies (in blue).

The work presented in this dissertation can also benefit those with brain injuries and mental disorders. For example, patients with severe motor impairment (such as those with locked-in syndrome) have limited behavioral capabilities, yet it should be possible to express thoughts using preserved mental abilities (Sorger et al., 2012). Here, we worked to improve signal acquisition and analyses approaches while almost exclusively using mental tasks.

Together with the small optode setups featured in this thesis, we have set realistic foundations for applying our work in this and other patient groups sharing similar symptoms. Additionally, in **Chapter 2** we showed that AR technology can be successfully combined with fNIRS-BCI setups in the context of communication and control. Beyond these applications, AR technology can be used in neurofeedback therapy in patients suffering from anxiety disorders such as phobias to facilitate anxiety regulation. This is particularly interesting since AR provides a unique scenario where a realistic, anxiety-inducing stimulus can be presented in a controlled manner by imposing virtual stimuli, such as personalized threatening spider, over real objects and environments, such as the patient's arm (Gamito et al., 2011).

Future directions

A community effort

The ever-growing fNIRS community is well aware of the limitations of fNIRS technology and it has made collaborative effort to minimize and account for these. For example, several tools have been developed for designing informed and optimized optode setups that guarantee good signal quality and coverage (Machado et al., 2014; Aasted et al., 2015; Wijeakumar et al., 2015; Brigadoi et al., 2018; Machado et al., 2018; Zimeo Morais et al., 2018). A wide range of methods have been developed and implemented in analysis software to correct for the physiological and non-physiological noise sources, both offline (Homer 2 and Homer 3 (Huppert et al., 2009); Nirs toolbox (Santosa et al., 2018) and Nirstorm (Tadel et al., 2011)) and in real time (Lührs and Goebel, 2017). Further, validation and standardization efforts of these tools have promoted reproducibility. We hope that this collaborative effort will remain in the years to come.

Miniaturization of technology

Monitoring brain activity using fNIRS in real life situations has become increasingly accessible over recent years thanks to the development of miniaturized and wearable fNIRS devices. These systems do not use fiber optic bundles, making them more lightweight and more resistant to movement artifacts (Pinti et al., 2018). These are highly desirable features for real-life, fNIRS-based BCI applications, and we expect this progress to continue over the next years. Further, with the miniaturization of the technology and the improvement of

neuronavigation systems and auxiliary measurement devices, we expect to see a more streamlined integration of these tools and fNIRS systems. Of particular interest for the future of BCI applications is the development of hybrid BCIs that combine EEG and fNIRS measurements. Previous work has shown that they can achieve better performance than with unimodal BCIs (Fazli et al., 2011; Khan et al., 2014; Khan and Hong, 2017; Shin et al., 2018; Rezazadeh Sereshkeh et al., 2019). However, these systems are not frequently used in practical applications because the amount of hardware needed to capture two different types of signals simultaneously results in bulky and complex systems. We hope that the progress in miniaturization happening separately for fNIRS and EEG systems is extended to their integration.

Need for user-centered designs

It is important to emphasize that more work is required to realize these goals since the knowledge gained in this dissertation reflects basic scientific investigations that will consequently benefit these target patient groups. We addressed some of the limitations currently faced by fNIRS-BCI applications that hinder the translational potential of BCIs. We did so in ideal laboratory conditions, measuring healthy, young, motivated individuals and having minimal technical and temporal constraints. Naturally, BCI researchers will need to seek collaboration in the future with end-users and, when applicable, with their immediate caretakers, family members and medical staff. Interviews, surveys and focus groups will help researchers and developers understand and identify the needs and reality of the users. Further, direct contact with end-users will enable researchers to iteratively validate the methodological developments. This user-centered design approach has the potential to yield higher user satisfaction and better system adoption (Sujatha Ravindran et al., 2020).

Our contribution as researchers

Since their inception, BCIs have inspired countless science fiction novels and movies and have attracted substantial media coverage and attention. This can be a good thing, particularly when BCI applications are represented positively. Such coverage draws attention to struggles faced by individuals that would benefit from this technology, thereby creating a social awareness and interest in technological advancements. It can also serve as a platform for publicizing opportunities for participation in research studies. However, the image of BCI technology portrayed in these platforms can reflect dystopian views. These scenarios rarely contain technological limitations such as low information transfer rates or signal quality-related problems, and largely ignore end-user discomfort. Importantly though, dystopian scenarios stimulate open discussions about ethical concerns raised by BCI technology.

Simultaneously, unrealistic descriptions of BCI technology can inflate hopes of potential and future end-users. BCI researchers are therefore instrumental, having the expertise to educate end-users and their immediate social circle (when dealing with clinical populations), as well as the responsibility to help them manage their expectations about the technology. This can be done in a localized manner (e.g. in the aforementioned focus groups and interviews), or in bigger settings (e.g. science communication events or media platforms). Regardless of the chosen output channel, it is important to find a good balance between exhibiting enthusiasm about progress and potential of BCI applications and openly describing the current limitations and state of the technology. It is equally important to consider primary users (end-users) and a variety of secondary users when applicable, as their contribution is essential to move toward mature BCI technologies.

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Acknowledgements

First and foremost, I have to thank my supervisors. Bettina, thank you for giving me the opportunity to pursue a PhD under your guidance. I have learned a lot from and with you during these years. Thank you, too, for trusting that we could complete the various running projects whether I was in Maastricht or somewhere else. Rainer, thank you for your guidance and for the timely feedback that always proved useful. Rico, even though our interaction was not as frequent as I would have hoped for, I always enjoyed talking to you and appreciated your ideas.

Michael, my un-official supervisor, thank you for the many discussions and for sitting through countless long meetings with me. Your contribution was essential to complete this thesis. Dimo, your expertise was instrumental to carry out these projects. Thank you for always being ready to help. To the hemodynamic BCI group and occasional guests, thank you for the assistance and the interesting discussions. Special thanks to Simona and Rodion for assisting during the data collection, and to all of our participants, for their time and dedication.

Christl, José, Eva and Riny: thank you. You have helped me so much during these years. It was always a pleasure to walk by your offices and chat with you. Thank you, Jordi and Noël, and Johan and Erik for your support.

To the BrainInnovation team, thank you for your long-lasting assistance and for making me feel part of the group. Special thanks to Judith - I learned a lot with you. And to Faruk, the segmentation wizard, thank you for the excellent tips.

I would like to thank all my officemates, Michele, Tyler, Isma, Emily, Valentin, Sanae, Anita, Roef and Vaish, for making the office a cozy place to work. Valentin, I learned a lot from you. Vaish, thank you for being such a nice, calming and happy presence.

Anita, Shruti, Laurien and Michael, my powerhouse, thank you for the countless (non)scientific conversations and good memories. Tabea and Hannah, the same goes to you. I greatly missed not having you around. You are all awesome friends, colleagues and teammates. Iñigo, mi hermano no oficial, gracias por sacarme siempre una sonrisa and to Wieland (together with Laurien), for introducing me to the amazing world of gardening and

wine photography. To Maria and Panda, without whom my German family would not be complete: thank you for making me feel at home.

Agus, amigo, gracias por estar dispuesto a ayudarme con lo que fuera y por ser tan buena compañía. Siempre me he sentido comprendida y escuchada contigo. Patxi, agradezco tu amistad, y tus abrazos sanadores. Geral, gracias por tu (son)risa eterna. Echo de menos tu espíritu alegre. Marta, gracias por ser tan agradable y por ser una excelente compañera de viajes locos. Linda, Yawen, Stefano, Alix, Deni, Hannah [Marifé], Rick, Sri, Faruk, Marian, Ingo, Lars: hanging out with you - whether it was at the basketball court, at an occasional dinner or at the department - was always fun. To Sasja and Alexandra, thank you for the attentiveness. Seeing either of you at the front desk or the corridors was a mood lifter. Talking about mood lifters, I could not *not* mention my beloved Bandito brothers. Thank you for the fun times (and for the excellent coffee). To the rest of the members of the CN department: thank you for building such a nice working environment. It has been a pleasure to share these years with you.

To Peppe, Dennie, Anna, Martijn, Pieter, Monika, Nicola, Grace, Meche, thank you for the fun memories. Gara, Georgina, Almudena, Cristina y Mora, me siento muy afortunada de poder haber compartido parte de esta aventura con vosotras. Thank you, Sanae for being such a cheerful and inspiring company. Emma, my youngest friend, thank you for being a sunshine during these years. Thank you Anne, Rekha and Nici for your support and friendship. To the friends in Glasgow, thank you for making the trips even more fun. Uning, Medoza, and Nur, thank you for your friendship. Your strength is inspiring.

Sarri, zure hitz eta aholkuen falta handia sentitzen dut.

Zarauzko kuadrila eta gainontzeko lagunei, eskerrik asko doktoretzako gorabeherak erlatibizatzen laguntzeagatik eta distantzia oztopo ez dela berresteagatik.

Familiakoei, eskerrak bihotzetz zuen maitasun eta babesengatik. Zorionekoa ni, halako familia baten kide izateagatik! Ama eta aita, zuen esfortzu eta eskuzabaltasunek ez dute parekorik – eskerrik asko erraztu dizkidazueten aukera guztiengatik.

Tyler, my rock, thank you for being such a supportive partner. I love you. I cannot wait to start our next chapter *together*.

About the author

Amaia Benitez Andonegui was born on June 21st, 1991 in Zarautz, Spain. She attended school and high school in her hometown, at La Salle Ikastetxea and Lizardi Institutua, respectively. Between 2009 and 2013, she carried out her undergraduate studies in Biomedical Engineering at Tecnun College of Engineering in Donostia, Spain. In 2012 she spent a Erasmus semester at Chalmers University of Technology in Gothenburg, Sweden. In 2013 she was admitted to the Research Master program in Cognitive Neuroscience at Maastricht University. Her Master thesis focused on optimizing fNIRS optode placement to measure activity in the supplementary motor area. This research was supervised by Dr. Sorger and Prof. Goebel. Between 2015 and 2020, she conducted her doctoral research under the supervision of Dr. Sorger, Prof. Goebel and Dr. Möckel at the Department of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, and the Department of Knowledge Engineering, Faculty of Science and Engineering, at Maastricht University. Currently she works as a research associate at the Department of Cognitive Neuroscience at Maastricht University on mapping axes of motion in the human motion complex using 7 Tesla magnetic resonance imaging with Prof. Goebel.

Publications

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Benitez-Andonegui, A., Burden, R., Benning, R., Möckel, R, Lührs, M., Sorger, B. (2020). *An augmented-reality fNIRS-based brain-computer interface: a proof- of-concept study*. Frontiers Neuroscience, Vol. 14(346). doi: 10.3389/fnins.2020.00346

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Under review

Benitez-Andonegui, A., Lührs, M., Nagels-Couner, L., Ivanov, D., Goebel, R., Sorger, B. *The effect of considering individual functional and anatomical MRI on fNIRS optode-layout design*

Benitez-Andonegui, A., Dumitrescu, S., Tursic, A., Goebel, R., Ivanov, D., Lührs, M., Sorger, B. *Investigating the impact of vasculature on short distance channel correction in fNIRS*

Conference contributions

Benitez-Andonegui A, Burden R, Benning R, Möckel R, Lührs M, Sorger B (2019, December*). An augmented-reality fNIRS-based brain-computer interface: a proof-of-concept study*. Presented at rtFIN Maastricht The Netherlands

Tursic A, Muñoz-Moldes S, Lührs M, Eck J, **Benitez-Andonegui A**, Goebel R (2019, December). *The effect of session-specific region definition in multi-session fMRI neurofeedback*. Presented at rtFIN Maastricht The Netherlands

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