Shedding light on motor-independent communication

Shedding Light on Motor-Independent Communication: fNIRS-based Brain-Computer Interfacing for Everyday Life

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THESIS

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Content

Abbreviations

ALS	Amyotrophic Lateral Sclerosis
BCI	Brain-Computer Interface
BOLD	Blood-oxygen-level-dependent
COI	Channel-Of-Interest *
DoC	Disorder of Consciousness
EEG	Electroencephalography
fMRI	functional Magnetic Resonance Imaging
fNIRS	functional Near-Infrared Spectroscopy
GLM	General Linear Model
HbO	Oxygenated hemoglobin
HbR	Deoxygenated hemoglobin
LIS	Locked-In Syndrome
MEG	Magnetoencephalography
MCS	Minimally Conscious State
MD	Mental Drawing
MT	Multi-Trial
MCP	Multi-Channel Pattern
MVPA	Multi-Variate Pattern Analysis
MSA	Multiple System Atrophy
MS	Multiple Scleroses
SOI	Signal-Of-Interest *
SVM	Support Vector Machine
SN	Spatial Navigation
ST	Single-Trial
UWS	Unresponsive Wakefulness Syndrome

*see Definitions

Definitions

COI and SOI are abbreviations proposed in the empirical chapters of this dissertation. These abbreviations are thus relatively new in the field of fNIRS. They are akin to the well-known abbreviation ROI for "region of interest". In fMRI data analysis, signal is often extracted from specified ROI's, *i.e.,* regions of interest based on functional or structural features (see Poldrack (2007)).

In the current work we propose the following use of the abbreviations:

COI A single participant-specific fNIRS channel, *i.e.,* source-detector pair. See chapter 2 and 3.

SOI A single participant-specific fNIRS channel by chromophore (HbO, HbR or HbT) combination. See chapter 3 and 4.

Reference

Poldrack, R.A. (2007). Region of interest analysis for fMRI. *Social Cognitive and Affective Neuroscience, 2*(1), 67-70. doi:10.1093/scan/nsm006

1 General Introduction

Natural human communication depends on the integrity of our neuromuscular system. Our muscles and the nerves serving them are crucial for both verbal and non-verbal communication. When we speak, we engage muscles in our tongue, lips, jaw and pharynx. We use a myriad of different muscles when we nod our head, raise our hand, make a facial expression, etc. What happens if something is amiss? What happens if our brain loses the fine-grained control over our muscles? What happens if the muscles themselves stop responding to our brain's commands?

Locked-In Syndrome

The general motivation of this work is a condition called "locked-in syndrome" (LIS). Patients with LIS are almost completely paralyzed while at the same time being awake and aware (Laureys, Boly, Moonen, & Maquet, 2009). These fully conscious humans are literally "locked" in their body. The term LIS was introduced in 1966 to describe patients with infarction of the ventral pons (Plum & Posner, 1966). These patients suffered quadriplegia and paralysis of the lower cranial nerves, and thus lost the ability to communicate naturally (Patterson & Grabois, 1986). Nevertheless, these patients could see, hear, feel and think. Communication with these patients could still be established through vertical eye gaze and/or upper eyelid movement.

Three LIS subtypes were proposed in 1979 (Bauer, Gerstenbrand, & Rumpl, 1979). The LIS as described by Plum and Posner (1966) is referred to as "classical LIS", with total immobility except for vertical eye movements and blinking. When any additional voluntary movement is possible, the diagnosis "incomplete LIS" is given. Voluntary movements are most often found in the fingers, toes and head (Bruno & Laureys, 2012), occasionally

free eye movements remain possible (Bauer et al., 1979). When all motor functions cease to respond to brain signals, thus also vertical eye movements and blinking being absent, we are dealing with the rare case of a "total LIS". In these conscious patients, not a single behavioral sign of being aware can be detected.

Etiology

Acute LIS is often caused by vascular or traumatic brain injury (Bruno & Laureys, 2012). A common cause is infarction to the brain stem (Lulé et al., 2009), specifically the pons (Bruno et al., 2008; Patterson & Grabois, 1986). Trauma-related brain injury can result from, *e.g.*, a car crash, a fall but even doing gymnastics[1] or having a severe cough[2]. Rare causes of LIS are mesencephalic lesion, subarachnoid hemorrhage, vascular spasm of the basilar artery, brain stem tumor, central pontine myelinolysis, encephalitis, pontine abscess, drug toxicity[3], vaccine reaction, infection[4] and prolonged hypoglycemia (Bruno & Laureys, 2012; Bruno et al., 2008). All the above causes are "acute"/"sudden onset", meaning that a healthy individual suddenly, *i.e.,* over the course of a few days/weeks, finds itself in a locked-in state.

[1] The English woman Tracey Okines tore an artery in her neck during a cartwheel (Green, 2020; Wilson, Hinchcliffe, Okines, Florschutz, & Fish, 2011).

[2] A rheumatologist in Illinois, USA had an vertebral artery dissection after a persistent cough (Ansari-Ali, 2020).

[3] For example: toxic progressive leukoencephalopathy, or "chasing the dragon syndrome", a disease typically caused by the inhalation of fumes from heroin when heated on aluminum foil.

[4] The 19-year Irish woman Patricia Ingle contracted chlamydia psittacosis, *i.e.* an airborne infection, from a parrot at her job in a pet store (Ingle, 2016).

There are also patients that slowly descend into a LIS state. This is the case in late stages of neuromuscular diseases, such as amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS) and multiple systems atrophy (MSA). Muscle control is gradually lost over the course of these diseases.

Prevalence

LIS is a very rare condition, with a prevalence of less than 1/1.000.000 (Bruno & Laureys, 2012). In France the prevalence was estimated to be around 0.8/100.000 inhabitants (Snoeys, 2010). Snoeys (2010) extrapolated this estimated prevalence to Flanders, Belgium, which resulted in about 48 Flanders inhabitants with LIS. In Dutch nursing homes the prevalence of classic LIS was found to be 0.7 out of 10.000 long-term somatic nursing home beds (Kohnen, Lavrijsen, Bor, & Koopmans, 2013).

Diagnosis

On average it takes clinicians 78 days to diagnose a patient with LIS (León-Carrión, van Eeckhout, Domínguez-Morales Mdel, & Pérez-Santamaría, 2002). Initially, patients are often completely paralyzed or comatose. Typically, family members are the first to notice subtle signs of consciousness (Laureys et al., 2009; León-Carrión et al., 2002; Vanhaudenhuyse et al., 2018). Reasons for diagnosing the disease with a considerable delay are that LIS diagnosis is complex and requires a highly specialized medical team. Unsurprisingly, there is a high rate of misdiagnosis – 37-41 % – in patients with severe brain damage (Childs, Mercer, & Childs, 1993; Schnakers et al., 2009; Vanhaudenhuyse et al., 2018). If LIS patients are not capable of signaling their awareness due to their severe motor deficits, they are at risk of being misdiagnosed as having a disorder of consciousness (DoC) such as unresponsive wakefulness

syndrome (UWS)[5] or minimally consciousness state (MCS). In both these disorders, wakefulness/arousal from the autonomic nervous system is present, meaning that they can breathe, digest, thermoregulate and have a sleep-wake rhythm (Bruno, Vanhaudenhuyse, Thibaut, Moonen, & Laureys, 2011). While patients in UWS are not conscious at all and unable to communicate, MCS patients show minimal signs of awareness and might show communicative behavior (Laureys, 2005). Unlike LIS patients, MCS patients are not able to consistently or reliably communicate and are generally considered to have diminished cognitive functioning. Signs of consciousness that distinguish MCS from UWS patients are, for example, command following (*e.g.*, making a sound/movement on command), visual pursuit (*e.g.*, "fixate on the mirror" while mirror is moved 45° to left and right) or being able to demonstrate object recognition (*e.g.*, "Touch the apple, not the cup") (Giacino, Kalmar, & Whyte, 2004; Schnakers, Giacino, & Laureys, 2010). These behaviors signal some degree of preserved cognitive processing. However, even for medical professionals, it is often difficult to distinguish reflexive from voluntary behavior. A case study of a 41-year-old man illustrates the tragedy of misdiagnosis (Vanhaudenhuyse et al., 2018). After a car accident, the man was considered to be in UWS for 20 years. The patients' relatives requested a new diagnostic evaluation because they had the impression that their relative was actually conscious. Renewed diagnostic testing found that he was in fact in incomplete LIS. Through careful behavioral testing with the coma recovery scale (Giacino et al., 2004), functional communication was established through eye movement and some residual movement in his thumb. Neuroimaging confirmed that

[5] Previously referred to as "vegetative state", a diagnosis with an intrinsically negative connotation (Laureys et al., 2010).

the lesion was limited to the brainstem with otherwise intact cortical functioning. This patient's story is one of extreme social isolation, which, unfortunately, is not uncommon (Andrews, Murphy, Munday, & Littlewood, 1996; Childs et al., 1993; Naro, Calabrò, Pollicino, Lombardo, & Bramanti, 2017; Schnakers et al., 2009; Torrisi et al., 2018). Behavioral assessment remains the gold standard to detect consciousness in clinical cases (Vanhaudenhuyse et al., 2018). If practiced correctly, *i.e.*, applying the coma recovery scale (Giacino et al., 2004) for at least five days (Wannez, Heine, Thonnard, Gosseries, & Laureys, 2017), many misdiagnoses can be avoided. Note however, that this and other scales rely on at least some degree of preserved motor output. What about the small subset of total LIS patients, which cannot move a single muscle? The golden standard (*i.e.*, behavioral assessment) would fail to detect remaining consciousness in these patients. A term related to total LIS is "functional LIS" (Bruno, Vanhaudenhuyse, et al., 2011). In patients suffering a functional LIS, higher cortical functioning can only be detected through functional neuroimaging techniques (Monti, Coleman, & Owen, 2009; Monti et al., 2010; Naro et al., 2017; Owen & Coleman, 2008; Owen et al., 2006).

Prognosis

The initial phase of acute LIS is most critical, with the highest mortality in the first few months of the initial cause (Bruno et al., 2008; Doble, Haig, Anderson, & Katz, 2003). In a few cases, the LIS state is transient and patients recover fully (Bauer et al., 1979). Unfortunately, many do not recover and after one year are said to be in chronic LIS. Once a patient is medically stabilized for more than a year, life expectancy is on average 10 years for 83 % and 20 years for 40 % of the patient population (Doble et al.,

2003). The statistical distribution of life expectancy is relatively wide. Bruno et al. (2008) found an average life expectancy of 7 ± 5 years, ranging from three days to 27 years. Survival rates and life expectancies are closely linked to the specific etiology of LIS, with vascular etiology typically associated with a higher morbidity than non-vascular etiology (Bruno et al., 2008; Patterson & Grabois, 1986). Another factor is the age of the person at which the initial brain injury occurred, with younger persons being more likely to pull through the initial critical phase compared to older persons (Bruno et al., 2008). Lastly, the age of the crucial event is related to the etiology due to the simple fact that vascular causes are more common in older people (Patterson & Grabois, 1986).

For those patients with progressive motor-neuron disorders, *i.e.*, ALS, MS, MSA, the prognosis is determined by the progression of their disease. Many of these patients know they will enter total LIS eventually, as control of the eye muscles is lost in late stages of the diseases (Bauer et al., 1979).

A Life Worth Living

It is popular belief that a life with LIS is not a life worth living (Demertzi, Jox, Racine, & Laureys, 2014), and consequently euthanasia is a much sought after option (Bruno, Bernheim, et al., 2011). As with many severe brain disorders, inferring LIS patients' subjective experience is difficult. However, there is convincing evidence that life quality of LIS patients is not as poor as commonly assumed (Linse et al., 2017; Lulé et al., 2009). The majority of chronic LIS patients, *i.e.*, 72 %, self-assess their well-being as good and report being happy, with a minority, *i.e.*, 28 %, declaring unhappiness (Bruno, Bernheim, et al., 2011). Another study compared 19 classical LIS

patients with 20 healthy control subjects, and found no significant difference in self-reports of quality of life (Rousseau, Pietra, & Nadji, 2012). Even in a sample of end-stage ALS patients, assessed via eye-tracking, a good psychological wellbeing was reported (Linse et al., 2017). Requests for euthanasia are – contrary to popular belief – rare (Bruno, Bernheim, et al., 2011; Doble et al., 2003; Haig, 1998; Rousseau et al., 2012). An important factor in finding happiness in a LIS state, is restoration of possibilities to interact with one's surrounding. Despite losing all physical autonomy, appropriate assistive technology can enable cognitive/mental autonomy (Lulé et al., 2009).

Humans have the ability to adapt and overcome highly difficult situations. There are ample examples of LIS patients finding new purpose that go beyond merely coping with their disorder. For example, a 42-year old LIS patient[6] obtained a degree in ancient history using her patient-computer device even though it took her three weeks to complete a normally three-hour exam (Chapman, 2014). Doble et al. (2003) reported an attorney who continued sharing legal advice with colleagues through fax and email. A caregiver interpreted his eye blinks in Morse code and transcribed his messages. These examples demonstrate that LIS patients can lead a meaningful life and contribute to society.

Restoring Communication

LIS patients need to be able to communicate with the outside world to exercise their cognitive autonomy. Unsurprisingly, communication is a major determinant of quality of life in LIS patients (Rousseau et al., 2012).

[6] Dawn Faizey-Webster suffers from incomplete LIS after near-fatal pre-eclampsia at 26-weeks pregnancy. She used buttons either side of her head to move the cursor on the screen and blinked to register the letters.

In patients with classic or incomplete LIS, communication can be established through blinking or eye movement. In its most simple form, this can mean "look up for yes and down for no" (Haig, 1998; Kopsky, Winninghoff, Winninghoff, & Stolwijk-Swüste, 2014). The degrees of freedom can be further heightened through use of a communication grid or letter board (Haig, 1998). A conversation partner/transcriber typically recites a language-specific frequency-ordered alphabet and the patient blinks when the chosen letter is read aloud. Jean-Dominique Bauby[7] wrote his book 'The Diving Bell and the Butterfly' in this manner. It took him about 200.000 blinks with his left eye to write his autobiography. Nevertheless, human transcribers can be prone to bias and misinterpretation, moreover, caregivers are not always available or have the time. A solution has been found in patient-computer devices that LIS patients can use independently.

Patient-Computer Devices

Most patient-computer devices work with eye-tracking systems. Typically the eye movement or blinks of patients are registered with infrared sensors and converted for communication, use of the internet, reading, writing, etc. (Rousseau et al., 2012; Spataro, Ciriacono, Manno, & La Bella, 2014). For incomplete LIS patients, an ultrasound or infrared system can detect residual movement. Such patient-computer devices rely on overt/behavioral signs by the LIS patient. These devices thus can benefit patients in classic or incomplete LIS. Patients that find themselves in a total LIS state can per definition not communicate via overt signs. For these patients muscle-independent signals can offer a communication means.

[7] Jean-Dominique Bauby was editor-in-chief of the French magazine 'Elle'. He suffered a stroke at the age of 43 which caused LIS.

Brain-Computer Interfaces

A Brain-Computer Interface (BCI) circumvents all normal output pathways of peripheral nerves and muscles through use of voluntarily evoked brain signals (Wolpaw et al., 2000). Firstly, a person intentionally modulates its own mental state, through *e.g.* imagery or selective attention. This modulation in mental state is accompanied by an altered brain state (see Figure 1, left). Secondly, the brain state is captured by a functional neuroimaging technique (see Figure 1, top). Thirdly, brain states are analyzed. Specific brain-signal features, depending on the type of BCI employed, are extracted as input for an algorithm (see Figure 1, right). Fourthly, the output – hopefully the intended meaning – can then be used to communicate or control a device such as an electronic wheelchair or a robotic limb[8] (see Figure 1, bottom). Lastly, there is possibility to feed the generated output back to the BCI user. This way, the BCI user becomes aware of the output, can evaluate its accuracy and further reinforce or adapt their mental state modulation.

When LIS patients use a BCI, the computer thus performs the translational task that the neuromuscular system cannot execute anymore. When these systems are developed and tested, the most important outcome is the correspondence between intended meaning and output of such a system, *i.e.*, the BCI accuracy. Therefore, usually new BCI systems are elaborately tested on healthy participants until a sufficient BCI accuracy is reached (in so-called "proof-of-principle" studies).

[8] BCI for motor control or motor revalidation are not discussed in this work. The focus is entirely on BCIs for restoration of communication. See Mane, Chouhan, and Guan (2020) for a review on BCI for stroke revalidation.

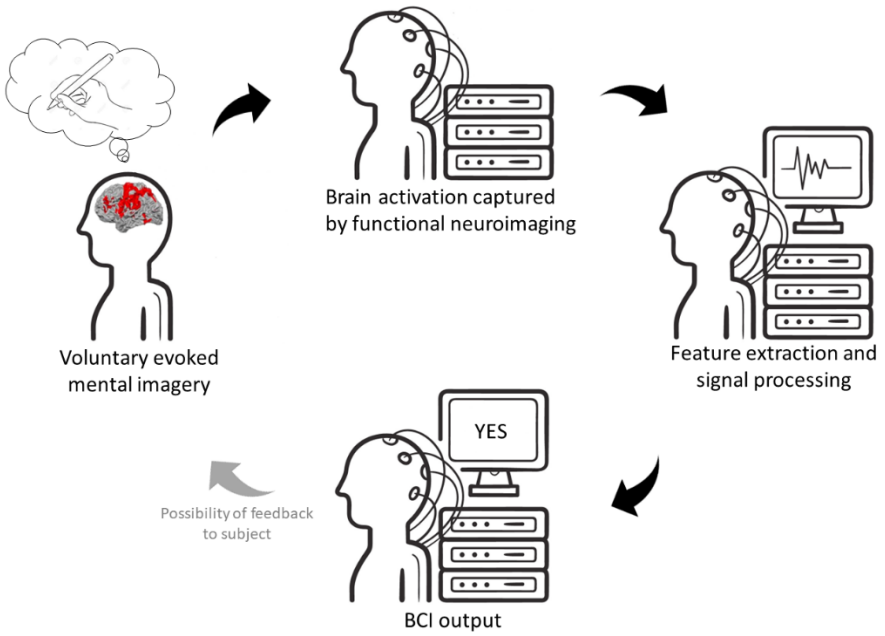

Figure 1. **Schematic of a Brain-Computer Interface.** *Left*: the participant alters his/her brain state through *e.g.* mental imagery. *Top*: the resulting brain activation is captured by a functional neuroimaging method. *Right:* the computer extracts specific signal features and processes these features. *Bottom:* BCI output such as a simple 'yes' or 'no'. Lastly, there is a possibility to give feedback about the BCI output to the subject.

The field of BCI is relatively young, with the first studies ranging back to about 40 years ago. The first international meeting on BCI technology was organized in 2000 (Wolpaw et al., 2000). A distinction is made between BCIs that rely on electrical impulses, *i.e.*, neuroelectric signals, or blood flow, *i.e.*, hemodynamic signals. The input for neuroelectric BCIs is a direct measure of cortical activity, whereas for hemodynamic BCIs the input is an indirect measure of brain activation. When a brain area is "active", electrical impulses can be detected with millisecond precision. The hemodynamic signals are a slow/delayed metabolic response that develop in the order of seconds (Wolpaw, Birbaumer, McFarland, Pfurtscheller, &

Vaughan, 2002). In the following, common functional neuroimaging methods used in the context of BCI will be reviewed shortly, though by no means exhaustively.

Neuroelectric BCIs

Most BCI research has focused on neuroelectric signals due to their fast detectability. Several electrophysiological methods capture the electrical activity of the brain, as described next.

Electroencephalography

The electroencephalography (EEG) signal finds its origin in synchronized activity in pyramidal cells (Jackson & Bolger, 2014). If these cells are aligned in parallel, a dipole can be measured on the head due to volume conduction (Jackson & Bolger, 2014). The technical equipment that measures these dipoles are electrodes, typically attached to the head with electrode gel. EEG is the most commonly used method in the context of BCI due to its many advantages. EEG is a non-invasive, fast, mobile and comparatively inexpensive method. Different EEG-BCIs employ specific features of the electrophysiological signal: slow cortical potentials (SCP), sensory motor rhythms (SMR), steady state visual evoked potentials (SSVEP) and event related potentials (ERP). BCIs based on SCP and SMR do not require a stimulus computer, whereas SSVEP and ERP require exogenous – typically visual – stimulation by flashing letters/symbols (Allison, Dunne, Leeb, Millán, & Nijholt, 2012). Seminal work by Birbaumer et al. (1999) demonstrated LIS patients' spelling letters using an SCP-BCI. Currently the most frequently used feature for EEG-BCI in the context of motor-independent communication is the ERP, more specifically the P300 component. This component, a positive deflection ± 300 ms after stimulus

onset, is measured over the parietal cortex. A stimulus computer will typically show a matrix of letters. Rows and columns are consecutively highlighted/flashed. The BCI user is asked to focus on the chosen letter, through counting the times this letter is flashed (Farwell & Donchin, 1988). When the chosen letter is flashed, a P300 component occurs. P300-based BCIs have enabled communication in ALS patients (Kübler et al., 2009; Nijboer et al., 2008; Sellers & Donchin, 2006; Sellers, Vaughan, & Wolpaw, 2010), brain stem stroke patients (Sellers, Ryan, & Hauser, 2014) and cervical spinal cord injury (Ikegami, Takano, Saeki, & Kansaku, 2011).

Magnetoencephalography

Another non-invasive neuroelectric method explored in the context of BCI is magneto-encephalography (MEG). MEG captures the magnetic field induced by the neuroelectric brain activation. It has the advantage of being more spatially specific compared to EEG, but it has a major disadvantage of being impractical (Reichert, Dürschmid, Heinze, & Hinrichs, 2017). An MEG system includes a large, non-mobile device, typically only found in research facilities and hospitals. MEG-BCIs have successfully enabled communication in healthy participants (Lin et al., 2013; Mellinger et al., 2007), but no communication studies have been performed in patients.

Invasive Methods

Invasive neuroelectric techniques, such as intracortical recordings (ICor) and electro-corticography (ECoG), are implanted under the skull. Due to the inherent risks of neurosurgery, the majority of studies were performed on patients that have medical indications for brain surgery such as epilepsy or tumor treatment (Schalk & Leuthardt, 2011). Results of these studies are encouraging but lack of data on long-term use and health risks are major

drawbacks (Schalk & Leuthardt, 2011). See Schalk and Leuthardt (2011) for a review of ECoG and Brandman, Cash, and Hochberg (2017) for a review of ICor for BCI purposes.

Hemodynamic BCIs

When there is neural activation in a specific area, a hemodynamic response will follow due to neurovascular coupling (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001; Phillips, Chan, Zheng, Krassioukov, & Ainslie, 2016). In other words, more blood will be sent to the active brain area to provide the cells with oxygen and glucose. The use of the hemodynamic signal is less common in the context of BCI than the neuroelectric signal. Hemodynamic BCIs typically have a lower information transfer rate[9] compared to electrophysiological methods due to their reliance on the inherently 'slower' metabolic response. Despite being an indirect and relatively slow measure of brain activity, hemodynamic responses have the advantage of being more localized to a specific brain area compared to the widespread neuroelectric effects. This advantage of spatial specificity can thus be exploited for BCI use.

Functional Magnetic Resonance Imaging

When an active brain area demands blood supply, this supply is typically more than the area needs. With functional Magnetic Resonance Imaging (fMRI) this excess can be detected due to the differential magnetic properties of oxygenated and deoxygenated blood. Blood oxygenation level-dependent (BOLD) contrast imaging can determine which brain areas are relatively active. For BCI purposes, the human ability to purposefully

[9] Information transfer rate (ITR) is an evaluation metric for BCI systems. It reflects the amount of information transferred per unit of time, typically expressed in bits/min (McFarland, Sarnacki, & Wolpaw, 2003).

evoke brain activation through mental imagery (Bardin et al., 2011; Monti et al., 2010; Owen & Coleman, 2008; Sorger et al., 2009; Sorger, Reithler, Dahmen, & Goebel, 2012) or selective attention (Naci & Owen, 2013) is exploited. Seminal work by Monti et al. (2010) demonstrated that yes/no questions can be answered through mental imagery in an fMRI scanner. Healthy participants were asked to imagine playing tennis (motor imagery) for encoding a "yes" and imagine walking through their house (spatial imagery) for encoding a "no". The **spatial specificity** of fMRI images was subsequently used to decode participants' intentional changes in brain activity. The researchers inferred a "yes" answer when they saw heightened activity in the supplementary motor area. When activity was seen in the parahippocampal gyrus, a "no" answer was inferred. The answers of healthy participants were decoded with 100 % accuracy. One DoC patient, a 22 year old man thought to be in UWS, was even able to use this fMRI-BCI to answer autobiographical yes/no questions (Monti et al., 2010). Shortly after, Bardin et al. (2011) designed a binary fMRI-BCI based on the **temporal specificity** of the BOLD response. Participants chose a single sport imagery task and were asked to perform it in one of two timeframes, one for "yes" and one for "no". Work from our lab has combined both the **spatial and temporal specificity** of the BOLD response in a four-choice fMRI-BCI (Sorger et al., 2009). Through use of two imagery tasks (motor imagery and mental calculation) and four distinct timeframes (differential on- and offsets), four answer options could be encoded. The average accuracy of healthy participants was observed to be as high as 94.9 % on a single-trial basis. Based on the same spatiotemporal characteristics of the hemodynamic response, Sorger et al. (2012) developed an fMRI-based letter speller with a high accuracy of 82 % in healthy participants. A

strength of these fMRI-BCIs (Bardin et al., 2011; Monti et al., 2010; Sorger et al., 2009; Sorger et al., 2012) is that they require minimal to almost zero preparation time and participant training. FMRI-BCIs can enable almost instant communication, in stark contrast with EEG paradigms that often require ample time to train both participants and classifiers (Pires, Nunes, & Castelo-Branco, 2012). The fMRI paradigms by our group (Sorger et al., 2009; Sorger et al., 2012) are sufficiently robust to correctly decode an answer from a single trial. Despite these encouraging results, an MRI machine is a large, expensive and immobile device. Communication via an fMRI-BCI is thus only possible in a hospital or research institution. Moreover, highly trained researchers or clinicians are required to analyze functional brain activation in these dynamic paradigms. There is a need to transfer theses successful hemodynamic paradigms to a portable method.

Functional Near-Infrared Spectroscopy

The first studies using functional near-infrared spectroscopy (fNIRS) to measure brain activation were conducted in 1993 (Chance, Zhuang, UnAh, Alter, & Lipton, 1993; Hoshi & Tamura, 1993; Kato, Kamei, Takashima, & Ozaki, 1993; Villringer, Planck, Hock, Schleinkofer, & Dirnagl, 1993). Since then, neuroscientific publications using fNIRS are increasing rapidly (Boas, Elwell, Ferrari, & Taga, 2014; Naseer & Hong, 2015; Pinti, Scholkmann, Hamilton, Burgess, & Tachtsidis, 2018). FNIRS is a portable brain imaging method that relies on the same hemodynamic signals as fMRI (Cui, Bray, Bryant, Glover, & Reiss, 2011; Huppert, Hoge, Diamond, Franceschini, & Boas, 2006; Scarapicchia, Brown, Mayo, & Gawryluk, 2017), with the important difference that it measures relative optical changes instead of magnetic changes.

Near-infrared light emitters and sensors, respectively referred to as source and detector optodes, are placed on the head (see Figure 2). The optodes are typically integrated in a cap, similar to an EEG cap. The source optodes emit two infrared light wavelengths of constant intensity[10] through the skin, skull, meninges and finally into the brain. The light can travel largely unaltered through the extracerebral tissue due to the low absorption of biological tissue that is mostly composed of water (León-Carrión & León-Domínguez, 2012). On the other hand, chromophores present in blood – such as oxygenated (HbO) and deoxygenated hemoglobin (HbR) – are light absorbing molecules. HbO and HbR have differential optical properties in the visible and near-infrared light range (Irani et al., 2007). HbO has a high absorption factor for a wavelength between 800 and 850 nm, and HbR for a wavelength between 650 and 700 nm (León-Carrión & León-Domínguez, 2012; Nishiyori, 2016). The infrared light photons scatter throughout the entire brain. Depending on the cerebral blood flow (CBF), chromophore concentrations in a certain brain area change over time. This in turn causes more (or less) light to be absorbed in a certain area. A detector optode captures only a fraction of the light photons sent into the brain. Nevertheless, it is known that a large percentage of photons captured by a detector optode scatter within a banana-shaped path (Gratton, Maier, Fabiani, Mantulin, & Gratton, 1994).

[10] This is the case only with continuous wave fNIRS. Most fNIRS hardware is based on continuous wave technology, as are all studies reported in this dissertation. Two alternative methods are frequency domain fNIRS and time domain fNIRS. Both technologies provide more information than continuous wave fNIRS, *i.e.,* time of flight, but are technically much more challenging (Irani, Platek, Bunce, Ruocco, & Chute, 2007; Minagawa-Kawai, Mori, Hebden, & Dupoux, 2008; Scholkmann et al., 2014; Wolf, Ferrari, & Quaresima, 2007).

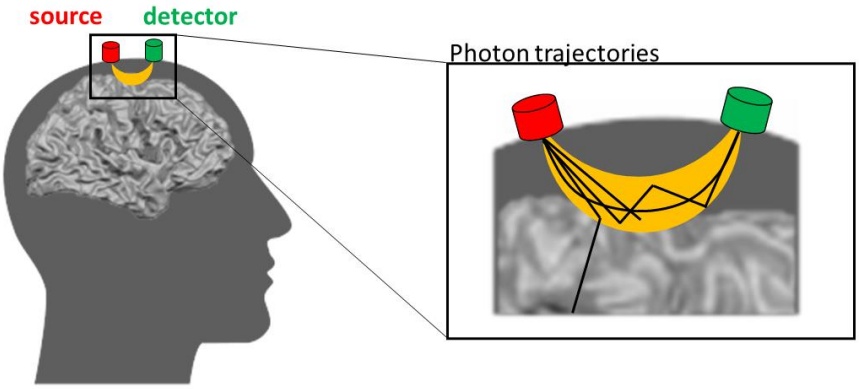

Figure 2. **Principles of Functional Near-Infrared Spectroscopy.** *Left*: The light-emitting source optode (red) and detector optode (green) are placed on the skin. The majority of the photons that are captured by the detector optode (green) travel within a banana-shaped area (yellow). *Right*: Possible photon trajectories. Two photons scatter, one reaches the detector and one leaves the sample. A third photon travels straight from source to detector optode, also called a "ballistic" photon (León-Carrión & León-Domínguez, 2012). A fourth photon is absorbed by chromophores in the cortex.

Using the modified Beer-Lambert law (León-Carrión & León-Domínguez, 2012) together with reasonable assumptions, it is possible to quantify relative changes in HbO and HbR. The sampling rate of fNIRS often depends on the number of optodes mounted[11], but is typically in the order of tens of Hz (Chen et al., 2020). The distance between a source and detector optode determines the depth sensitivity of a channel (Brigadoi, Salvagnin, Fischetti, & Cooper, 2018). Common inter-optode distances are between 2 and 7 cm (León-Carrión & León-Domínguez, 2012). When the source-detector distance is around 4/4.5 cm, the top 2-3 mm of cortex is measured (Chance et al., 1988; Tamura, Hoshi, Hazeki, & Okada, 1997) and

[11] This is called time multiplexing, in which sources emit light one at a time to be able to distinguish different channels. Alternative methods to avoid cross-talk between channels exist, for example frequency multiplexing in which sources emit nonoverlapping frequencies (Meryem et al., 2021).

extracranial contribution are negligible (Smielewski et al., 1997; Smielewski, Kirkpatrick, Minhas, Pickard, & Czosnyka, 1995). The spatial resolution is in the range of 5-10 mm (Quaresima & Ferrari, 2019). For comparison, common spatial resolution in fMRI is in the order of 3.5 mm (Molloy, Meyerand, & Birn, 2014) and in EEG, *i.e.*, with a 32-channel array, in the order of 7 cm (Michel & Brunet, 2019).

FNIRS has many advantages compared to other brain imaging methods. It is easy to operate, relatively inexpensive, safe, mobile and relatively robust against motion artifacts (Cutini, Moro, & Bisconti, 2012; Irani et al., 2007; León-Carrión & León-Domínguez, 2012; Naci et al., 2012; Pinti, Aichelburg, et al., 2018; Scholkmann et al., 2014). FNIRS can be considered an effective compromise between the high temporal resolution of EEG and the robustness of the hemodynamic signal in fMRI (Benitez Andonegui, 2021).

Due to its many advantages, the use of fNIRS in BCI research and clinical settings is growing steadily (León-Carrión & León-Domínguez, 2012; Zephaniah & Kim, 2014). Research in healthy participants showed feasibility of binary (Naseer, Hong, & Hong, 2014) and six-choice (Benitez-Andonegui et al., 2020) fNIRS-BCIs. FNIRS-BCIs have been tested in a few patient studies. Naito et al. (2007) tested a yes/no fNIRS-BCI in 40 LIS patients suffering from ALS. To answer “yes”, patients were asked to imagine calculating or singing (prefrontal activation tasks). To answer “no”, patients were asked to merely rest. Twenty-seven out of 40 patients reached a BCI accuracy above 75 %. Abdalmalak et al. (2017) tested a single LIS patient suffering from Guillain–Barré syndrome using time-resolved fNIRS. The patient was asked to imagine playing tennis for encoding a “yes”, and to rest for encoding a “no”. The patient was able to answer questions with an

accuracy of 100 %. Borgheai et al. (2020) performed an fNIRS-BCI study in six ALS patients. An accuracy of 81.3 % was established using a visuo-mental paradigm[12]. One of these six patients used the fNIRS-BCI longitudinally over 5 sessions in 5 months. BCI performance did not decline over this extended period.

Methodological challenges in the transfer of fMRI-BCI paradigms to fNIRS remain. FNIRS has an inherently lower spatial resolution compared to fMRI. Secondly, fNIRS can only detect brain activation in superficial brain areas, deeper structures cannot be reached. Thirdly, fNIRS is sensitive to physiological noise from extracranial tissue (Zhang, Noah, & Hirsch, 2016), resulting in a lower signal-to-noise ratio compared to fMRI. These issues result in a less robust signal, *i.e.*, the decoding accuracies are generally lower with fNIRS compared to fMRI, and require several trials to correctly decode a single answer. However, there are still ample possibilities to further improve fNIRS-BCIs to be more efficient, reliable across time, individualizable, suited for daily use, comfortable, BCI-user friendly, BCI-operator friendly, etc.

Research Aim and Thesis Outline

Problem Statement and Aim

Despite the large body of studies on BCIs for communication, rarely are BCI communication systems used in patients' daily life. The reasons are multifold, including a lack of commercially available communication BCI products, the technical complexity of BCIs but also the subject-specific performance of BCIs. The most commonly used BCI-input modality, *i.e.*, EEG

[12] This design is an adaptation of the classical oddball paradigm. It relies on visual tasks and arithmetic operations (Borgheai et al., 2020).

(Kübler et al., 2009; Lazarou, Nikolopoulos, Petrantonakis, Kompatsiaris, & Tsolaki, 2018; Marchetti et al., 2013; Won, Kwon, Jang, Ahn, & Jun, 2019), is a practical candidate for home use. However not all users achieve proficiency in EEG-based BCI control, coined "BCI illiteracy" (Blankertz et al., 2008; Dickhaus, Sannelli, Müller, Curio, & Blankertz, 2009; Kübler & Muller, 2007; Nijholt et al., 2008). About 20 % of users are unable to control an EEG-based BCI (Allison & Neuper, 2010; Dickhaus et al., 2009). This might be due to the inability of EEG-BCI communication paradigms to be individualized to users. Thus, there is a need to develop alternative and flexible brain-based communication techniques. Hemodynamic brain signals as measured with fMRI have been successfully explored in this context (Bardin et al., 2011; Monti et al., 2010; Sorger et al., 2009; Sorger et al., 2012). Despite the benefits of fMRI-BCI for diagnostics and establishing short-term communication, fMRI is costly and tied to clinical or research institutions. LIS patients and their families are in need of BCI communication in everyday life. FNIRS is a functional neuroimaging method which relies on the same hemodynamic brain signal as fMRI (Cui et al., 2011; Huppert et al., 2006; Scarapicchia et al., 2017). While spatially less specific than fMRI, it opens the possibility to transfer the fMRI paradigms to the portable fNIRS technology when combined with necessary methodological advancements. FNIRS is relatively easy-to-apply, inexpensive, safe and portable (Irani et al., 2007; Scholkmann et al., 2014). These factors make it an ideal candidate for future daily application and might even hold the promise of operation of the system by family members.

This thesis aims to develop and validate straightforward, robust, efficient, and cost-effective fNIRS-based communication paradigms that can

be tailored to individual users and eventually be used in daily life. Successful fMRI paradigms will be transferred to the fNIRS technology, together with methodological developments. Steps will be taken towards an individualizable BCI through exploring different encoding paradigms and sensory encoding modalities. The focus lies on the development of paradigms that are perceived as pleasant and easy by the user. Given that technical and analytical complexity are a known hurdle to clinical use, answers will be decoded from subject-specific signals using readily available software and existing analysis pipelines. Methodological challenges of fNIRS – such as sufficiency of a single trial to decode an answer – will be explored.

Outline

In the current thesis, three fNIRS-based BCI studies are reported. All studies were performed on healthy participants to gauge the potential of the proposed BCI paradigms in terms of decoding accuracy and participant experience. All studies were performed with continuous wave spectroscopy hardware (NIRx Medical Technologies; RRID:SCR_002491). We consistently used a small number of optodes with future clinical applicability in mind. User preparation time was limited, typically in the order of 15 to 30 min. In all experiments mental imagery, often mental drawing (MD), was used for encoding answers. Existing fNIRS-data analysis software was used to decode answers. Analysis of signals from a single channel, *i.e.,* channel of interest (COI), or even chromophore, *i.e.,* signal of interest (SOI), are reported to gauge robustness and potentially allow for a further reduction of the number of optodes used in future studies. All results are reported for

single- and multi-trial[13] analyses. Across all three studies, the subjective experiences of participants were explored using questionnaires.

Following this introduction (**chapter 1**), in **chapter 2**, we explore an auditory yes/no communication paradigm in a controlled laboratory setting. Twenty participants were measured with fNIRS using nine optodes covering the left-hemispheric fronto-parietal cortex. Participants either performed mental drawing – for encoding "yes" – or did not change their mental state – for encoding "no". Participants' answers were decoded offline using univariate and multivariate statistics.

In **chapter 3**, the auditory yes/no paradigm is further developed by exploring the potential benefit of using an active mental task for each answer option. Eighteen participants were investigated using the same fNIRS setup, covering left-hemispheric fronto-parietal cortex. Two mental imagery tasks, *i.e.*, mental drawing for encoding "yes" and spatial navigation for encoding "no", were presented in distinct auditory cued time windows. This design enables the combination of both spatial and temporal fNIRS-signal features to encode an answer, which serves as an experimental safeguard. Although several studies showed spatial discernibility of mental tasks using fNIRS (Hong, Naseer, & Kim, 2015; Sitaram et al., 2007), this study is the first in using two different mental tasks for encoding two answer options in an fNIRS communication experiment. Data were analyzed post-hoc in simulated real-time to make realistic predictions for future online experiments. An in-house fNIRS suitability questionnaire, based on participants' physical features such as hair color, was explored for predicting general data quality.

[13] Multi-trial analysis is a joint analysis of several consecutive trials.

In **chapter 4**, the fNIRS-BCI is extended to a four-choice temporal-encoding paradigm. This constitutes a crucial advancement, as fNIRS-BCIs available at the time only enabled binary communication (Power, Kushki, & Chau, 2012; Weyand & Chau, 2015). Six participants were asked to perform mental imagery, *i.e.*, mental drawing, in one of four time windows. This design thus exploits the temporal specificity of the hemodynamic response. To add to the encoding flexibility, three sensory encoding modalities were tested. Participants were guided by either visual, auditory, or tactile instructions. This is the first fNIRS-BCI study to explore the tactile encoding modality. To ensure reliability over time, all six participants were asked an identical set of six autobiographical questions across three consecutive days. To check reliability across environments, two participants were tested outside the laboratory in a cafeteria. Answers from the four participants tested in the laboratory were decoded post hoc in simulated real-time. The answers of the two participants in the cafeteria were decoded online. The trade-off between number of optodes and decoding accuracy was investigated.

In **chapter 5**, the outcomes of the three empirical studies are reviewed and synthesized. Subsequently, the limitations of the presented studies and recommendations for future fNIRS-BCI studies are discussed.

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2 Yes or No? Binary Brain-based Communication utilizing Motor Imagery and fNIRS

Based on:

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Abstract

Past research into motor-independent communication for the severely disabled has mainly focused on developing brain-computer interfaces (BCIs) implementing neuroelectric signals. More recently, also hemodynamic brain signals have been explored for BCI purposes. Here, we introduce a novel, straightforward, and easy-to-implement yes/no communication paradigm relying on mental imagery (mental drawing) and portable functional near-infrared spectroscopy. To hemodynamically encode answers to binary questions, participants either performed mental drawing (for encoding "yes") or did not change their mental state (for encoding "no"). Participants' answers were decoded offline using univariate and multivariate statistics. In approximately half of the participants, accuracies reached 70 % or higher, which is considered a sufficient performance for binary communication BCIs. As the proposed communication technique requires relatively little cognitive capabilities, it might not only serve as a useful communication means but also as a diagnostic tool for detecting preserved conscious awareness in non-responsive patients.

Introduction

Communication is an essential element of human interaction. In the so-called 'locked-in' syndrome (LIS, Plum and Posner (1972)), fully aware and conscious patients have lost the ability to naturally communicate due to severe motor paralysis. To help affected patients in this fateful condition, motor-independent communication through brain-computer interfaces (BCIs) has been suggested (Wolpaw et al., 2000). BCIs rely on brain signals that an individual can intentionally generate to encode an intention (*e.g.*, to communicate a "yes" or a "no" answer). These brain signals are then measured with a functional neuroimaging method and finally decoded back into their originally intended meaning using signal-classification methods. In the field of BCI an accuracy of at least 70 % is considered sufficient for a two-class communication BCI (Kübler, Mushahwar, Hochberg, & Donoghue, 2006).

For almost 30 years now, BCI research has focused on developing communication BCIs using neuroelectric signals mainly based on noninvasive electroencephalography (EEG) (*e.g.*, Farwell and Donchin (1988); Leuthardt, Schalk, Wolpaw, Ojemann, and Moran (2004); Mellinger et al. (2007)). Though these 'classic' communication BCIs have been applied successfully in affected patients (*e.g.*, Birbaumer et al. (1999); Nijboer et al. (2008)), not all individuals achieve proficiency in EEG-based BCI control. A phenomenon referred to as 'BCI illiteracy' (Dickhaus, Sannelli, Müller, Curio, & Blankertz, 2009). Thus, there is an urgent need to explore further possibilities for brain-based communication.

Recently, hemodynamic brain signals as measured with functional magnetic resonance imaging (fMRI) (Bardin et al., 2011; Monti et al., 2010; Naci & Owen, 2013; Sorger et al., 2009) and functional near-infrared

spectroscopy (fNIRS) (Chaudhary, Xia, Silvoni, Cohen, & Birbaumer, 2017; Gallegos-Ayala et al., 2014; Naito et al., 2007) have been suggested and tested in this context. For example, our group has developed a letter speller based on differently timed mental-task performance and real-time fMRI that allows convenient back-and-forth communication of any word (Sorger, Reithler, Dahmen, & Goebel, 2012). The robust letter speller requires almost zero pre-training or preparation time and can be of great benefit for short-term communication. However, the fMRI-based BCI approach is costly and tied to clinical or research institutions making it unsuitable for everyday-life usage. A primary need of LIS patients and their families, however, is immediate access to and frequent use of BCI communication.

FNIRS is a functional neuroimaging method that relies on the same (hemodynamic, *i.e.*, vascular) brain response as fMRI (León-Carrión & León-Domínguez, 2012). While being spatially less specific than fMRI, fNIRS is relatively easy to apply, inexpensive, safe and, most importantly, portable (Scholkmann et al., 2014). These factors open the possibility to transfer the developed fMRI communication paradigms to the more compact and portable fNIRS technology, making fNIRS an ideal candidate for future daily-life application. Due to its straightforward implementation it could be readily handled maybe even by the patient's care givers.

Here, we suggest a novel, straightforward yes/no communication procedure employing mental imagery and fNIRS. In our suggested procedure, participants performed two localizer runs, one at the beginning of the experiment and one at the end. Each of these runs consisted of twenty 10 s periods of mental task performance that alternated with twenty-one 20 s baseline blocks, adding up to 10 min 20 s per run. Between localizer runs, six answer-encoding runs were performed, during which

participants were asked to answer biographical questions (e.g., “Do you live in Maastricht?”) by intentionally modulating their brain activation. For encoding “yes”, participants were asked to start mental drawing as soon as “yes” was aurally presented and to halt mental-task performance as soon as “stop” was presented. For encoding “no”, participants were asked to stay at rest for the whole length of the run. Each answer-encoding run consisted of five 10 s answer-encoding trials, alternated with six 20 s baseline periods, adding up to 2 min 50 s (see Figure 1). Participants’ brain responses were decoded offline.

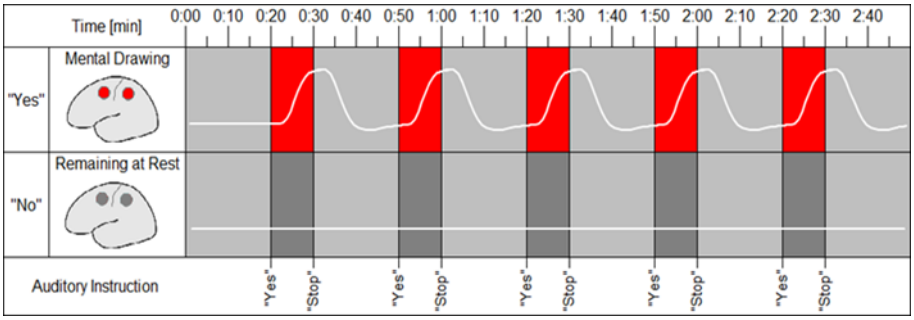

Figure 1. **Encoding Scheme for an Answer Run** including expected HbO changes (white curve/line) in motor imagery-related brain regions. When a participant wants to encode “yes”, he/she performs motor imagery causing hemoglobin to rise. When a participant wants to encode “no”, he/she stays at rest causing no relative change in hemoglobin. Note that participants encoded the same answer five times (five trials) in one run.

Materials and Methods

Participants

Twenty healthy subjects (nine female, three left-handed, age = 26.0± 8.0 years [mean ± SD], all with normal or corrected-to-normal vision and reportedly normal hearing) participated in the study. Table 1 documents individual participants’ characteristics. All participants gave written

informed consent according to procedures approved by the local ethics committee and received financial compensation.

Mental Drawing Paradigm

To intentionally evoke fNIRS signals, participants were instructed to: "Imagine drawing simple geometric figures (such as circles, triangles, cubes, etc.) or small contour drawings (e.g., a butterfly, star, car, tree, boat, or house) with the right hand at a comfortable but consistent speed. Imagine using a pen. This might support your imagination." Participant preparation: Prior to the experiment, participants were familiarized with the general procedure of the study. They shortly practiced mental drawing and answer encoding until they felt comfortable (ca. 15 min). Moreover, a list of 45 binary biographical questions, simple yet unobtrusive enquiries about their lives, was provided. Six of those questions were selected by an independent experimenter: three to be answered with "yes" and "no", to assure equal distribution of answer options. After placement of the cap with the fNIRS optodes, participants were seated comfortably in a noise-dimmed cabin, which was equipped with a loudspeaker and microphone to enable verbal communication between participant and experimenter during the experiment.

Data Acquisition

Self-induced hemodynamic brain signals were obtained using a NIRScout-816 system (NIRx Medizintechnik GmbH, Berlin, Germany) equipped with six detector and three source optodes (LEDs emitting wavelengths of both 760 nm and 850 nm). Sources were positioned according to the international 10-20 EEG system on FC3 (1), C3 (2) and CP3 (3) and detectors were positioned on FC5 (1), C5 (2), CP5 (3), FC1 (4), C1 (5) and CP1 (6). This

limited number of optodes was chosen to ensure clinical applicability (*i.e.*, reasonable optode-placement time allowing for rapid bedside measurements of patients). Recorded optical signals were sampled at a rate of 12.5 Hz. Due to the limited number of sources and detectors, the optodes' montage covered a confined area above the left-hemispheric fronto-parietal (sensorimotor) cortex (see Figure 2). Auditory stimuli were presented using in-house stimulation software (Gijsen, 2015).

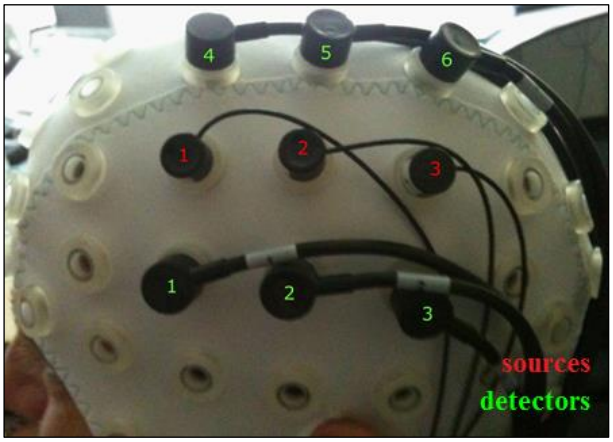

Figure 2. **FNIRS Optode Set-up** with the three source optodes in red (optodes 1, 2 and 3 in the middle horizontal line) and the six detector optodes in green (optodes 1, 2 and 3 in the lower horizontal line and optodes 4, 5 and 6 in the higher horizontal line).

Subjective Ratings

After each run, participants rated the experienced fNIRS comfortability according to a Likert-scale ranging from 0 (extremely uncomfortable) to 10 (extremely comfortable). We predicted that comfortability ratings would decrease over time. After completion of the experiment, the participants rated the general easiness and pleasantness of the employed mental-

imagery paradigm (mental drawing) again using a Likert-scale ranging from 0 (extremely difficult/unpleasant) to 10 (extremely easy/pleasant).

Data Analysis

FNIRS time series were analyzed using Satori (v0.92, Brain Innovation B.V., Maastricht, The Netherlands). During preprocessing, raw data time course values were converted to oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) values. Linear trend removal, temporal lowpass filtering (Gaussian full width at half maximum [FWHM]: 40 data points) and high-pass filtering (cutoff: 10 cycles [localizer runs] or 2 cycles [answer encoding runs] per time course) were applied. These filtering parameters correspond approximately to a band-pass filter of 0.1-0.016 Hz for the localizer runs and 0.1-0.012 Hz for the encoding runs. The subsequent data analysis was focused on the 14 'direct-neighbor' channels (*i.e.*, channels emerging from sources-detector combinations of close proximity; see Figure 3). Two types of analyses were conducted: univariate general linear model (GLM) analysis and multi-channel pattern (MCP) analysis.

GLM Analysis

First, a single channel of interest (COI) was determined individually for each participant using the data of the first localizer run. For this purpose, channel-wise (whole-run) GLM analysis was performed separately for HbO and HbR time series using a predictor corresponding to the motor imagery condition and applying the statistical contrast "motor imagery vs. resting". For selecting the COI we calculated a criterion value by averaging the obtained HbO and HbR t-values per channel. The channel with the highest criterion value was considered the COI and selected for further analysis. As a next step, the data of the first "yes" and "no" answer-encoding run per

participant was analyzed as follows: For each of the ten trials (five “yes” and five “no” trials) the individual criterion value was calculated. Then, a mean across these ten individual criterion values was computed. This average value was used as ‘cut-off’ value for decoding the answers of the remaining four answer-encoding runs. Values above or below the cut-off value resulted in decoding the answer-encoding data as “yes” or “no”, respectively. Encoded answers were compared post hoc to the actually intended answers given by the participant. Next to individual and group-mean single-trial (ST) accuracies, we computed multi-trial (MT) accuracies for each individual and for the group. Multi-trial accuracies were derived by integrating the five separate yes/no decisions per run using majority voting (*e.g.*, three answers encoded as “yes” and two answers encoded as “no” were considered as a “yes” answer). Resulting single-trial accuracies were evaluated in a confusion matrix per participant using a Chi square test to assess if decoding accuracies were significantly above chance level ($p < 0.05$).

MCP Analysis

MCP analysis was conducted using a support vector-machine as classifier (Chang & Lin, 2001). For this analysis, all channels (n = 14) were used to define the spatial features for the MCP analysis. In order to ‘train’ (and ‘test’) the classifier, means of raw values for HbO and HbR were estimated in a time window from 6 s to 17 s after trial onset of the mental drawing trials. This window was defined for the mental drawing trials as it corresponds to the time points where the mean hemodynamic response was expected to be the highest. For the rest conditions an 11 s time window was chosen from 11 s to 22 s after trial onset of the rest conditions, during which the mean hemodynamic response is expected to be at

baseline. The single-trial data of the two localizer runs served as training data. Analysis of the six answer-decoding runs resulted in five single-trial predictions (corresponding to the five separate answer-encoding trials) per run. As in the GLM approach, each prediction was compared to the actual answer given by the participant. Again, mean single- and multi-trial accuracies were calculated individually and for the group as described above for the GLM approach. Resulting single-trial accuracies were tested for significance ($p < 0.05$) using permutation tests (10.000 permutations). For both the GLM and MCP analysis, the average sensitivity – P(yes decoded | yes encoded) – and specificity – P(no decoded | no encoded) – was calculated. Correlations were run between the single-trial and multi-trial accuracies of both approaches. Means and SEs were calculated with the subjective ratings.

Results

GLM Analysis

For each subject, a COI could be selected based on the procedure described above (see Table 1 for selected channels and individual criterion values). Figure 3 illustrates how often each channel was selected across participants. Using the GLM approach, participants' answers could be decoded correctly with an average accuracy of 64.25 % on a single-trial basis (theoretical chance level being 50 %). Individual single-trial accuracies varied from 35.00 - 95.00 % (see Table 1). In eight participants, single-trial accuracies were significantly above chance level as assessed with a Chi-Square test (see Table 1). The classifier showed no bias, as "yes" and "no" answers were decoded respectively on 50.25 % and 49.75 % of the 400 trials. The average sensitivity was 65.00 % and the average specificity was

65.50 %. On a group level, the multi-trial accuracy was 65.00 %. Individual multi-trial accuracies varied from 25.00-100.00 % (see Table 1). For the group of nine subjects with individual single-trial accuracies of 70 % or higher, the average single-trial accuracy was 79.44 % (SE = 2.82), whereas their average multi-trial accuracy was 84.09 % (SE = 4.20). For the eleven other subjects, the average single-trial accuracy was 51.82 % (SE = 2.88), whereas their average multi-trial accuracy was 47.73 % (SE = 5.28).

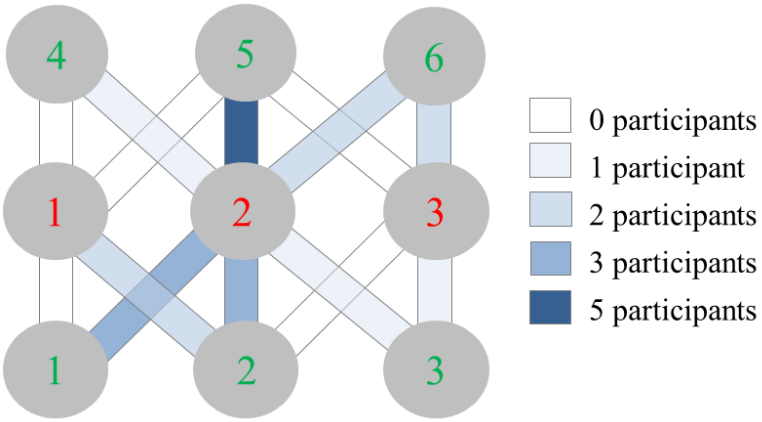

Figure 3. **Frequency of Best Channel Selection within the GLM Approach.** The red and green numbers indicate source and detector optodes, respectively. Note that the most frequently selected channels correspond to brain areas commonly associated with motor imagery (Koessler et al., 2009).

MCP Analysis

Using the multi-variate approach, participants' answers could be decoded correctly from single trials with an average accuracy of 62.33 %. Individual single-trial accuracies ranged from 33.33 % to 76.67 %. In eleven subjects, single-trial decoding accuracies were significantly above chance level as revealed by permutation tests (Table 1). "Yes" and "no" answers were decoded respectively on 62.00 % and 38.00 % of the 600 trials. The

sensitivity was 75.67 % and the specificity was 51.67 %. The multi-trial accuracy was 63.33 % on the group level and individual multi-trial accuracies ranged from 33.33 % to 100.00 %. When focusing the analysis on the ten subjects with single-trial accuracies of 70 % or above, the single-trial accuracy was 72.33 % (SE = 0.87), whereas the multi-trial accuracy was 85.71 % (SE = 2.38). For the group of ten subjects with individual single-trial accuracies below 70 %, the average single-trial accuracy was 52.33 % (SE = 3.06), whereas their average multi-trial accuracy was 59.09 % (SE = 7.22).

Table 1: **Participant Characteristics, Subjective Rating, Channel Selection and Classification Results.**

			MD SR				GLM accuracies		MCP accuracies	
P	H	S	E	P	COI	Crit.	ST (%)	MT (%)	ST (%)	MT (%)
1	R	M	8	7	2-4	16.69	75.00°	75.00	53.33*	66.67
2	R	F	9	8	2-5	5.28	55.00	50.00	33.33	33.33
3	R	F	10	10	3-3	101.44	70.00	75.00	70.00*	66.67
4	R	M	9	8	2-5	313.42	95.00°	100.00	76.67*	83.33
5	R	F	8	7	1-2	291.52	75.00°	75.00	70.00*	66.67
6	L	M	4	6	2-1	44.25	60.00	75.00	56.67	50.00
7	R	F	9	9	2-2	90.16	60.00	50.00	73.33*	100.00
8	R	M	7	6	3-6	71.26	45.00	50.00	53.33	50.00
9	R	M	7	7	2-1	177.18	70.00	75.00	76.67*	83.33
10	R	F	8	9	2-5	90.60	40.00	25.00	70.00*	66.67
11	R	F	6.5	6	2-3	73.27	60.00	50.00	66.67	66.67
12	R	F	7.5	5	1-2	26.03	45.00	25.00	63.33	83.33
13	R	M	6	4	2-6	2.59	85.00°	100.00	43.33	33.33
14	R	F	9	8	2-5	85.33	55.00°	75.00	70.00*	66.67
15	R	M	10	8	2-2	44.18	75.00°	100.00	73.33*	83.33
16	R	M	8	6	2-2	49.52	85.00°	100.00	73.33*	83.33
17	R	M	9	8	3-6	35.18	65.00	50.00	56.67	83.33
18	L	M	8	8	2-6	24.08	35.00	25.00	46.67	16.67
19	L	M	8	7	2-5	114.92	50.00	50.00	50.00	33.33
20	R	F	8	7	2-1	58.75	85.00°	75.00	70.00*	50.00
Mean			7.92	7.20			64.25	65.00	62.33	63.33
SE			.07	.07			3.72	5.56	2.77	4.93

Notes. P = participant, H = handedness, R = right, L = left, S = sex, M = male, F = female, MD SR = mental drawing subjective rating, E = average easiness rating across runs, P = average pleasantness rating across runs, COI = channel of interest, Crit. = Criterion, ST = single trial, MT = multi-trial, ° $p < .05$ based on Chi-Square, * $p < .05$ based on permutation testing.

Subjective Ratings

FNIRS comfortability ratings were medium to high (see group means in Figure 4). Comfortability decreased across time and dropped considerably for the last run (second localizer). Participants generally experienced the mental drawing task as pleasant (M = 7.2, SE = .07) and easy to perform (M = 8.0, SE = .07).

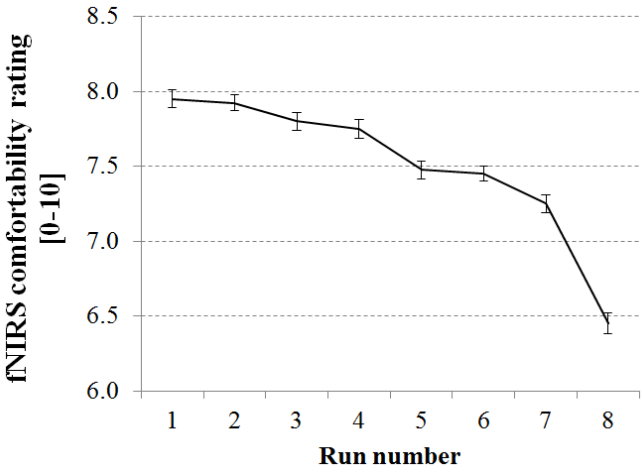

Figure 4. **FNIRS comfortability ratings** (group means and SEs) across runs. Values range from 0 (extremely uncomfortable) to 10 (extremely comfortable). Note that the first and eighth run were localizer runs.

Accuracy Correlations

Correlations between the accuracies of the different approaches were all insignificant ($p > .05$): GLM MT and MCP MT ($r = .21$); GLM ST and MCP ST ($r = .36$).

Discussion

A novel yes/no communication paradigm using mental drawing and fNIRS was tested in healthy participants. In LIS patients an fNIRS-based binary BCI has been tested recently (Chaudhary et al., 2017; Gallegos-Ayala et al.,

2014). However, in those studies a classifier was trained for several sessions over several days. The current approach has the potential of enabling immediate communication in the order of ca. 30 min (±15 min training; ±10 min localizer, ±6 min encoding). Of course, this should be tested using real-time decoding and in affected patients. We deem this will be successful as Naito et al. (2007) found an accuracy rate above 75 % in 23 out of 40 LIS patients with their fNIRS-based binary BCI using mental calculation/singing. Our results indicate that it is possible to obtain sufficiently high, *i.e.*, ≥ 70 % (Kübler et al., 2006), and reliable answer-decoding accuracies in healthy subjects by using the current paradigm and various data analysis methods. On average, multi-trial accuracies were only marginally higher than single-trial accuracies. However, when focusing on participants reaching an accuracy of 70 % or higher, there is a trend for multi-trial accuracies to be higher than single-trial accuracies in both GLM and MCP analysis. Closer inspection of these participants' data indicated relatively prominent hemodynamic responses, suggesting that the multi-trial approach is most advantageous when single-trial measurements have a sufficiently high signal-to-noise ratio.

The GLM approach might be particularly suited in the context of a communication BCI due to its simplicity. We expect that at least some LIS patients are also able to use the binary BCI presented here, as accuracies of 70 % or higher were reached by approximately half the participants after a mere 15 min of training. Since our communication BCI relies on only a single fNIRS channel, preparation time can in principle (when having determined the COI in a previous fNIRS session) be rather short. The similar sensitivity (65.00 %) and specificity (65.50 %) emphasizes that there is no bias to either "yes" or "no". The MCP approach might be especially useful in the context

of detection of remaining consciousness in non-responsive patients because in contrast to the GLM approach, it does not require the calculation of a yes/no cut-off value. Nevertheless a localizer containing differential activity (mental imagery vs. rest) is still required to train the classifier, which might not be easily obtained in this patient group. Encouraging is the high specificity (75.67 %) of this approach. In three of the four cases in which participants intentionally changed their brain states, this change was detected.

The two data analysis approaches differ in the number of subjects reaching a level of significance (8 in the GLM vs. 11 for the MCP approach; see Table 1). In addition, GLM analysis accuracies do not correlate significantly with any of the MCP analysis accuracies. However, comparison of the two methods is hampered by several fundamental differences: (1) In the GLM analysis, the data from only one channel was considered, whereas all channels are considered in the MCP analysis. (2) In the MCP analysis, more single-trials could be considered, resulting in a higher chance of getting significant results. (3) Due to the fundamentally different nature of both approaches, different significance tests were employed (Chi-square vs. permutation testing).

A general shortcoming of our study, affecting both the GLM and MCP analysis accuracies, is the absence of localizer data for the “no” condition. As there was no separate localizer to identify signal characteristics while participants did not change their brain state, the training data for encoding “no” answers was selected as the time window in the end of the resting period after each task performance. Obtaining proper localizer data for the “no” condition should be done it future experiments, albeit this would be at the cost of additional measurement time.

We noted large differences between individual participants' classification accuracies: some participants performed exceptionally well whereas for others classification accuracy was at chance level. Blood pressure, respiration and heart rate are known to influence the fNIRS signal (Bauernfeind, Wriessnegger, Daly, & Müller-Putz, 2014). Future studies taking into account these physiological measures may filter out such influences in order to improve the contrast-to-noise ratio of the fNIRS measurements. Moreover, given the very short training period, participants with chance level performance may be retested after providing them with additional training.

We monitored comfortability over time and measured perceived easiness and pleasantness, as it is known that subjective motivation can influence BCI performance (Kleih, Nijboer, Halder, & Kübler, 2010; Nijboer, Birbaumer, & Kubler, 2010). Comfortability ratings across the experimental session decreased slightly with a drop in the last run. This could be due to the fact that performing a localizer run after the answer-encoding runs was experienced as comparatively boring. Overall, application of our BCI in affected patients is encouraged by the fact that our participants gave overall positive easiness and pleasantness ratings.

Conclusion

The presented yes/no communication procedure using fNIRS and mental imagery might constitute a useful communication means for LIS patients. Moreover, as the suggested encoding paradigm requires relatively little effort from individuals, it has potential as a diagnostic means to detect preserved conscious awareness in non-responsive patients.

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3 Brain-Based Binary Communication using Spatiotemporal Features of fNIRS Responses

Based on:

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Abstract

'Locked-in' patients lose their ability to communicate naturally due to motor system dysfunction. Brain-computer interfacing offers a solution for their inability to communicate by enabling motor-independent communication. Straightforward and convenient in-session communication is essential in clinical environments. The present study introduces a functional near-infrared spectroscopy (fNIRS)-based binary communication paradigm that requires limited preparation time and merely nine optodes. Eighteen healthy participants performed two mental imagery tasks, mental drawing and spatial navigation, to answer yes/no questions during one of two auditorily cued time windows. Each of the six questions was answered five times, resulting in five trials per answer. This communication paradigm thus combines both spatial (two different mental imagery tasks, here mental drawing for "yes" and spatial navigation for "no") and temporal (distinct time windows for encoding a "yes" and "no" answer) fNIRS signal features for information encoding. Participants' answers were decoded in simulated real-time using general linear model analysis. Joint analysis of all five encoding trials resulted in an average accuracy of 66.67 % and 58.33 % using the oxygenated (HbO) and deoxygenated (HbR) hemoglobin signal respectively. For half of the participants, an accuracy of 83.33 % or higher was reached using either the HbO signal or the HbR signal. For four participants, effective communication with 100 % accuracy was achieved using either the HbO or HbR signal. An explorative analysis investigated the differentiability of the two mental tasks based solely on spatial fNIRS signal features. Using multivariate pattern analysis (MVPA) group single-trial accuracies of 58.33 % (using 20 training trials per task) and 60.56 % (using 40 training trials per task) could be obtained. Combining the five trials per

run using a majority voting approach heightened these MVPA accuracies to 60.56 % and 75 %. Additionally, an fNIRS suitability questionnaire capturing participants' physical features was administered to explore its predictive value for evaluating general data quality. Obtained questionnaire scores correlated significantly (r = -.499) with the signal-to-noise ratio of the raw light intensities. While more work is needed to further increase decoding accuracy, this study shows the potential of answer encoding using spatiotemporal fNIRS signal features or spatial fNIRS signal features only.

Keywords

Functional Near Infrared Spectroscopy (fNIRS), Brain Computer Interface, Mental Imagery, Mental Drawing, Motor Imagery, Spatial Navigation, Binary Communication, Yes/no Decoding.

Introduction

Active human communication depends fully on the functional integrity of the motor system. When the motor system ceases to function, *e.g.*, due to neuromuscular impairments, consequences can be detrimental for communication. Severe motor paralysis most often occurs through infarction of the pons (Patterson & Grabois, 1986) or in late stages of diseases such as amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS). In some cases this leads to a state of being fully awake and aware (Laureys, 2005; Monti, Coleman, & Owen, 2009) but without any ability to communicate in a natural way, commonly referred to as the 'locked-in' syndrome (LIS; see Laureys (2005); Monti et al. (2009); Plum and Posner (1982)). In 'classical' LIS, vertical eye movements and eye blinking are spared and can thus be used for basic communication. Nevertheless, in progressive motor-neuron disorders such as ALS, control of the eye muscles is lost in late stages of the disease, resulting in a 'complete' or 'total' LIS (Bauer, Gerstenbrand, & Rumpl, 1979).

In LIS patients, voluntarily evoked brain signals can be exploited to restore basic communication independent of motor function. This can be achieved through a brain-computer interface (BCI), which relies on intentionally generated brain signals that are measured with a functional neuroimaging method, *e.g.*, electroencephalography (EEG; Farwell and Donchin (1988); Leuthardt, Schalk, Wolpaw, Ojemann, and Moran (2004)), magnetoencephalography (MEG; Mellinger et al. (2007); Reichert, Dürschmid, Heinze, and Hinrichs (2017)) or functional magnetic resonance imaging (fMRI; Bardin et al. (2011); Monti et al. (2010); Naci and Owen (2013); Sorger et al. (2009); Sorger, Reithler, Dahmen, and Goebel (2012)). A BCI then processes these inputs such that they can be used for motor

control, communication, neurofeedback, *etc*.

EEG is the most widely used neuroimaging method for BCI purposes. Encouraging communication results have been reported using EEG-based BCIs (Birbaumer et al., 1999; Farwell & Donchin, 1988; Leuthardt et al., 2004; Nijboer et al., 2008). Recent binary communication paradigms established accuracies consistently above 70 % (Halder et al., 2010; Käthner, Kübler, & Halder, 2015), even reaching an accuracy of 87.5 % in one patient (Han et al., 2019). EEG-based BCIs have been mainly tested with visual paradigms using event-related potentials that, at least partly, depend on patients ability to fixate (Brunner et al., 2010; Treder & Blankertz, 2010). However, the population of LIS patients is heterogeneous, with varying degrees of visual impairment/oculomotor control (Riccio, Mattia, Simione, Belardinelli, & Cincotti, 2012), cognitive impairment (Schnakers et al., 2008; Wilson, Hinchcliffe, Okines, Florschutz, & Fish, 2011) and brain areas affected. Given this patient heterogeneity, a wide range of neuroimaging methods should be explored as each has its limitations. In a recent hybrid EEG-fNIRS study (Rezazadeh Sereshkeh, Yousefi, Wong, Rudzicz, & Chau, 2019) it was found that the EEG signal was detrimental in most healthy participants. Nevertheless, certain participants truly benefited from use of the fNIRS signal. The high spatial resolution of hemodynamic neuroimaging, such as fMRI and fNIRS, combined with the – typically used – auditorily guided imagery paradigms might be beneficial for certain BCI users.

A seminal fMRI paradigm (Monti et al., 2010) enabled binary communication in disorders of consciousness patients through the use of tennis imagery for encoding a “yes” response and spatial navigation imagery for a “no” response. In the 16 healthy control subjects, a decoding accuracy of 100 % was obtained. Work from our lab has extended this type

of paradigm to a four-choice BCI (Sorger et al., 2009), with an average accuracy of 94.9 % (theoretical chance level being 25 %), and a free-letter spelling BCI (Sorger et al., 2012), with an average accuracy of 82 % (theoretical chance level: ca. 3.7 %), successfully tested in healthy participants. Given the immobility of fMRI hardware, the current challenge is to transfer these fMRI-based paradigms to a mobile setup employing functional near-infrared spectroscopy (fNIRS), thereby enabling convenient BCI-based communication of patients in daily-life settings, *e.g.*, in their home environments.

The use of fNIRS as a method to measure brain signals is gaining popularity, with the number of publications increasing rapidly (Boas, Elwell, Ferrari, & Taga, 2014) since its first use in 1993 (Chance, Zhuang, UnAh, Alter, & Lipton, 1993; Hoshi & Tamura, 1993; Kato, Kamei, Takashima, & Ozaki, 1993; Villringer, Planck, Hock, Schleinkofer, & Dirnagl, 1993). The mobility of fNIRS hardware makes it highly suited for bedside testing (Cutini, Moro, & Bisconti, 2012; León-Carrión & León-Domínguez, 2012), hence its growing use in brain-computer interfacing (Zephaniah & Kim, 2014). However note that its mobility comes at the cost of a generally lower accuracy compared to fMRI-based paradigms. The reason for these relatively lower classification accuracies in fNIRS-based paradigms is threefold: (1) fNIRS possesses an inherently lower spatial resolution than fMRI (2) fNIRS has a limited spatial coverage and is thus only able to sample superficial regions of the cortex (3) fMRI has a higher SNR than fNIRS (Cui, Bray, Bryant, Glover, & Reiss, 2011), as fNIRS suffers from global/physiological noise from extracranial tissue (Zhang, Noah, & Hirsch, 2016).

In the context of communication, most hemodynamic BCI systems

rely on mental imagery for intentional generation of brain signals. Commonly used mental imagery tasks (see Naseer and Hong (2015) for a more extensive review) include mental speech (Rezazadeh Sereshkeh, Yousefi, Wong, & Chau, 2018; Sorger et al., 2012), mental calculation/counting (Naito et al., 2007; Power, Kushki, & Chau, 2012; Sorger et al., 2009; Sorger et al., 2012) and motor imagery (Abdalmalak, Milej, Diop, et al., 2017; Coyle, Ward, & Markham, 2007; Monti et al., 2010; Sorger et al., 2009; Sorger et al., 2012). Most fNIRS based-BCI communication studies focus on binary communication, as multi-class fNIRS-based BCIs are not yet enabling effective BCI control (Power et al., 2012; Weyand & Chau, 2015).

In most binary fNIRS-communication paradigms, a "yes" answer is encoded through mental imagery, whereas a "no" answer is encoded by rest (Abdalmalak, Milej, Norton, et al., 2017; Nagels-Coune et al., 2017; Naito et al., 2007; Naseer, Hong, & Hong, 2014). In healthy subjects, group average accuracies range between 62 % and 82 % (Nagels-Coune et al., 2017; Naseer et al., 2014). In a subset of 23 out of 40 patients, an average accuracy above 75 % was found using tasks activating prefrontal cortex such as mental calculation or mental singing (Naito et al., 2007). Recently Abdalmalak, Milej, Norton, et al. (2017) asked a LIS patient to imagine playing tennis for encoding a "yes", while resting to encode a "no". An accuracy of 100 % was reached over five repetitions of three questions. The drawback from previously mentioned studies is that one cannot distinguish a real "no" answer from possible disengagement from the task. This problem can be circumvented through the use of a different, active mental task for each answer option. The evoked spatially different brain-activation patterns can then be exploited for encoding two answer alternatives.

Several studies have demonstrated the potential of spatial discernibility of mental tasks using fNIRS. For example, Sitaram et al. (2007) were able to distinguish left- from right- hand motor imagery with an accuracy of 73 % using a support vector machine (SVM) classification. Furthermore, Hong, Naseer, and Kim (2015) could distinguish mental calculation, right- and left-hand imagery with an accuracy of 75.6 % using 3-class linear discriminant analysis (LDA). However, to our knowledge, no study has tested the use of two mental tasks directly in a communication experiment. In a recent study, participants imagined different mental speech content for answering yes/no questions intuitively, *i.e.*, imagining saying "yes" or "no" repeatedly (Rezazadeh Sereshkeh et al., 2018). An average accuracy of 64.1 % was attained over two experimental sessions. Note, however, that only a 3-class ("yes", "no" & "rest") accuracy was reported, thus the 2-class accuracy ("yes" vs "no") cannot be inferred from the report.

The current study aimed to increase the feasibility and success of an fNIRS-BCI in healthy participants, thereby potentially increasing the applicability in LIS patients. We used an approach that combines temporal encoding (distinct time windows for encoding "yes" and "no") with spatial encoding (two channels, each coding for a distinct mental imagery task, here motor imagery for "yes" and spatial navigation for "no"), as has been done in Sorger et al. (2009) and Sorger et al. (2012) in fMRI-based communication BCIs. In mental drawing trials, participants were asked to imagine drawing small geometric shapes with their right hand. In spatial navigation trials, participants imagined walking through their home and visualized the visual scene in different rooms. Similar tasks were previously used in the seminal fMRI work of Monti et al. (2010) and have been suggested to be explored in the context of fNIRS-BCI (Abdalmalak, Milej,

Diop, et al., 2017). We expected motor cortex activation during motor imagery (Sitaram et al., 2007), and parietal activation during spatial navigation imagery (Abdalmalak, Milej, Diop, et al., 2017; Cabrera & Dremstrup, 2008; McKendrick et al., 2016). To increase general fNIRS-BCI feasibility by decreasing setup time, we opted for a sparse fNIRS optode setup with nine optodes covering large parts of left-hemispheric fronto-parietal cortex.

The current study included 18 healthy participants who were briefly trained prior to undergoing the fNIRS recording session. Participants were asked six binary questions (*e.g.*, "Do you have a driver's license?") which they answered by performing one of the two tasks in auditorily cued time windows. Conventional univariate analyses were employed in simulated real-time to decode the participants' answers from the recorded fNIRS data. Additionally, a multivariate approach was applied to explore the discernibility of the two tasks based on their spatial brain activation patterns only. Comfort ratings were obtained throughout the experiment as other studies have reported that participants may withdraw from fNIRS recordings due to headset discomfort (Cui et al., 2011; Rezazadeh Sereshkeh et al., 2018; Suzuki, Harashima, & Furuta, 2010). In addition, we evaluated whether the presence of specific physical features of participants (*e.g.*, hair thickness, root density or color) affected fNIRS-signal quality and subsequent decoding results (Coyle, Markham, & Ward, 2005; Cui et al., 2011; Fang, Pan, Liu, Wang, & Li, 2018; Khan et al., 2012; Koizumi et al., 1999). To this end, an in-house questionnaire was administered. Moreover, participants' experience with the mental tasks in terms of ease and pleasantness were assessed, since they are known to positively correlate with decoding accuracy (Weyand & Chau, 2015).

In summary, due to the unique combination of temporal and spatial encoding of mental tasks, and the use of an active mental task for each answer option, we expected that our paradigm would outperform the standard paradigms reviewed here.

Material and Methods

Participants

The current dataset was collected in the same session as the data published in a previous study by Nagels-Coune et al. (2017). Eighteen of the twenty participants performed the present paradigm in addition to the previously reported paradigm. The localizer runs (block 1 and block 2) have already been used in the context of the earlier study (Nagels-Coune et al., 2017). All eighteen healthy participants (eight females, age = 26.00 ± 8.19 years [mean ± SD]) reported normal hearing. The participants' characteristics of relevance to the fNIRS measurements are shown in Table 1. Written informed consent was acquired from each participant before the experiment. The experimental procedure conformed to the Declaration of Helsinki and was approved by the local ethics committee. All participants were compensated with a gift voucher for their participation.

Participant Preparation

Introducing the Two Mental Tasks

Following the informed consent procedure, participants were introduced to two mental imagery tasks. For the mental drawing (MD) task, participants were instructed to imagine drawing simple geometric shapes with their right hand. The three left-handed participants were thus requested to imagine drawing with their non-dominant hand. For the spatial navigation

(SN) task, participants imagined walking through their house while vividly visualizing the visual scene of each room (see Supplementary Material for the standardized mental task instructions). Participants chose objects they would like to imagine drawing and a familiar environment they would like to imagine navigating through.

Table 1. **Participant Characteristics and Signal-of-Interest**

P	H	Cap Size	fSS	Mental Drawing SOI		Spatial Navigation SOI	
				HbO	HbR	HbO	HbR
01	Right	56	12	CP3-CP5	CP3-CP5	FC3-FC1	CP3-CP5
02	Right	56	14	FC3-FC1	C3-C1	C3-FC5	FC3-FC5
03	Right	56	13	FC3-FC5	CP3-CP5	CP3-CP5	FC3-C5
04	Right	56	10	C3-FC5	FC3-C5	FC3-C5	FC3-C5
05	Left	56	10	C3-FC5	FC3-FC1	CP3-CP5	CP3-CP5
06	Right	56	16	CP3-C5	C3-C5	CP3-C5	CP3-C5
07	Right	56	14	FC3-FC5	FC3-FC5	FC3-FC5	FC3-FC5
08	Right	56	1	C3-FC5	C3-FC5	FC3-C1	C3-FC1
09	Right	56	13	C3-CP5	CP3-CP1	C3-FC5	CP3-C1
10	Right	56	14	C3-C5	C3-CP5	FC3-FC1	FC3-FC1
11	Right	56	10	FC3-C5	CP3-CP1	CP3-CP5	C3-C1
12	Right	58	17	FC3-FC5	FC3-FC5	FC3-FC5	FC3-FC1
13	Right	56	13	C3-C1	C3-C1	FC3-FC5	FC3-FC5
14	Right	58	14	CP3-CP1	C3-C5	C3-C5	C3-C5
15	Right	60	17	C3-C5	C3-C5	FC3-FC5	C3-C1
16	Right	56	10	CP3-CP1	C3-C5	FC3-FC5	C3-C1
17	Left	56	13	FC3-FC5	CP3-CP5	FC3-FC1	FC3-FC1
18	Left	56	13	C3-CP1	C3-C1	FC3-C5	FC3-C5

Notes. P = participant, H = handedness, cap size (in cm) and fSS = fNIRS suitability score (max score = 21). The last four columns show the signals-of-interest (SOIs), selected on the basis of the data of localizer runs in block 1. Abbreviations: HbO, oxygenated hemoglobin; HbR, deoxygenated hemoglobin.

Selection of Binary Questions

Prior to the experiment, participants answered 45 unobtrusive binary questions (see Supplementary Material), *e.g.*, "Do you have a driver's license?" in a questionnaire. Six questions, three answered with "yes" and three answered with "no", were selected for the main fNIRS experiment to ensure an equal distribution of both answers.

fNIRS Suitability Questionnaire

Due to fNIRS being an optical neuroimaging method, participants' physical features may alter the penetration/absorption of light and consequently signal strength (Coyle et al., 2005). To evaluate whether this influenced our results, we created an in-house questionnaire that quantifies participants' suitability for fNIRS measurements. The questionnaire (see Supplementary Material) captured the following physical features that are thought to influence fNIRS signal strength via distortion of optical contact between the skin and optodes (distortion skin-optode contact) or via light absorption: hair length (distortion skin-optode contact), hair color (light absorption; Coyle et al. (2005); Khan et al. (2012); Koizumi et al. (1999); Lloyd-Fox, Blasi, and Elwell (2010)), hair thickness (light absorption affected by hair follicle density; Coyle et al. (2005); Fang et al. (2018)), hair density (distortion skin-optode contact; Lloyd-Fox et al. (2010); Orihuela-Espina, Leff, James, Darzi, and Yang (2010)), hair structure (distortion skin-optode contact; Lloyd-Fox et al. (2010)); skin color (light absorption by melanin concentration; Orihuela-Espina et al. (2010)), and head size (light absorption affected by altered inter-optode distance). Each feature was rated on a scale ranging from 0 (desirable feature) to a maximum of 4 (undesirable feature). Scores were summed with a maximum score of 21. The higher the suitability score, the less suitable for fNIRS measurement the participant was deemed.

Cap Placement and Mental Task Training

Participants' head circumference was measured and an appropriately sized cap was selected. Cap sizes used in this experiment ranged from 54 to 60 cm (see Table 1). Prior to placing the cap, participants were asked to moisten the left side of the head to aid the placement of the optodes. Similar to EEG cap placement, nasion-inion distance was measured to

ensure proper cap positioning. Participants were then seated in a sound-attenuating cabin, which was kept entirely dark during the fNIRS measurement as ambient light can influence near-infrared spectroscopy measurements (Kovalenko, Roskosky, & Freedman, 2014; Pinti et al., 2018). While the optodes were placed in optode holders, participants were given the opportunity to practice the two mental tasks. This procedure took on average 17 min (standard deviation: ± 8 min).

fNIRS-based Communication Paradigm

We employed an auditorily cued encoding paradigm in which fNIRS signals were evoked through differently timed (temporal encoding) mental imagery tasks (spatial encoding). The auditory cues, *i.e.,* concise spoken commands, guided participants' mental imagery by indicating the start and end of each encoding window. The cues and their accompanying time point triggers were presented using an in-house software (StimulGL; Gijsen (2015)). Our design encompassed two localizer runs (block 1), six encoding runs, and finally another two localizer runs (block 2).

Localizer Block 1

In the two localizer runs, participants performed the two tasks in a fixed order, with the MD run preceding the SN run. These localizer runs were conducted to gauge participant's hemodynamic responses to the mental tasks and select task-sensitive channels for answer decoding. In the first localizer run, participants performed 20 MD trials with a duration of 10 s each, interleaved with 20 s rest periods. The localizer started with an initial rest period of 20 s, after which the participants heard the auditory cue "start". This cue marked the start of the MD task, by which participants were instructed to perform the mental imagery task until they heard the

cue “rest”. They then halted the mental imagery and remained at rest for 20 s, until the next “start” cue urged them to commence the mental imagery again. This procedure was repeated 20 times, resulting in 20 MD trials. The second localizer followed the same protocol.

Six Answer Encoding Runs

In this stage of the experiment, participants were asked to answer binary questions by performing one of two mental tasks in a particular time window. Participants were informed that to encode a “yes” answer, they had to perform MD imagery when they heard “yes”. In the “yes” encoding runs, participants were instructed to ignore the “no” cues and to not perform SN (or any other task). Conversely, to encode a “no” answer, they had to perform SN imagery when they heard “no”. In this case, the “yes” cues were ignored (see Figure 1).

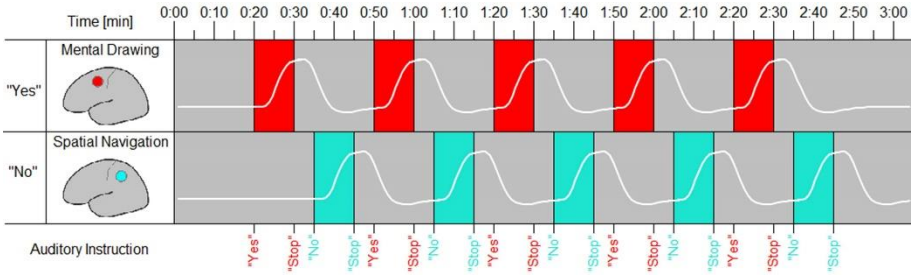

Figure 1. **Encoding Scheme for Answering a Binary Question.** The red periods require mental drawing (MD) imagery, whereas the green periods required spatial navigation (SN) imagery. If participants chose to answer “yes”, they started performing the MD task when they heard a “yes”, halted their imagery when they heard the cue “stop”, and ignored the auditory cues related to the “no” response. The hypothesized HbO response for a “yes” answer is shown by the upper white waveform. If participants chose to answer “no”, they started performing the SN task when they heard a “no”, halted their imagery when they heard the cue “stop”, and ignored the auditory cues related to the “yes” response. The hypothesized HbO response for a “no” answer is shown by the lower white waveform.

Six questions were asked, each at the start of a separate answer encoding run. The question was read aloud through a microphone by the experimenter. The fNIRS recording started when the participant reported having his/her answer, *i.e.*, "yes" or "no", and the corresponding task, *i.e.*, MD or SN, clearly in mind. The time intervals within which a "yes" or "no" answer could be given followed 20 s after termination of the question. The "yes" interval was initiated by the auditory "yes" cue and terminated 10 s later by an auditory "stop" cue. The "yes" interval always proceeded the "no" interval, which was marked by the auditory cue "no" and "stop" 10 s later. Hence, if participants had chosen to answer "yes", they started performing the MD. If participants had chosen to answer "no", they ignored the "yes" cue. The cue, "stop", indicated participants to stop the mental imagery. Again, if participants had chosen to answer "no", they also ignored this "stop" cue and remained at rest until they heard the cue "no". At this point they started performing the SN task until the "stop" cue was heard. This procedure was repeated five times per encoding run, resulting in five "yes" and five "no" trials.

Summarized, participants thus answered questions by performing the MD mental task within a first time interval marked by "yes" and "stop" cues, or the SN mental task within a second time interval marked by "no" and "stop" cues.

Localizer Block 2

The procedure in localizer block 1 was repeated to increase the amount of available data for classifier training. This repetition was warranted, as we were unsure with respect to the minimum amount of data necessary for effectively training the classifier in the multivariate approach.

Comfortability Ratings

In between the ten fNIRS runs, participants were allowed to take a short break to slightly adjust their body posture, or drink some water. After each run, participants were asked to give a comfortability rating between 0 and 10, with 0 meaning “very uncomfortable” and 10 being “very comfortable”.

Ease and Pleasantness of the Mental Tasks

After the ten fNIRS runs, the cap was removed and participants were asked to rate the ease and pleasantness of the MD and SN tasks with a score from 0 to 10. An easiness rating of 0 indicated great difficulty of mental task execution, whereas a rating of 10 indicated extreme ease of task execution. A pleasantness rating of 0 indicated an extremely unpleasant experience when performing the mental task, whereas a score of 10 indicated an extremely pleasant experience.

fNIRS Data Acquisition

Hemodynamic signals were obtained using a continuous-wave fNIRS system (NIRScout-816 system, NIRx Medizintechnik GmbH, Berlin, Germany; RRID:SCR_002491) and NIRStar (v. 12.0) software (NIRx Medizintechnik GmbH, Berlin, Germany; RRID:SCR_014540). Three source optodes, LEDs emitting light with wavelengths of 760 nm and 850 nm, were used in combination with six detector optodes. These nine optodes were placed in optode holders on the cap according to the international 10-20 EEG system. The three sources optodes were positioned on FC3, C3 and CP3, whereas the six detector optodes were positioned on FC5, C5, CP5, FC1, C1 and CP1 (see Figure 2). Defining a channel as a unique source and detector optode pair, this setup resulted in 18 channels.

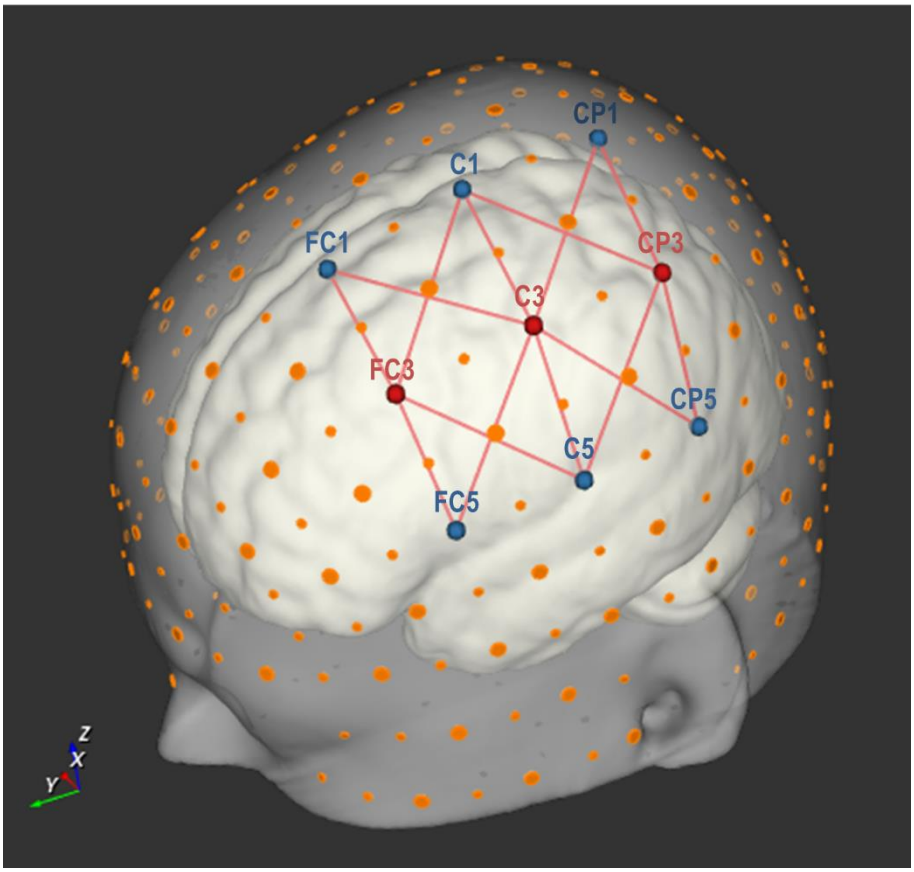

Figure 2. **Optode Set-up** with three source and six detector optodes, placed on nine points according to the international 10-20 EEG system. Large orange dots represent reference points of the 10-20 system, whereas small orange dots represent reference points of the extended 10-10 EEG system (Oostenveld & Praamstra, 2001). The red lines represent 14 source-detector pairs (each forming an fNIRS channel). Image created using NIRSite (v.1) software (NIRx Medizintechnik GmbH, Berlin, Germany; RRID:SCR_002491).

Channels FC3-CP1, FC3-CP5, CP3-FC1 and CP3-FC5 were excluded from all analyses, as the spatial separation between the sources and detectors exceeded 60 mm in the largest cap size (60 cm) used in this experiment. An optode separation of that size was considered undesirable since it largely exceeds the recommended inter-optode distance of 30 mm and gives rise to noisy and unstable signals (Gratton et al., 2006). The

remaining 14 channels analyzed in this experiment are depicted by the red connecting lines in Figure 2. This optode montage covered a confined area above the left-hemispheric fronto-parietal (sensorimotor) cortex. The frontal optodes covered brain areas commonly associated with motor imagery, such as premotor cortex and possibly parts of the supplementary motor areas in certain head sizes (Abdalmalak et al., 2016; Koessler et al., 2009; Sitaram et al., 2007). The posterior optodes captured part of the parietal cortex, expected to be associated with SN imagery (Abdalmalak, Milej, Diop, et al., 2017; Cabrera & Dremstrup, 2008; McKendrick et al., 2016). Optical signals were recorded with a sampling rate of 12.5 Hz.

Data Analysis

Analyses of the fNIRS signal

The main outcome of the spatiotemporal encoding paradigm, *i.e.*, communication accuracy, was obtained with a General Linear Model (GLM) approach (univariate analysis). In addition, spatial discernibility of the two mental tasks was investigated using a SVM (multivariate analysis). See Figure 3 for an illustration of the analyses workflow.

General Data (Pre)-Processing

FNIRS time series were analyzed in simulated real-time using Turbo-Satori software (v1.2.8, Brain Innovation B.V., Maastricht, The Netherlands). In the first pre-processing step, raw wavelengths were converted to optical densities. The optical density data were then converted to oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) values using the modified Beer-Lambert law. Linear trend removal and moving average filtering (low-pass cut-off frequency: 0.3 Hz, filter order: 2; high-pass cut-off frequency: 0.01 Hz, filter order: 1) were applied. The low-pass filter aimed

to remove high-frequency artifacts induced by heartbeat and breathing, whereas the high-pass filter served to remove low-frequency drifts.

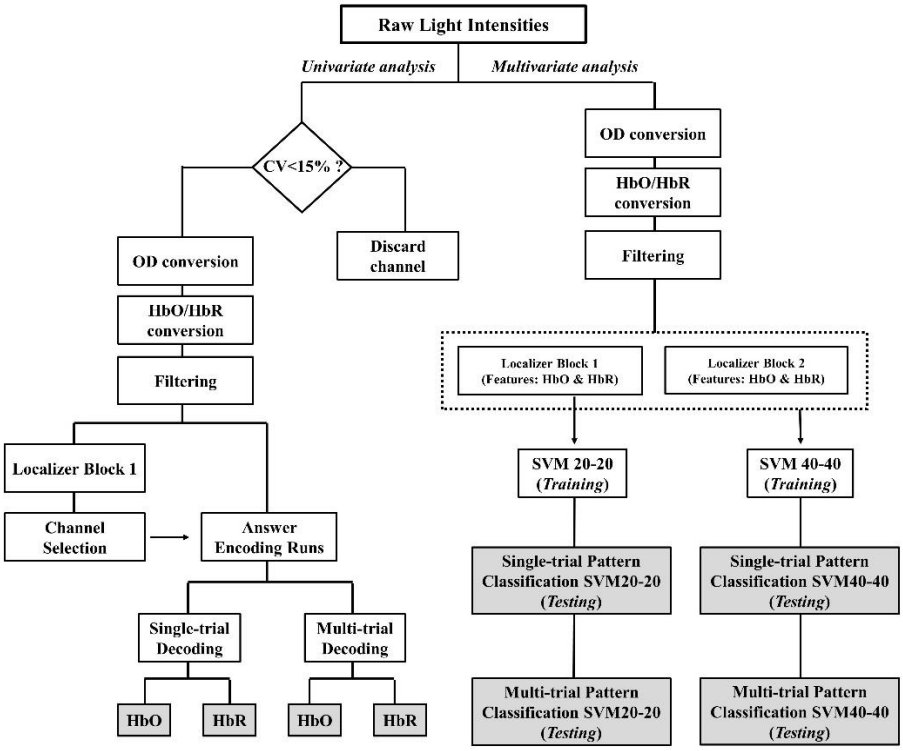

***Figure 3*. Schematic Depiction of the fNIRS Signal Analyses.** The two main pipelines were univariate analysis and multivariate analysis. Each pipeline resulted in four accuracy outcomes. These outcome variables are represented in grey colored boxes. Abbreviations: CV = coefficient of variance; OD = optical density; HbO = oxygenated hemoglobin; HbR = deoxygenated hemoglobin; SVM20-20 = support vector machine with 20 training trials of each task; SVM40-40 = support vector machine with 40 training trials of each task.

Communication Accuracy (Univariate Analysis)

Channel Exclusion

To ensure proper signal quality, we excluded channels showing a signal-to-noise ratio below a given criterion value. To that aim, the channel-wise

coefficient of variance percentage (CV %) was calculated on the unfiltered raw wavelength data by dividing the temporal standard deviation by the mean value (see Piper et al. (2014) for a detailed description). A CV % higher than 15 indicates insufficient signal-to-noise ratio (Pfeifer, Scholkmann, & Labruyère, 2018; Piper et al., 2014; Schmitz et al., 2005; Schneider et al., 2011). Consequently, all channels with a CV % higher than 15 for either one or both wavelengths in the first two localizers (block 1) were excluded from channel-of-interest selection. This channel-wise exclusion was also performed on the last set of localizers (block 2) to gauge the intra-individual variability in channel exclusion across all localizer runs.

Given the limited number of 14 channels in the current experiment, one runs the risk of excluding a potentially informative channel due to its high CV %. Therefore, all univariate analyses were repeated omitting the CV % criterion, thus allowing different channels to be selected for subsequent analyses (see Supplementary Material). Only when the overall accuracy differed significantly between both approaches, the accuracies of the analyses without the CV % criterion are also reported in the results section.

Channel Selection

From the channels that were not excluded in the previous step, a single channel was chosen for each mental imagery task (MD and SN) based on the data of localizer block 1. HbO and HbR signals were analyzed separately. Four GLM analyses (HbO / HbR × MD / SN) were conducted with a predictor for the mental imagery trials and applying the contrast “MD / SN vs. rest”. The four channels with the highest t-value in each of the four GLM analyses were coined “signals of interest” (SOIs) and were considered for the following single- and multi-trial analyses of the answer encoding data.

Answer Decoding

Participant's answers were decoded through comparison of the five individual trial pairs (single-trial approach) or through comparison of the integrated five trials per answer option (multi-trial approach).

In the single-trial approach a GLM analysis was run with the statistical contrast "yes" vs. "no" for each yes/no trial pair (5 trial pairs per encoding run). This resulted in four t-values per trial pair, one for each SOI (HbO/HbR x SN/MD), based on mental task predictors that encompassed two individual trials. These t-values were used to decode the participants' answer as follows: When the t-value of the MD SOI was larger than the t-value of the SN SOI, a "yes" answer was decoded. Whereas when the t-value of the MD SOI was smaller than the t-value of the SN SOI, a "no" answer was decoded. The single-trial approach resulted in 30 decoded answers (6 runs x 5 trial pairs) per participant. The decoded answers were compared to the originally encoded answers and each individual participant's accuracy was calculated.

In the multi-trial approach, a GLM analysis was run with the statistical contrast "yes" vs. "no". The five trials per answer option were used to infer a t-value for each SOI (HbO/HbR x SN/MD). Decoding followed the same rationale of t-value comparison as in the single-trial approach. This procedure was repeated for all six answer-encoding runs for both the HbO and HbR signal separately. The decoded answers were compared to the originally encoded answers and each individual participant's accuracy was calculated. The multi-trial approach resulted in 6 decoded answers (6 runs) per participant. The decoded answers were compared to the originally encoded answers and each individual participant's accuracy was calculated.

To assess the significance of the participants' decoding accuracies in

the univariate analyses, we determined the empirical chance level based on binomial distributions (Noirhomme et al., 2014). The following settings were determined: $\alpha = .05$, number of independent outcomes $k = 2$ and number of independent trials $n = 30$ or $n = 6$ for single- and multi-trial accuracies respectively. The resulting upper-bound empirical chance levels for evaluating single- and multi-trial accuracies were therefore 19 trials (63.33 %) and 5 trials (83.33 %) respectively. If 19 or more trials were decoded correctly in the single-trial approach, this was considered a significant result. If 5 or more trials were decoded correctly in the multi-trial approach, this was considered a significant result.

The rate of correct detection of "yes"/"no" answers was calculated by dividing the amount of correctly detected "yes"/"no" answers by the total amount of encoded "yes"/"no" answers per participant, *i.e.*, 15 for the single-trial and 3 for the multi-trial analysis.

Multivariate Analyses

Single-trial Results

Two classifiers were trained to discriminate the spatial activation patterns in all 14 channels induced by the two different mental tasks. This was done using either 20 or 40 trials of each mental task. One classifier was trained on two runs: one for MD (MD1) and one for SN (SN1), with each 20 trials (SVM20-20). The other classifier was trained on four runs: two for MD (MD1 & MD2) and two for SN (SN1 & SN2), resulting in 40 trials for each task (SVM40-40). We considered a temporal window spanning -2 s to 20 s (where 0-10 s corresponds to the trial interval) and linearly fitted each HbO/HbR concentration channel time course separately with a design matrix consisting of a double-gamma hemodynamic response function per trial and an additional linear confound predictor. Resulting estimates were

t-values which were stored in volume map files for each time course. These files were used as input for the classifier testing on an independent dataset, *i.e.*, the six answer-encoding runs' data. Per answer-encoding run, the five 'active' trials, *i.e.*, trials in which we knew the participant was performing a task, were tested. The five 'inactive' trials in which participants rested were not analyzed. This resulted into a total of thirty testing trials (6 runs x 5 'active' trials) per participant. The proportion of testing trials for which the decoded answer matched the true answer was subsequently calculated. Lastly, to determine the empirical chance level for each individual participant, permutation testing was performed with an in-house MATLAB script (ver. R2015a). To this end, task labels were randomly reassigned to each trial in the training dataset, on which the classifier was subsequently trained. Testing was then done on an independent, non-permuted testing dataset. This procedure was repeated 2000 times. Chance level was calculated as the proportion of permutations revealing accuracies lower or equal to the accuracy obtained using the real (non-permuted) dataset.

The rate of correct detection of MD/SN was calculated by dividing the amount of correctly detected MD/SN patterns by the total amount of encoded MD/SN trials, *i.e.*, 15 per task.

Multi-trial Results

Multi-trial accuracies were derived from the single-trial multivariate results reported above. The five yes/no decisions per run were integrated using majority voting (*e.g.*, three answers encoded as "yes" and two answers encoded as "no" were considered as a "yes" answer, and vice versa). The proportion of decoded answers matching with the true answer was calculated for each participant. The upper-bound empirical chance level for each individual participant was 83.33 %, based on binomial distributions.

The rate of correct detection of MD/SN was calculated by dividing the amount of correctly detected MD/SN patterns by the total amount of encoded MD/SN runs, *i.e.*, three per task.

fNIRS Suitability Questionnaire and Signal Quality

The total fNIRS suitability score was obtained by summing all features, with a maximum score of 21 (see Table 1 for suitability score per participant). This score was correlated with the number of channels with a CV under 15 %, which is a metric for fNIRS signal quality (Balardin et al., 2017), through calculation of a one-tailed Pearson's *r* in SPPS (ver. 22). Furthermore linear regression analyses were performed using SPPS (ver. 22). FNIRS signal quality, *i.e.*, SNR, was treated as predictor variable and the eight decoding accuracies obtained from the univariate analyses (single-/multi-trial x HbO/HbR) and multivariate analyses (single-/multi-trial x SVM20-20/SVM40-40) were treated as criterion variables.

Comfortability, Ease and Pleasantness Ratings

Mean and standard deviation are reported for comfortability, ease and pleasantness ratings. Pearson's *r* was calculated between ease and pleasantness and accuracy outcomes of all univariate (single-/multi-trial x HbO/HbR) and multivariate (single-/multi-trial x SVM20-20/SVM40-40) analyses. Statistical significance was evaluated using a criterion of $\alpha = .05$.

Results

Communication Accuracy (Univariate Analysis)

Channel Exclusion

On average 37 % of channels were excluded due to their low SNR in localizer block 1. Descriptively, the channels with a relatively longer source-

detector distance, *e.g.*, diagonal channels such as FC3-C1, as compared to the shorter optode distances, *e.g.*, straight channels such as FC3-FC1, were excluded more often. Large variation was observed between individual participants, ranging from 0 to 13 excluded channels. In contrast, the SNR measure was highly consistent across the four localizer runs (block 1 & block 2) within individual participants (see Supplementary Material, Figure S1).

Channel Selection

The four SOIs selected for further data-analysis steps are reported per participant in Table 1. In the HbO selection, the same channel was selected for mental drawing and spatial navigation imagery in three participants, *i.e.*, participant 6, 7 and 12. In the HbR selection the same channel was selected for both tasks in four participants, *i.e.*, participant 1, 4, 7 and 14. Overall the channel selection was quite variable across participants (see Table 2). For the MD task, channels FC3-FC5 (HbO) and C3-C5 (HbR) were chosen most frequently. For the SN task, channels FC3-FC5 (HbO) and FC3-FC5, FC3-C5, FC3-CP1 and C3-CP3 (HbO) were chosen most frequently. The event-related averages of the four channels-of-interest are depicted for two exemplary participants, participant 4 and 17 (Figure 4 and 5).

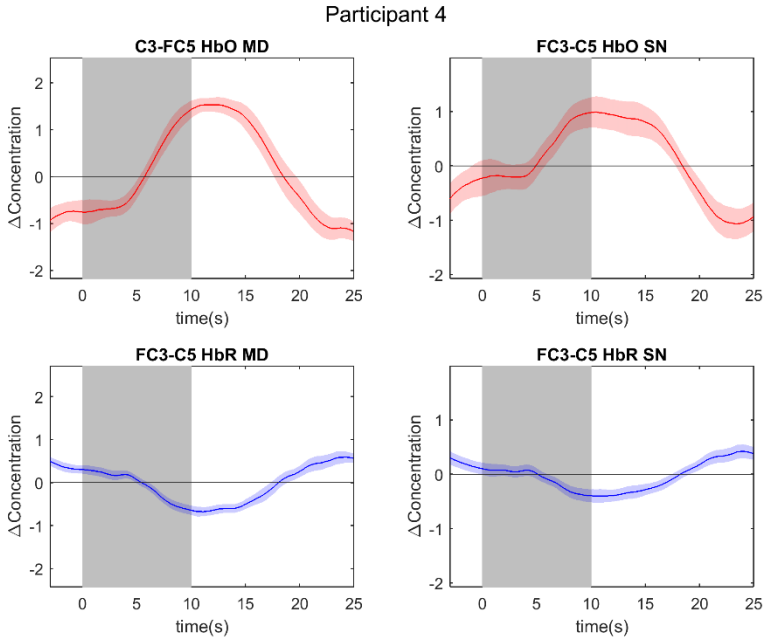

Figure 4. **Event-related Averages of Channels of Interest in Participant 4.** The two graphs on the left are event-related averages from the first localizer run (mental drawing; MD). The two graphs on the right are event-related averages from the second localizer run (spatial navigation; SN). The top two graphs depict the oxygenated hemoglobin (HbO) response, whereas the bottom two graphs depict the deoxygenated hemoglobin (HbR) response. Each graph is the event-related average of 20 individual trials, with the darker average signal line and its standard deviation (lighter colored band surrounding the average signal line). The grey band from 0 to 10 s signifies the mental imagery time interval. Notice the clear and typical hemodynamic response during both tasks: a positive deflection in HbO and a negative deflection in HbR.

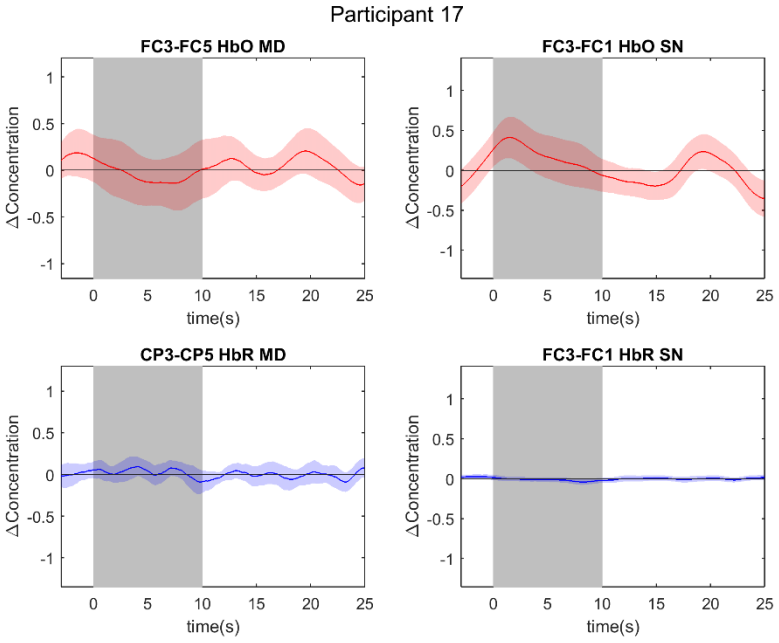

Figure 5. **Event-related Averages of Channels of Interest in Participant 17.** The two graphs on the left are event-related averages from the first localizer run (mental drawing; MD). The two graphs on the right are event-related averages from the second localizer run (spatial navigation; SN). The top two graphs depict the oxygenated hemoglobin (HbO) response, whereas the bottom two graphs depict the deoxygenated hemoglobin (HbR) response. Each graph is the event-related average of 20 individual trials, with the darker average signal line and its standard deviation (lighter colored band surrounding the average signal line). The grey band from 0 to 10 s signifies the mental imagery time interval. Notice the absence of a typical hemodynamic response during both tasks: there is no clear positive deflection in HbO, nor a negative deflection in HbR.

Channel (Source-Detector)	Absolute frequency			
	Mental Drawing		Spatial Navigation	
	HbO	HbR	HbO	HbR
FC3-FC5	4	2	5	3
FC3-C5	1	1	2	3
FC3-FC1	1	1	3	3
FC3-C1	0	0	1	0
C3-FC5	3	1	2	0
C3-C5	2	4	1	1
C3-CP5	1	1	0	0
C3-FC1	0	0	0	1
C3-C1	1	3	0	3
C3-CP1	1	0	0	0
CP3-C5	1	0	1	1
CP3-CP5	1	3	3	2
CP3-C1	0	0	0	1
CP3-CP1	2	2	0	0
Total	**18**	**18**	**18**	**18**

Table 2. **Frequency of Signals of Interest (SOI's) Selection** in 18 participants. A channel is formed by the combination of two optodes (source-detector). Abbreviations: HbO, oxygenated hemoglobin; HbR, deoxygenated hemoglobin.

Single-trial Results

Univariate analysis of single-trial data resulted in an average decoding accuracy of 56.85 % (SD = 11.17 %) and 54.81 % (SD = 13.58 %) for HbO and HbR respectively (see Figure 6). Individual accuracies ranged from 33.33 % to 90 %. Two participants' HbO data decoding accuracy was significant (indicated with a ♦ symbol in Figure 6). The average rate of correct detection of "yes" answers in the HbO signal was 60.00 %, whereas "no" answers were correctly detected 53.70 % of the time. The HbR decoding accuracy was significant in four participants (indicated with a ♦ symbol in Figure 6). Participant 4 was the sole significant participant in both HbO and HbR accuracies. The average rate of correct detection of "yes" answers in the HbR signal was 62.22 %, whereas "no" answers were correctly detected 47.41 % of the time.

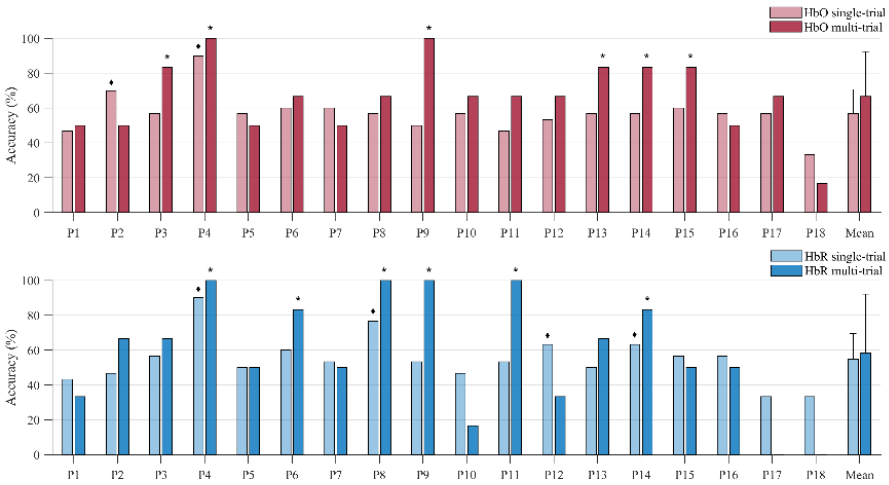

Figure 6. **Decoding accuracies of individual participants and the sample mean** obtained with the single-trial (light-colored bars) and the multi-trial (dark-colored bars) univariate approach. Decoding accuracies were attained through channels-of-interest, preceded by a channel exclusion step. The upper plot show results based on analysis of HbO data (red bars), the lower plot is based on HbR data (blue bars). The ♦ symbol indicates participants whose single-trial accuracy was significant, whereas the * symbol indicates those participants whose multi-trial accuracy was significant.

Multi-trial Results

Univariate analysis of multi-trial decoding resulted in an average accuracy of 66.67 % (SD = 20.6 %) and 58.33 % (SD = 32.96 %) for HbO and HbR respectively (see Figure 6). The control analysis without channel exclusion, yielded a significantly lower group average of 58.33 % (SD = 25.73 %) for the HbO data (paired samples t-test; t = 2.70; p = .015; see Supplementary Material). In the main analysis, *i.e.*, with channel exclusion, individual accuracies ranged from 0 % to 100 %. Six participants' HbO data decoding accuracy was found to be significant (indicated with a * symbol in Figure 6). The answers by participants 4 and 9 were decoded with 100 % accuracy. The average rate of correct detection of "yes" answers in the HbO signal was 83.33 %, whereas "no" answers were correctly detected in 50.00 % of

the cases. The HbR decoding accuracy was significant in six participants (indicated with a * symbol in Figure 6), with 100 % accuracy in participants 4, 8, 9 and 11. The answers of participants 4, 9 and 14 were significantly decoded in both HbO and HbR signal. For illustrative purposes the event-related averages of a "yes" and a "no" answer are depicted for participant 4 and 19 in Figure 7 and 8. The average rate of correct detection of "yes" answers in the HbR signal was 72.22 %, whereas "no" answers were correctly detected 44.44 % of the time.

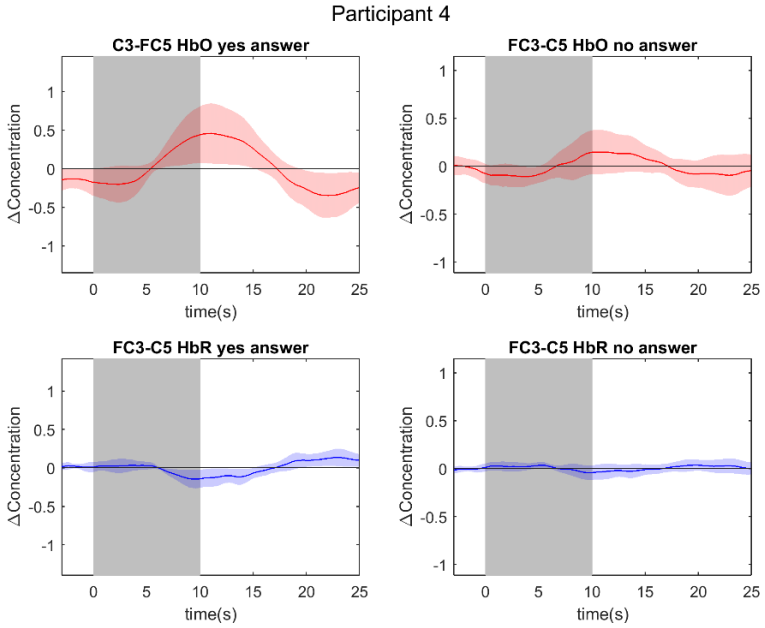

Figure 7. **Event-related Averages of Channels of Interest in Participant 4.** The two graphs on the left are event-related averages from the first answer decoding run, in which the participant encoded a "yes" answer. The two graphs on the right are event-related averages from the sixth answer decoding run, in which the participant encoded a "no" answer. The top two graphs depict the oxygenated hemoglobin (HbO) response, whereas the bottom two graphs depict the deoxygenated hemoglobin (HbR) response. Each graph is the event-related average of five individual trials, with the darker average signal line and its standard deviation (lighter colored band surrounding the average signal line). The grey band from 0 to 10 s signifies the mental imagery time interval. Notice the clear and typical hemodynamic response function during both tasks: a positive deflection in HbO and a negative deflection in HbR.

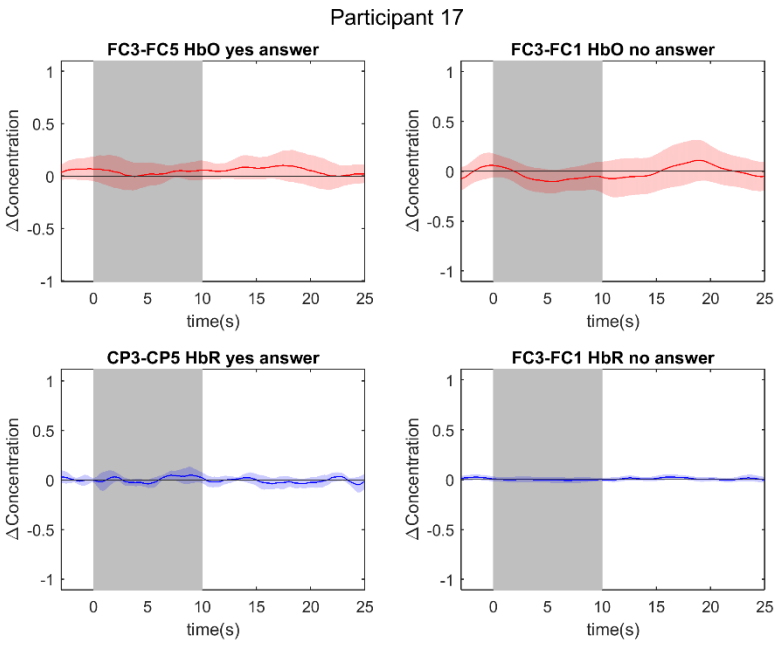

Figure 8. **Event-related Averages of Channels of Interest in Participant 17.** The two graphs on the left are event-related averages from the fifth answer decoding run, in which the participant encoded a "yes" answer. The two graphs on the right are event-related averages from the sixth answer decoding run, in which the participant encoded a "no" answer. The top two graphs depict the oxygenated hemoglobin (HbO) response, whereas the bottom two graphs depict the deoxygenated hemoglobin (HbR) response. Each graph is the event-related average of five individual trials, with the darker average signal line and its standard deviation (lighter colored band surrounding the average signal line). The grey band from 0 to 10 s signifies the mental imagery time interval. Notice the absence of a typical hemodynamic response function during both tasks: there is no clear positive deflection in HbO, nor a negative deflection in HbR.

Multivariate analyses

Single-trial Results

The SVM20-20 classifier achieved an accuracy of 58.33 % (SD = 13.05 %). Individual accuracies ranged from 33.33 % to 76.67 %. Spatial activation patterns could be distinguished significantly above chance level, assessed by permutation testing, in four out of 18 participants (indicated with a ⌑

symbol in the top plot in Figure 9). The average rate of correct detection of MD was 52.59 %, whereas SN was correctly detected 64.07 % of the time.

The SVM40-40 classifier achieved an accuracy of 60.56 % (SD = 13.15). Individual accuracies ranged from 30.00 % to 83.33 %. Spatial activation patterns could be distinguished significantly above chance level, assessed by permutation testing, in seven out of 18 participants (indicated with a ⌑ symbol in the bottom plot in Figure 9). The average rate of correct detection of MD was 59.26 %, whereas SN was correctly detected 62.59 % of the time.

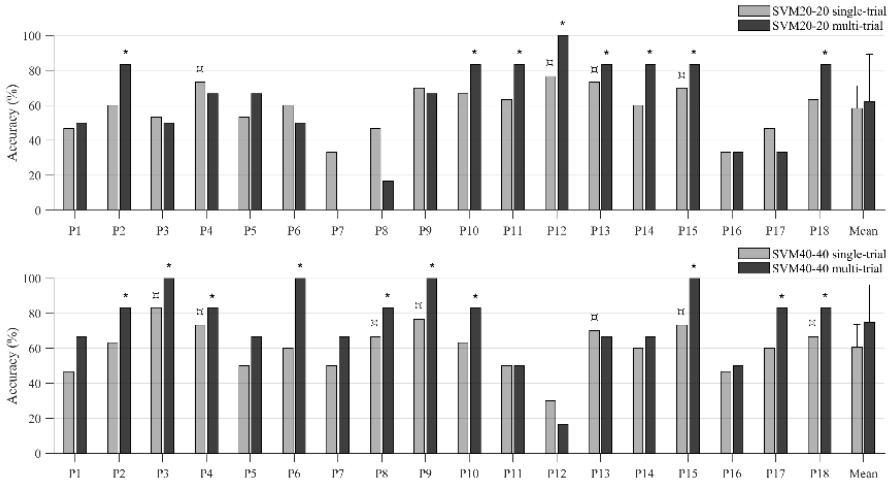

Figure 9. **Decoding Accuracies of Individual Participants and the Sample Mean** obtained with the single-trial (light-colored bars) and the multi-trial (dark-colored bars) multivariate approach. The upper plot shows decoding accuracies of the SVM20-20 classifier, the lower plot shows decoding accuracies of the SVM40-40 classifier. The ⌑ symbol indicates participants whose accuracy reached significance, as tested with permutation testing (for evaluating single-trial accuracies), whereas the * symbol indicates those participants whose multi-trial accuracy was significant. Abbreviations: SVM20-20 = support vector machine with 20 training trials of each task; SVM40-40 = support vector machine with 40 training trials of each task.

Multi-trial Results

The SVM20-20 classifier achieved an accuracy of 62.04 % (SD = 27.30 %). Individual accuracies ranged from 0.00 % to 100.00 %. Spatial activation patterns discernibility was significant in eight out of 18 participants (indicated with a * symbol in the top plot in Figure 9). The average decoding accuracy of these eight participants was 85.42 % (SD = 5.89 %). The average rate of correct detection of MD was 59.26 %, whereas SN was correctly detected 64.81 % of the time.

The SVM40-40 classifier achieved an accuracy of 75.0 % (SD = 21.58 %). Individual accuracies ranged from 16.67 % to 100.00 %. Spatial activation patterns discernibility was significant in ten out of 18 participants (indicated with a * symbol in the bottom plot in Figure 9). The average rate of correct detection of MD was 72.22 %, whereas SN was correctly detected 77.78 % of the time.

fNIRS Suitability Questionnaire and Signal Quality

We found that SNR, as measured by the number of channels passing the CV % criterion, was significantly correlated with fNIRS suitability scores (r = -.499, n = 18, p = 0.018; see Supplementary Material, Figure S3). Participants with low fNIRS suitability scores (indicating highly suitable participants) thus typically had good fNIRS signal SNR.

Regression analyses with accuracy as the criterion variable and SNR as the predictor variable revealed the following results (See Supplementary Material, Figure S4). Approximately 30 % of the variation in HbR multi-trial accuracy could be attributed to the variation in SNR (R^2 = .309 with F_{17} = 7.165, p = .017). In contrast, SNR was no significant predictor for any other criterion variable: HbR single-trial accuracy (R^2 = .083 with F_{17} = 1.442, p =

.247), HbO single-trial accuracy (R^2 = .045 with F_{17} = .755, p = .398), HbO multi-trial accuracy (R^2 = .029 with F_{17} = .480, p = *.499*), single-trial SVM20-20 (R^2 = .135 with F_{17} = 2.494, p = .134), multi-trial SVM20-20 (R^2 = .041 with F_{17} = .676, p = .423), single-trial SVM40-40 (R^2 = .009 with F_{17} = .144, p = .709) and multi-trial SVM40-40 (R^2 = .147 with F_{17} = 2.767, p = .116).

Comfortability, Easiness and Pleasantness

Participant's comfortability rating started out fairly high (8.03 ± 1.27) and then decreased over the remaining fNIRS runs (see Figure 10). The last run shows lowered although still acceptable comfort scores (6.53 ± 1.55). Not a single participant indicated a comfortability score lower than 5 during the experiment.

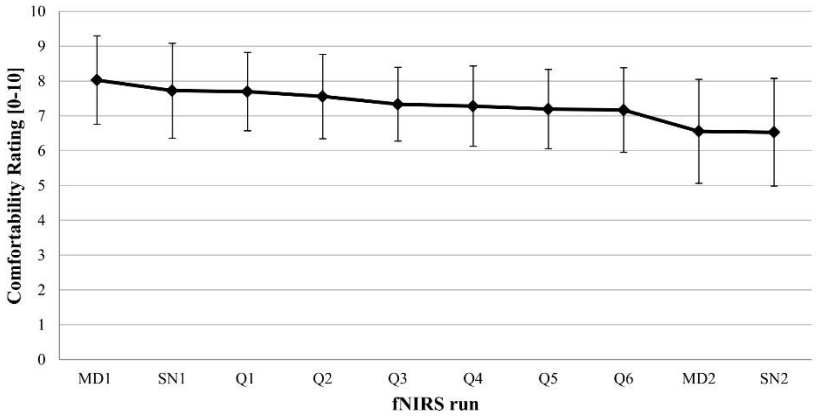

Figure 10. **Mean Comfortability Rating over Time.** A comfortability rating of 0 corresponds to "very uncomfortable" and 10 to "very comfortable". The ten fNIRS runs are depicted in the order they were conducted in the experiment. The first two runs, MD1 and SN2, were localizer runs (block 1) for mental drawing (MD) and spatial navigation (SN). The following six runs, Q1, Q2, Q3, Q4, Q5, Q6, represent the answer decoding runs, with a Q as an abbreviation for 'question run'. The last two runs, MD2 and SN2, were localizer runs (block 2). Error bars reflect standard deviations.

Overall both tasks were deemed easy and pleasant. On average the SN task was considered more difficult to perform (6.28 ± 1.32) and less pleasant (6.61 ± 1.45) than the MD task (7.94 ± 1.48; 7.28 ± 1.49). The difference between the two tasks in terms of ease was statistically significant (t = 4.70, $p < .001$). The difference in pleasantness showed a similar trend, yet it was not statistically significant (t = 1.86, $p = .081$). Ease and pleasantness ratings correlated significantly with the accuracy of the SVM40-40 analysis, whereas all other correlations were not significant (see Table 3 for all correlations).

Pearson's p *p*-value	Multi HbO	Multi HbR	Single HbO	Single HbR	Single SVM 20-20	Multi SVM 20-20	Single SVM 40-40	Multi SVM 40-40
Ease MD	0.288	0.220	0.101	0.034	0.010	0.017	0.508	0,383
	0.123	*0.190*	*0.345*	*0.447*	*0.484*	*0.945*	*0.016**	*0.117*
Ease SN	0.360	0.147	0.156	0.041	0.325	0.364	0.609	0.499
	0.071	*0.281*	*0.268*	*0.435*	*0.094*	*0.137*	*0.004**	*0.035**
Pleasant MD	0.320	0.210	0.127	-0.051	-0.116	-0.208	0.736	0.748
	0.098	*0.202*	*0.308*	*0.421*	*0.323*	*0.408*	*0.000**	*0.000**
Pleasant SN	0.295	0.023	0.023	-0.163	0.145	0.076	0.637	0.423
	0.117	*0.464*	*0.464*	*0.259*	*0.283*	*0.765*	*0.002**	*0.080*

Table 3. **Correlation Table of Ease and Pleasantness Ratings with the Eight Accuracy Outcomes Variables.** Abbreviations: MD = mental drawing; SN = spatial navigation; Multi = multi-trial; Single = single-trial; HbO = oxygenated hemoglobin; HbR = deoxygenated hemoglobin; SVM = support vector machine; * = correlation is significant at 0.05 level (1-tailed).

Discussion

We presented a novel binary communication paradigm that aimed to exploit spatiotemporal characteristics of fNIRS signals evoked by differently timed mental imagery tasks. The paradigm involved minimal training and a sparse optode setup of only nine optodes (three sources, six detectors). Participants were asked to perform mental drawing (MD) for encoding a "yes" answer and spatial navigation (SN) for encoding a "no" answer in

different auditorily cued time windows. The applied goal was to test decoding success and feasibility of the current paradigm compared to previous paradigms. Answers were decoded in simulated real-time using a set of predefined fNIRS channels using a univariate analysis approach. We also performed an explorative multivariate analysis on the data from all channels to investigate the differentiability of the two mental tasks based solely on spatial fNIRS signal features. In addition, the link between participants' physical characteristics and the fNIRS signal was explored with a novel fNIRS suitability questionnaire.

Univariate Analysis

Channel Selection

We hypothesized that relatively frontal optodes covered brain regions commonly associated with motor imagery, whereas posterior optodes covered brain areas associated with SN imagery. On a group level, we found that frontal optodes were selected most often, irrespective of the type of task. However, note that a channel exclusion step was performed before the channel selection step, thus one should interpret these findings with caution. On an individual level, spatially different channels were selected as SOI for each task in most participants. The absence of a spatial encoding aspect, *i.e.*, selecting the same SOI for both tasks, in a few participants (three in HbO and four in HbR; see Table 1) posed no decoding problem. Our paradigm aimed at exploiting spatial as well as temporal characteristics of fNIRS signals. Hence, in those few participants we solely relied on the temporal aspect, the fNIRS signal evoked by differently timed mental imagery tasks, to decode participant's answers. For example, participant 4 had the same SOI for both tasks in the HbR signal but had a decoding

accuracy clearly above chance level, with a single-trial accuracy of 90 % and a multi-trial accuracy of 100 %. The incorporation of both spatial and temporal features is an experimental safeguard in the presented fNIRS paradigm.

Communication Accuracy

The single-trial GLM approach, with average decoding accuracies of 56.85 % (HbO) and 54.81 % (HbR), enabled effective communication in a limited subset of participants. In the fNIRS literature, no univariate single-trial accuracies have been previously reported. Multiple trials seem to be necessary at the current time, unfortunately at the cost of a lower information transfer rate. The multi-trial GLM approach resulted in higher group decoding accuracies in comparison to the single-trial approach. In four participants a 100 % decoding accuracy was reached in the multi-trial approach, which was not attained in any participant using a single-trial approach. Average multi-trial decoding accuracy was higher in HbO (66.67 %) than in HbR (58.33 %), but on an individual level the same number of participants (six) reached significance. The similar individual decoding results across HbO and HbR were an unexpected finding. Generally, the lower amplitude and SNR of HbR, as compared to HbO, is thought to hinder detection of task-evoked changes (Leff et al., 2011). In line with this, it has been demonstrated that HbO signal is more robust than HbR for motor imagery specific activation (Mihara et al., 2012). Likewise, Rezazadeh Sereshkeh et al. (2018) reported that HbO signals yielded the highest accuracies in their 3-class BCI using imagined speech, and Hwang et al. (2016) reported that HbO features yield more discriminative information than HbR features in 2-class communication. Despite this previous work, here we find individual HbR multi-trial decoding accuracies that are similar

to the ones seen in the HbO signal. It could be that the negative effect of the low SNR of the HbR signal is compensated by the relatively low sensitivity to physiological noise, *i.e.*, systemic artifacts in both extra-cerebral and intra-cerebral compartments, as compared to HbO (Kirilina et al., 2012). In the current study we could not correct for physiological noise, which might have been a disadvantage for the HbO signal especially. Whether the differential sensitivity to physiological noise should influence researchers' decision to select either HbO or HbR for BCI purposes should be investigated further. Therefore, in line with Pinti et al. (2018), we encourage future studies to report both HbO and HbR results.

As in previous fNIRS-BCI studies, only a subset of our participants reached an acceptable criterion for communication (Nagels-Coune et al., 2017; Naito et al., 2007; Rezazadeh Sereshkeh et al., 2018). The multi-trial approach enabled effective communication in six participants in the HbO signal, *i.e.*, participants 3, 4, 9, 13, 14, 15, and six participants in the HbR signal, *i.e.*, participants 4, 6, 8, 9, 11 and 14. When taking the HbO and HbR results together, effective communication was reached in half of our participants. Therefore, as stated above, we recommend reporting BCI success for both HbO and HbR in future studies. Note that our use of the empirical chance level as a criterion is significantly stricter than the commonly used '70 %' criterion that signifies a sufficient accuracy for communication in an individual user (Kübler, Mushahwar, Hochberg, & Donoghue, 2006). Our paradigm thus enables effective communication, greatly exceeding the common criterion of 70 % for effective communication (Kübler et al., 2006), in a subset of participants.

Our multi-trial accuracies of 66.67 % (HbO) and 58.33 % (HbR) are low compared to those reported in other binary communication paradigms

(Naseer et al., 2014; Rezazadeh Sereshkeh et al., 2018). This could be due to our sparse approach of a single session. Other studies encompassed multiple sessions (Rezazadeh Sereshkeh et al., 2018) or separate training sessions (Naseer et al., 2014). More training of our participants and more experimental trials could have resulted in better BCI performance (Kaiser et al., 2014) but would require more time investment, which in turn might affect the clinical applicability.

Our paradigm is the first to attempt using two active mental tasks to differentiate two answer options. However the low correct detection rate of the "no" answers, ranging from 44.44 % to 53.70 %, implies that the motor imagery task has mainly driven our univariate results. This finding questions the effective contribution of the spatial navigation task in our univariate analyses. Efforts have been made to investigate SN in naturalistic environments (McKendrick et al., 2016) and virtual reality environments (Kober, Wood, & Neuper, 2013) using fNIRS. However, to our knowledge no previous fNIRS study has explored the fNIRS signal in response to SN imagery. This study thus constitutes the first exploration of SN imagery in fNIRS. Future studies should investigate this mental task more thoroughly using an extended optode setup, as it is possible that our optode setup was not suited for SN. Alternatively, other promising mental imagery tasks can be explored. With respect to the spatial encoding aspect of the current paradigm (two distinct mental tasks and associated channels-of-interest for encoding "yes" and "no" encoding), follow-up work is required to ensure effective and balanced contributions of both tasks.

Multivariate Analysis

The multivariate analysis explored the possibility of distinguishing the spatial patterns induced by MD versus SN, disregarding any temporal information. From a clinical perspective, we compared the classifier results for both a limited (localizer block 1) and a full (localizer block 1 and 2) training set. Both our single-trial decoding accuracies, 58.33 % (SVM20-20) and 60.93 % (SVM40-40), were rather low in comparison with previous studies. Classification results of 73 % in two-class discrimination (Sitaram et al., 2007) and 64.1 % to 75.6 % in three-class discrimination (Hong et al., 2015; Rezazadeh Sereshkeh et al., 2018) are reported. However, the limited amount of trials in the current study should be noted, whereas other studies have trained and tested their classifiers on a significantly higher number of trials. In addition, our setup of nine optodes is quite sparse in comparison to previous work (Hong et al., 2015; Rezazadeh Sereshkeh et al., 2018; Sitaram et al., 2007). Note that the correct detection of the MD and SN tasks was more balanced, as compared to the univariate analyses. Correct detection of MD ranged from 52.59 % to 72.22 %, while correct detection of SN ranged from 62.59 % to 77.78 %. This implies effective contribution of both mental imagery tasks in our multivariate analyses.

Interestingly, in the current experiment, a simplistic majority voting approach applied on the single-trial SVM decisions, resulted in heightened accuracies of 62.04 % (SVM20-20) and 75 % (SVM40-40). This type of trial combination is rarely reported in BCI literature (Nagels-Coune et al., 2017), but it seems to affect the decoding accuracy in a positive manner and could potentially be useful in clinical BCI applications.

A limitation of our multivariate approach is that the two mental imagery tasks never co-occurred within localizer runs. Classifiers were thus

trained on each distinctive task in one (SVM20-20) or two (SVM40-40) separate runs. In hindsight, it would have been better to perform both mental tasks within a run, as has been done by Valente, Kaas, Formisano, and Goebel (2019) in an MVPA-based BCI control study using fMRI.

Uni- vs Multivariate Results

Comparisons between the univariate and multivariate results should be drawn with caution given the fundamentally different nature of the methods. In the univariate analyses, the data from four channels-of-interest were considered, whereas all channels were considered in the multivariate analyses. Each analysis approach has its drawbacks for future BCI use, with the SVM approach requiring more measurement points and the GLM approach being dependent on a small subset of channels. There is no clear superiority of one approach over the other and one could think of these methods as two alternatives that can be explored depending on the BCI user's preferences and performance. Despite similar average decoding accuracies across uni- and multivariate analyses, accuracies varied largely within an individual participant. For example, the surprisingly low multi-trial decoding accuracy of 0 % in HbR for participants 17 and 18 is in stark contrast with their MVPA accuracy. In figure 5 and 8, one cannot recognize the expected hemodynamic response (positive HbO deflection and negative HbR deflection) or any other response in the signal of participant 17. The 0 % finding in the HbR signal for the multivariate analyses is thus probably due to noisy signal in combination with a low number of trials (6 trials), as both participants attain an accuracy of 33.33 % in the single-trial analysis. In addition, suboptimal channel selection due to our sparse optode setup might have contributed to these findings. Nevertheless, when looking at the

multivariate results of participant 17 and 18, we see responses above chance level. These diverging results between uni- and multivariate analyses imply that our general linear model approach, with its focus on a single channel-of-interest for each task, was not well suited to disentangle the differential spatial features of the fNIRS signal in certain participants.

Inter-Subject Variability

The inter-subject variability in our sample was substantial, both in terms of signal quality and accuracy outcomes. The large variability between participants has been recognized in other fNIRS studies (Holper, Shalom, Wolf, & Sigman, 2011; Power et al., 2012; Rezazadeh Sereshkeh et al., 2018). We have explored a few subject-specific factors that potentially influence the fNIRS signal quality and accuracy, such as hair and skin features (fNIRS suitability questionnaire) and subjective ease and pleasantness ratings of the mental tasks.

fNIRS Suitability Questionnaire

We developed an fNIRS suitability questionnaire to explore whether physical features such as hair and skin could predict fNIRS signal quality. In the current study, we found that participants who were deemed less suitable for fNIRS (as measured by our in-house questionnaire), generally had less channels with a sufficient SNR (as operationalized by CV %). The resulting significant correlation constituted a first indicator of the questionnaire's usefulness. Furthermore, the variation in SNR across participants could explain approximately 31 % of the variance in the HbR multi-trial accuracies ($R2 = .309$ with $F17 = 7.165$, $p = .017$). Note however that the fNIRS suitability questionnaire administered in the current study is an exploratory instrument and further work is needed to establish its

validity and reliability. In addition, it should be noted that we used common optode holders, as opposed to spring-loaded optode holders, in the current experiment. Common optode holders are thought to be more sensitive to signal disturbance due to hair than spring-loaded optode holders. It is thus expected that the established relationship between physical features and fNIRS signal quality will weaken in an experimental set-up with spring-loaded optode holders. However, given the participant discomfort they often cause (Lloyd-Fox et al., 2010), non-spring loaded optode holders will continue to be used in studies involving children, patients and other vulnerable populations. More extensive exploration of the effects of participants' hair, skin and head size on signal quality is required in the future. Ideally one would determine a suitability criterion that ensures sufficient SNR and thus enables detection of intentional brain activation.

Comfort, Ease and Pleasantness

Our participants generally experienced the fNIRS setup as comfortable. Despite the average decrease of comfortability across time, participants still felt comfortable in the last fNIRS runs and not a single participant indicated discomfort at any point.

Participants considered the MD significantly easier to perform than the SN. In addition the SN task was considered less pleasant than the MD task. Despite a clear trend, this difference did not reach significance. Ease and enjoyment have been shown to correlate with fNIRS decoding accuracy (Weyand & Chau, 2015). In line with these observations, ease and pleasantness correlated significantly with the SVM40-40 accuracies in the current study (see Table 3).

Unexplored User Characteristics

In half of our participants, the paradigm did not enable effective communication. While this may in part be due to the poor signal quality of the current data set, with on average 37 % of channels rejected per participant, other studies have similarly identified subgroups of participants in which fNIRS-BCI failed to work (Naito et al., 2007; Rezazadeh Sereshkeh et al., 2018). Given the general recognition of substantial inter-subject variability, the current challenge in fNIRS-based BCI research is to investigate what enables certain participants to use the BCI successfully but also what factors are hindering BCI success in other participants. Given the known correlations between EEG-BCI success and user characteristics (Weyand & Chau, 2015), a systematic investigation of user characteristics in relation to fNIRS-BCI performance is due. Factors that are thought to influence fNIRS hemodynamic signatures are age (Zich, Debener, Thoene, Chen, & Kranczioch, 2017), handedness (Kempny et al., 2016), user training (Kaiser et al., 2014), vividness of mental imagery (Cui, Jeter, Yang, Montague, & Eagleman, 2007), imagery content in combination with idiosyncratic cognitive abilities (Holper & Wolf, 2011) and mental fatigue (Sargent, Heiman-Patterson, Feldman, Shewokis, & Ayaz, 2018). Lastly, there is notable inter-subject variability in brain activation patterns elicited by certain mental tasks (Power et al., 2012; Weyand & Chau, 2015). Therefore, an individualized combination of two tasks may be most effective for controlling a binary BCI in individual users. A first effort to explore each participant's best discriminating subset of mental tasks has shown encouraging results (Weyand & Chau, 2015).

Limitations and Future Work

In the current study, three left-handed participants, *i.e.*, participants 5, 17 and 18, were asked to perform motor imagery with their non-dominant hand. Given the established hemispheric asymmetry related to handedness (Lee, Jin, & An, 2019; Maruff et al., 1999; Yokoyama, Ohtaka, Kato, Kubo, & Nakata, 2019), it is plausible that left hand imagery combined with right hemisphere fNIRS recordings would have resulted in heightened BCI decoding accuracies for these three participants. When excluding these three participants from our univariate analyses, single-trial accuracies rose to 58.44 % (HbO) and 58.00 % (HbR), previously 56.85 % and 54.81 %. Multi-trial accuracies rose to 70.83 % (HbO) and 62.50 % (HbR), previously 66.67 % and 58.33 % respectively.

The signal quality in the current data set may have been limited by our use of non-spring loaded optode holders. Recently the use of spring loaded optode holders is on the rise, as they are known to improve signal quality. Unfortunately the type of optode holders is not systematically reported in fNIRS studies, thereby limiting systematic comparison. Nevertheless, given the discomfort they often cause (Lloyd-Fox et al., 2010), non-spring loaded optode holders will continue to be used in patient studies. Therefore the current data might be representative for data we might encounter in patient population. It is known that the signal-to-noise ratio of fNIRS measurement remains a challenge in ecologically valid environments (Pinti et al., 2017; Zephaniah & Kim, 2014). Our presented fNIRS suitability questionnaire should be developed further and would ideally identify those participants with an insufficient SNR before the start of the experiment. Given this information, efforts can be made to ensure

good signal quality by for example tracking the optode-to-scalp coupling in real-time (Pollonini, Bortfeld, & Oghalai, 2016).

Another drawback of the current study is the absence of additional physiological measures. Taking measures of blood pressure, respiration and heart rate (Bauernfeind, Wriessnegger, Daly, & Müller-Putz, 2014), and regressing out these factors from our HbO and HbR signals might have improved our detection of task-specific activation. Moreover, given the absence of short-separation channels in the current study, we could not remove the influence of extra-cerebral tissue changes on the fNIRS signal (Brigadoi & Cooper, 2015). Methods such as the global component removal by Zhang et al. (2016) require optodes to cover a much larger area than the expected activated area and could thus not be applied. Mayer waves might thus have occurred in our dataset and have possibly reduced our decoding accuracies (Yucel et al., 2016). This might be especially the case for HbO as compared to HbR, given its higher sensitivity to physiological noise (Kirilina et al., 2012). Future studies should incorporate short-separation channels, as this can result in a significant improvement in both accuracy and reliability of fNIRS measurements (Brigadoi & Cooper, 2015). Such improvements are warranted for transference of fNIRS-BCI to clinical populations, as there is empirical evidence from EEG-based BCI that accuracies tend to be lower in patients as compared to healthy participants (Halder et al., 2010).

We advise future studies that employ a similar paradigm to focus on multi-trial decoding accuracies, as these proved most promising in our univariate analysis. This general linear model approach using a small set of fNIRS channels has enabled effective communication in half of our participants in either HbO or HbR signal. The good HbR decoding accuracies

were an unexpected finding and we thus advise future experiments to report both HbO and HbR signal outcomes. In addition, future experiments should perform online, real-time, analysis. This would enable direct within-session feedback, which may heighten motivation in the participants and subsequently BCI performance (Kleih, Nijboer, Halder, & Kübler, 2010; Nijboer, Birbaumer, & Kubler, 2010). Lastly, efforts to combine fNIRS with other modalities, such as EEG, have shown to improve classification accuracy significantly (Fazli et al., 2012; Rezazadeh Sereshkeh et al., 2019; Shin, Kwon, & Im, 2018; Zephaniah & Kim, 2014) and are worth further investigation.

Conclusion

The presented binary communication paradigm aimed to exploit spatiotemporal characteristics of fNIRS-signals evoked by differently timed mental imagery tasks. In various univariate analyses, the group average decoding accuracy was limited and did not exceed previously reported paradigms. The mental drawing imagery mainly drove our decoding results in the univariate analyses. Spatial navigation imagery should be explored more extensively in the context of fNIRS. Despite the rather low group average accuracies or number of participants exceeding chance level, it bears mention that those participants with a significant decoding accuracy performed excellent, with participants reaching decoding accuracies of 100 %. The multivariate results showed potential spatial discernibility in a subset of participants. Integration of the single-trial multivariate outcomes using a majority voting approach resulted in encouraging decoding accuracies. The hypothesized link between participants' physical characteristics and the fNIRS signal was confirmed with our novel fNIRS suitability questionnaire.

Supplementary Material

Binary Questions

- Do you have a brother?
- Do you own a car?
- Do you sleep before 12'o clock?
- Have you been beyond Europe already?
- Do you like sports?
- Have you ever driven a motor scooter?
- Do you like listening to classical music?
- Do you watch the news at 8'o clock?
- Were you born in Maastricht?
- Would ever like to visit the moon?
- Were you born in the Netherlands?
- Do you have a driver's license?
- Do you eat pork?
- Are you older 28 years?
- Do you have any sisters?
- Are you married?
- Is your favorite color red?
- Do you like cats?
- Do you drink coffee in the morning?
- Do you go on winter holidays?
- Do you have children?
- Do you have a smart phone?
- Were you born before 1985?
- Do you live in Maastricht?

- Do you have a dog?
- Do you live in a house?
- Did you study in Germany?
- Do you like spaghetti?
- Do you go on summer holidays?
- Do you have a laptop?
- Do you miss your hometown?
- Did you graduate in Cologne?
- Did you visit the school in Magdeburg?
- Do you want to stay forever in your current home town?
- Did you have a job while going to school?
- Do you like the summer season?
- Did you graduate in Maastricht?
- Have you ever visited USA?
- Do you like the color pink?
- Do you like to play football?
- Did you immediately find a job after your education?
- Do you like the winter season?
- Do you like to play volleyball?
- Do you like to swim in the sea?
- Do you like your hometown?

Standardized Mental Task Instructions

Mental task	Instruction
Mental drawing	During 'mental drawing', please imagine drawing simple geometric figures (such as circles, triangles, cubes, *etc.*) or small contour drawings (*e.g.*, a butterfly, star, car, tree, boat, or house). Do this with your right hand and in a comfortable but consistent speed. Try to imagine using a pen. This might support your imagination. Start from the beginning if necessary.
Spatial navigation	During 'spatial navigation', you should imagine to "go" through your house/apartment and look into the different rooms for a moment (*e.g.*, 2s). Do that in a comfortable but consistent speed. Try to really imagine vividly the various three-dimensional (3D) scenes. The order of the rooms does not matter. However, try to continuously perform this mental task (thus continuously try to imagine the 3D scene of the particular room). After having looked into all rooms of your house/apartment immediately start from the beginning and perform the spatial navigation task as long as it is indicated.
Resting	During 'resting' try relax and not to do anything, especially not to perform the mental tasks implemented in this study. Try to neglect irrelevant auditory instructions (*e.g.*, when encoding the answer "No"*).*

fNIRS Suitability Questionnaire

Hair	Features	Values	Evaluation
Hair Length	bald (naturally)	0	
	shaved	1	
	short I (<3cm)	2	
	short II (>3cm)	3	
	long (>20cm)	4	
Hair Color	(bald)	0	
	light (blond, white)	1	
	middle (dark blond, light brown, red, grey)	2	
	dark (dark brown, black)	3	
Hair (Root) Thickness	(bald)	0	
	fine	1	
	middle	2	
	dense	3	
Hair Density	(bald)	0	
	thin	1	
	middle	2	
	thick	3	
Hair Structure	(bald)	0	
	straight	1	
	undulating	2	
	curly	3	

Skin	Features	Values	Evaluation
Skin Color	light	1	
	tanned	2	
	dark	3	

Head	Features	Values	Evaluation
Head Size	< 58	0	
	58/60	1	
	> 60	2	

Total Score

Frequency of Accepted Channels per Participant

In 11 participants the same number of channels was excluded across all four localizer runs. In the remaining 7, the maximum difference in number of excluded channels between localizer runs was one (see Figure S1).

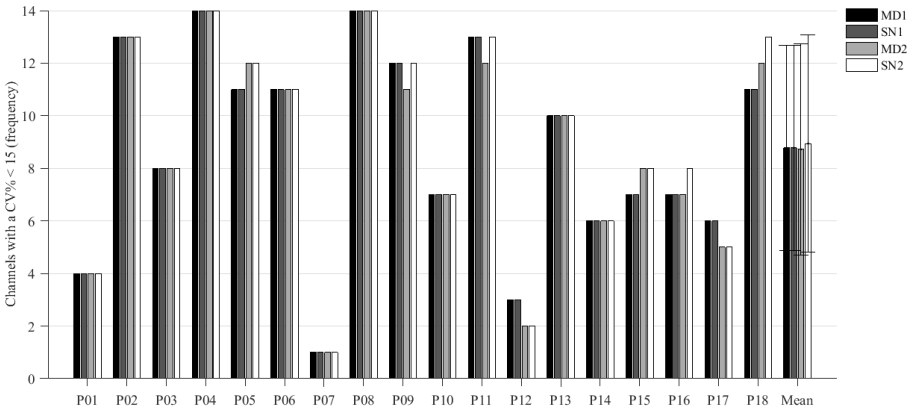

Figure S1. **Number of Channels with a Coefficient of Variance (CV %) Below 15** per participant and the sample mean. Legend abbreviations: MD1: mental drawing localizer 1 (block1); MD2: mental drawing localizer 2 (block 2); SN1: spatial navigation localizer 1 (block 1); SN2: spatial navigation localizer 2 (block 2)**.**

Univariate Results without the Channel Exclusion Step

Given the limited amount of 14 channels in the current experiment, one runs the risk of excluding a potentially informative channel due to its low SNR. Therefore, all univariate analyses were repeated omitting the CV % criterion, thus allowing different channels to be selected for subsequent analyses. Only when overall accuracy differed significantly between both approaches, the accuracies of the analyses without the CV % criterion were reported in the main manuscript.

Channel Selection

In table S1 the selected channels-of-interest (SOIs) can be seen per participant. When compared to table 1 (analysis with channel exclusion), there is a 58 % overlap in HbO SOIs and 69 % in HbR SOIs.

Participant	Mental Drawing SOIs		Spatial Navigation SOIs	
	HbO	HbR	HbO	HbR
01	C3-FC1	C3-FC1	C3-FC5	C3-FC5
02	FC3-FC1	C3-C1	C3-FC5	FC3-FC5
03	C3-CP5	CP3-CP5	CP3-CP5	FC3-C5
04	C3-FC5	FC3-C5	FC3-C5	FC3-C5
05	C3-FC5	FC3-FC1	CP3-CP5	C3-CP5
06	CP3-C5	C3-C5	FC3-C1	CP3-C5
07	CP3-CP1	CP3-CP1	C3-FC1	CP3-CP1
08	C3-FC5	C3-FC5	FC3-C1	C3-FC1
09	C3-CP5	CP3-CP1	C3-FC5	CP3-C1
10	C3-C5	C3-CP5	FC3-FC1	C3-CP1
11	FC3-C5	CP3-CP1	CP3-CP5	C3-C1
12	C3-CP1	CP3-CP1	C3-CP5	C3-CP5
13	CP3-C1	CP3-C1	C3-CP1	FC3-FC5
14	CP3-CP1	C3-C5	C3-C5	C3-C5
15	C3-C5	C3-C5	FC3-FC5	FC3-C5
16	FC3-C1	FC3-C1	C3-CP5	C3-C1
17	C3-CP1	C3-CP1	C3-FC1	FC3-FC1
18	C3-CP1	C3-C1	FC3-C1	FC3-C5

Table S1. **Channel Selection without Channel Exclusion.** The four columns show the channels-of-interest (SOIs), selected on the basis of the data of localizer runs in block 1 without the channel exclusion step. The cells with a grey background signify the channels that overlap in analyses with and without the channel exclusion step.

Single-trial Results

Univariate analysis of single-trial data resulted in an average accuracy of 55.93 % (SD = 13.89 %) and 53.33 % (SD = 14.69 %) for HbO and HbR respectively. Individual accuracies ranged from 26.67 % to 90 %. Five

participants' HbO data decoding accuracy was significant. Three participants' HbR data decoding accuracy was significant. Participant 4 was the sole participant whose answers were decoded significantly using HbO or HbR signal.

Multi-trial Results

Univariate analysis of multi-trial decoding resulted in an average accuracy of 58.33 % (SD = 25.72) and 57.41 % (SD = 33.93) using HbO and HbR data, respectively. Individual accuracies ranged from 0 % to 100 %. Four participants' HbO data decoding accuracy was significant. Seven participants' HbR data decoding accuracy were significant. The answers of participants 4, 9 and 14 were decoded significantly in both HbO and HbR signal.

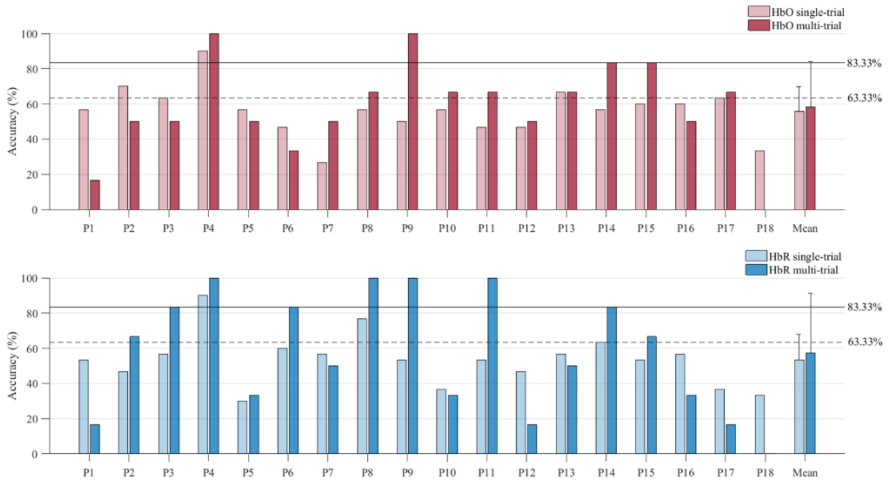

Figure S2. **Decoding Accuracies of Individual Participants and the Sample Mean** obtained with the single-trial GLM approach (light-colored bars) and the multi-trial approach (dark-colored bars). Decoding accuracies were attained through channels-of-interest, not preceded by a channel exclusion step. The upper plots show results based on analysis of HbO data (red bars), the lower plot is based on HbR data (blue bars). The horizontal lines represent the empirical chance levels of 63.33 % (dashed line, for evaluating single-trial accuracies) and 83.33 % (solid line, for evaluating multi-trial accuracies).

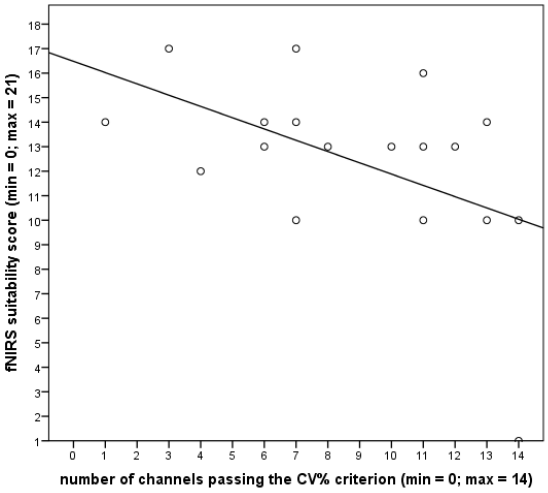

Figure S3. **Scatterplot with an SNR Measure on the x-axis and fNIRS Suitability Score on the y-axis.** SNR is operationalized as the number of channels passing the CV % criterion, with a higher number indicating better SNR. Note that the higher suitability scores on the y-axis indicate possibly less suitable participants for fNIRS measurements. The solid black line is the linear regression line.

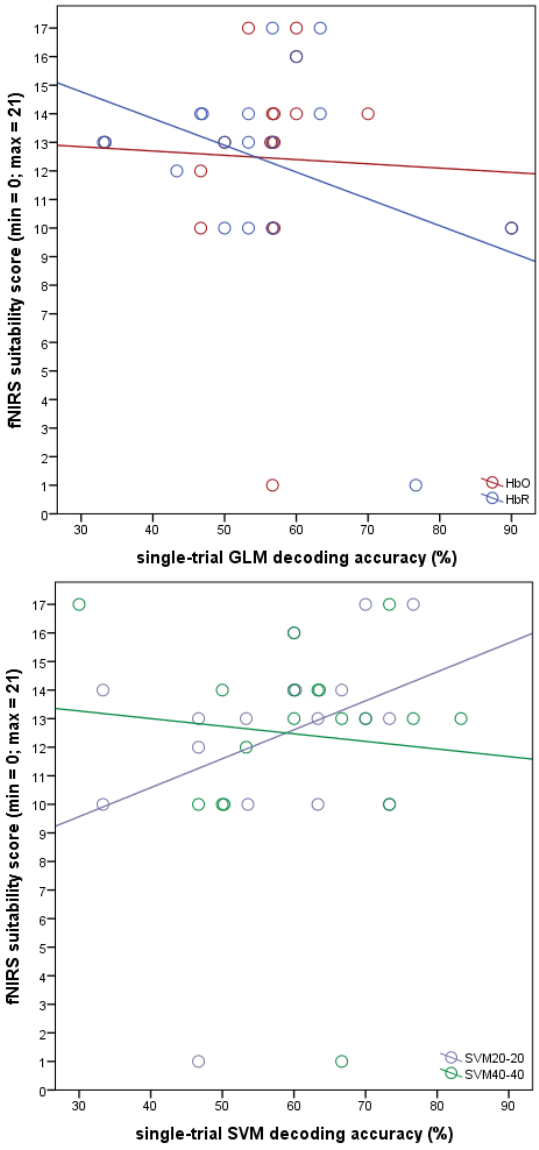

Figure S4. **Scatterplots with Single-trial Decoding Accuracy on the x-axis and fNIRS Suitability Score on the y-axis.** Upper panel: single-trial GLM decoding accuracy in function of fNIRS suitability score, grouped by data type (red circle = HbO; blue circle = HbR). The solid lines are linear regression lines per data type group. Lower panel: single-trial SVM decoding accuracy in function of fNIRS suitability score, grouped by classifier training (grey circle = SVM20-20; green circle = SVM40-40). The solid lines are linear regression lines per data type group (non-significant). Note that higher suitability scores on the y-axis indicate possibly less suitable participants for fNIRS measurements.

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4 See, Hear, or Feel to Speak: a Versatile Multiple-Choice fNIRS-BCI Feasible with Visual, Auditory, or Tactile Instructions

Based on:

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Abstract

Severely motor-disabled patients, such as those suffering from the so-called 'locked-in' syndrome, cannot communicate naturally. They may benefit from brain-computer interfaces (BCIs) exploiting brain signals for communication and therewith circumventing the muscular system. One BCI technique that has gained attention recently is functional near-infrared spectroscopy (fNIRS). Typically, fNIRS-based BCIs allow for brain-based communication via voluntarily modulation of brain activity through mental task performance guided by visual or auditory instructions. While the development of fNIRS-BCIs has made great progress, the reliability of fNIRS-BCIs across time and environments has rarely been assessed. In the present fNIRS-BCI study, we tested six healthy participants across three consecutive days using a straightforward four-choice fNIRS-BCI communication paradigm that allows answer encoding based on instructions using various sensory modalities. To encode an answer, participants performed a motor imagery task (mental drawing) in one out of four time periods. Answer encoding was guided by either the visual, auditory, or tactile sensory modality. Two participants were tested outside the laboratory in a cafeteria. Answers were decoded from the time course of the most-informative fNIRS channel-by-chromophore combination. Across the three testing days, we obtained mean single- and multi-trial (joint analysis of four consecutive trials) accuracies of 62.5 % and 85.19 %, respectively. Obtained multi-trial accuracies were 86.11 % for visual, 80.56 % for auditory, and 88.89 % for tactile sensory encoding. The two participants that used the fNIRS-BCI in a cafeteria obtained the best single- (72.22 % and 77.78 %) and multi-trial accuracies (100 % and 94.44 %). Communication was reliable over the three recording sessions with multi-trial accuracies of 86.11 % on

day 1, 86.11 % on day 2 and 83.33 % on day 3. To gauge the trade-off between number of optodes and decoding accuracy, averaging across two and three promising fNIRS channels was compared to the one-channel approach. Multi-trial accuracy increased from 85.19 % (one-channel approach) to 91.67 % (two-/three-channel approach). In sum, the presented fNIRS-BCI yielded robust decoding results using three alternative sensory encoding modalities. Further, fNIRS-BCI communication was stable over the course of three consecutive days, even in a natural (social) environment. Therewith, the developed fNIRS-BCI demonstrated high flexibility, reliability and robustness, crucial requirements for future clinical applicability.

Keywords

Functional near-infrared spectroscopy, brain-computer interface, motor imagery, mental drawing, sensory encoding modality, four-choice communication, temporal encoding, reliability over time

Introduction

The motor system plays a pivotal role in natural human communication. Any disruption to this system can negatively affect our ability to communicate. Severely motor-disabled patients lose the ability to communicate in an intuitive manner. For example, patients suffering from the 'locked-in' syndrome (Plum & Posner, 1982) are aware but have lost the ability to speak. Patients with the 'classic' locked-in syndrome and those in early stages of amyotrophic lateral sclerosis (ALS), can use eye movement for basic communication. However, some patients suffer from deficits in the oculomotor system, such as those with 'complete' locked-in syndrome (CLIS) or in late stages of ALS. These patients are particularly in need of motor-independent communication means that rely on central nervous system activation. Restoring basic communication in these patients can have a large impact on their quality of life (Kübler, Winter, Ludolph, Hautzinger, & Birbaumer, 2005; Rousseau, Pietra, & Nadji, 2012).

Brain-computer interfacing (BCI) enables motor-independent communication through brain-based encoding of intention. The BCI user willfully modifies her/his brain activation, which is recorded using functional neuroimaging and from which an answer is decoded. The most widely used imaging method in the context of BCI is the electroencephalogram (EEG), which records neuro-electric brain signals (Kübler et al., 2009; Lazarou, Nikolopoulos, Petrantonakis, Kompatsiaris, & Tsolaki, 2018; Marchetti et al., 2013; Won, Kwon, Jang, Ahn, & Jun, 2019).

However, not everyone can control an EEG-based BCI (Allison & Neuper, 2010). Especially in the late stages of ALS, when patients lose all ocular control and enter a CLIS state, interpretable visual signals are rare (Borgheai et al., 2020). This highlights the need for alternatives for the

heterogeneous population of patients who have to rely on a BCI. In this context, hemodynamic responses, relying on blood flow instead of electric signals, constitute a viable alternative. Successful communication has been demonstrated using functional magnetic resonance imaging (fMRI) paradigms in healthy participants (Sorger et al., 2009; Sorger, Reithler, Dahmen, & Goebel, 2012) and patients (Monti et al., 2010) when using two or three mental imagery tasks. Nevertheless, fMRI has its drawbacks, such as high costs, immobility and participant-specific contra-indications to being in a strong magnetic field (Irani, Platek, Bunce, Ruocco, & Chute, 2007; Naci et al., 2012; Scarapicchia, Brown, Mayo, & Gawryluk, 2017). There is a need for these promising hemodynamic paradigms to be transferred to a portable neuroimaging method that can be used in ecologically valid environments in which communication typically takes place (Naci et al., 2012; Sorger et al., 2009; Sorger et al., 2012).

Functional near-infrared spectroscopy (fNIRS) is such an alternative method. It being portable, relatively affordable and easier to operate than fMRI (Naci et al., 2012). This neuroimaging method measures the hemodynamic response using near-infrared light emitters and sensors, called optodes. The term 'channel' is used to define a specific optode pair (one emitter and one receiver optode). Cortical activity can be detected through relative concentration changes in oxygenated (HbO) and de-oxygenated (HbR) hemoglobin. Validation studies have shown that fNIRS signals correlate strongly with fMRI signals (Cui, Bray, Bryant, Glover, & Reiss, 2011; Huppert, Hoge, Diamond, Franceschini, & Boas, 2006; Scarapicchia et al., 2017), despite lower spatial resolution and signal-to-noise ratio of fNIRS.

In recent years, methodological advances in fNIRS hardware and signal processing have resulted in a steady increase of fNIRS publications (Naseer & Hong, 2015b; Pinti, Scholkmann, Hamilton, Burgess, & Tachtsidis, 2018). Similar to the fMRI paradigms, most fNIRS-BCI research has focused on binary communication via mental imagery tasks (Abdalmalak et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017; Naito et al., 2007), with a few studies showing effective decoding of four (Batula, Ayaz, & Kim, 2014; Naseer & Hong, 2015a) or six (Benitez-Andonegui et al., 2020) answer options. Mental imagery is typically guided with a single sensory encoding modality, mainly visual or auditory. Answer decoding is often done using multivariate classification techniques that rely on spatial features of the different mental imagery tasks (Batula et al., 2014; Hong, Khan, & Hong, 2018; Naseer & Hong, 2015b; Weyand & Chau, 2015). Despite the technological and methodological advances, most fNIRS-BCI studies so far have been limited to laboratory environments (Naseer & Hong, 2015b). FNIRS-BCIs have only been tested in a handful of patient studies (Abdalmalak, Milej, Norton, et al., 2017; Borgheai et al., 2020; Naito et al., 2007). For an fNIRS-BCI to reach end-users, its setup should be straightforward and flexible both in terms of answer encoding and decoding. Crucially, an fNIRS-BCI should also work reliably over time and in different environments.

Previous work from our lab has shown the potential of the temporal encoding paradigm (see Figure 1) in which answer options are presented in a serial manner (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020). Thereby, participants can perform a single mental imagery task when their chosen answer option is presented. Other fNIRS studies have used paradigms that strongly rely on spatial discrimination of brain-activation

patterns evoked by different mental imagery tasks (Batula et al., 2014; Hong et al., 2018; Naseer & Hong, 2015a; Weyand & Chau, 2015). The advantage of the temporal paradigm lies in its simplicity, which is enabled by the limited pre-training time it requires from the BCI user and the combined use of a single motor imagery task, (usually) a single fNIRS channel, and relatively basic univariate data analysis. Our lab has tested the temporal encoding paradigm using a two- (Nagels-Coune et al., 2020) and six-choice (Benitez-Andonegui et al., 2020) paradigm. In the current study, we aim to replicate the success of the temporal encoding paradigm using a four-choice paradigm. So far only two studies have tested a four-choice fNIRS-BCI in healthy participants. In a preliminary study by Batula et al. (2014), three participants used four motor imagery tasks, specifically right hand, left hand, right foot and left foot tapping, to communicate their answer. Data from the 18 fNIRS optodes was analyzed with a support vector machine, resulting in a mean single-trial accuracy of 45.7 %. Naseer and Hong (2015a) asked ten healthy participants to use four distinct mental imagery tasks, namely right-hand motor imagery, left-hand motor imagery, mental arithmetic and mental counting, to encode four answer options. Using 32 fNIRS optodes and linear discriminant analysis (LDA) to discern differentiable spatial patterns, a mean single-trial accuracy of 73.3 % was reached.

Next to a convenient fNIRS-BCI paradigm, there is a need for flexibility in term of the sensory modality that guides the user to encode an answer option. Many EEG-based BCIs have focused on the visual modality (Allison & Neuper, 2010; Brunner et al., 2010; Treder & Blankertz, 2010). However, vision is one of the most affected senses in patients in need of a BCI (Gill-Thwaites & Munday, 2004; Riccio, Mattia, Simione, Belardinelli, &

Cincotti, 2012; Rousseau et al., 2012). Therefore, the auditory encoding modality has been explored in EEG-based BCIs (Kübler et al., 2009; Simon et al., 2015; Sugi et al., 2018) and fMRI-based BCIs (Monti et al., 2010; Naci & Owen, 2013). Encoding displays in the tactile modality remain relatively unexplored, with only a few EEG-based BCIs reported (Guger et al., 2017; Kaufmann, Holz, & Kübler, 2013; Lugo et al., 2014; Muller-Putz, Scherer, Neuper, & Pfurtscheller, 2006). However, tactile encoding might provide a critical solution for patients who are unable to use either visual or auditory BCI paradigms. Kaufmann et al. (2013) reported a LIS patient in whom the tactile modality was of superior benefit compared to the visual and auditory modalities in the context of an EEG-based BCI. To our knowledge, no study has yet explored the tactile encoding modality in the context of an fNIRS-BCI. Moreover, no BCI study has systematically explored three different sensory encoding modalities within the same participants employing an identical BCI paradigm.

Another critical factor for end-users is the reliability of the fNIRS-BCI. Most fNIRS-BCI studies were performed in a single session (Abdalmalak, Milej, Norton, et al., 2017; Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017; Naito et al., 2007; Naseer & Hong, 2015a), with the exception of the recent single-case study by Borgheai et al. (2020). Test-retest reliability of fNIRS signals has been assessed in non-BCI fNIRS research (Blasi, Lloyd-Fox, Johnson, & Elwell, 2014; Plichta et al., 2006; Wiggins, Anderson, Kitterick, & Hartley, 2016). These studies have shown encouraging results at the group level but also found large variability on the individual level. Here, we will assess the reliability of the suggested 4-choice fNIRS-BCI in six individual participants over the course of three fNIRS sessions across three consecutive days. Next

to reliability over time, rehabilitation professionals have emphasized a need for BCIs to work reliably in different environments (Nijboer, 2015). The limited amount of studies that have tested an fNIRS-BCI in a non-laboratory environment, have usually done so in an environment familiar to the subject, for example their home or care center (Abdalmalak, Milej, Norton, et al., 2017; Borgheai et al., 2020; Li, Yang, & Cheng, 2021). However, a reliable fNIRS-BCI should also be able to perform in more noisy (social) environments. Therefore, two participants in our study will use the fNIRS-BCI in a cafeteria.

The simplicity of the temporal encoding paradigm developed in our lab (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017) is enabled by straightforward univariate analysis – using only the information of the participant-specific most-informative fNIRS channel-by-chromophore. Despite the initial success in communication with ALS patients using a single-channel single-wavelength approach by Naito et al. (2007), BCI studies rarely decode information from a single channel (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020). The majority of fNIRS-BCI studies use a large number of fNIRS channels and analyze data using a multivariate approach (Batula et al., 2014; Hong et al., 2018; Naseer & Hong, 2015a; Weyand & Chau, 2015). Large optode setups are generally experienced as uncomfortable and reports exist of participants withdrawing from fNIRS studies because of it (Cui et al., 2011; Rezazadeh Sereshkeh, Yousefi, Wong, & Chau, 2018; Suzuki, Harashima, & Furuta, 2010). Being able to use sparse channel setups would greatly increase clinical application and patient comfort. In addition, which chromophore, *i.e.*, HbO or HbR, is most suited for BCI purposes is still a matter of debate. HbO is most often used in BCI because of its high amplitude (Leff et al., 2011), but HbR is

thought to be less contaminated by physiological noise (Kirilina et al., 2012). Previous studies from our lab have reported a roughly comparable amount of participants in which HbO outperforms HbR and vice versa (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020). In light of this, we focus our analyses in the current study on a participant-specific most-informative fNIRS channel-by-chromophore and compare it with results obtained from averages of two and three channels, to gauge the trade-off between number of optodes and decoding accuracy.

The aims of the current fNIRS-BCI study are: (1) to replicate the success of the temporal encoding paradigm using a four-choice paradigm, (2) to explore three different sensory encoding modalities, *i.e.*, auditory, visual and tactile, within the same participants employing an identical BCI paradigm, (3) to assess the reliability of the fNIRS-BCI across time and environments, (4) to gauge the trade-off between number of optodes and decoding accuracy. To reach these aims, six participants answered four-choice questions using motor imagery, *i.e.*, mental drawing. Motor imagery was guided by the auditory, visual or tactile sensory encoding modality. Each participant performed three fNIRS sessions on three consecutive days. Two participants were tested in an ecologically valid environment, *i.e.*, a cafeteria, whereas the others were tested in a laboratory environment. Answer decoding was performed using a participant-specific most-informative fNIRS channel-by-chromophore. The possible advantage in terms of decoding accuracy of averaging two and three most-informative channels is explored. Finally, to capture the BCI users experiences, we administered several in-house questionnaires that assess motor imagery skills, mental imagery strategies, easiness and pleasantness of the three sensory encoding modalities, and level of comfort during our study.

Material and Methods

Participants

Eight participants were tested, of which two were excluded from this paper. One participant dropped out after session 2 due to personal matters, while a second participant was excluded following experimental error during the first recording session. The remaining six participants reported having no major disturbance of their visual, auditory or haptic capacities. The average age was 29.5 years (SD = 9.6) and all participants were right-handed females. Participants' characteristics that were of interest for the current BCI study are listed in Table 1. Written informed consent was acquired from each participant at the beginning of the first fNIRS session. The experimental procedure conformed to the Declaration of Helsinki and was approved by the institutional review board. All participants were compensated with gift vouchers for their participation.

Location: Lab or Cafeteria

Four participants were measured in a laboratory setting (see Table 1). These participants were measured in a separate room that was completely dark during the fNIRS session. The experimenters could communicate with the participants via a speaker system. Two participants were measured in the university cafeteria. In this location, there was considerable background noise from students passing by or sitting at a nearby table. In both locations, an overcap/shading cap was placed over the fNIRS cap to shield the detectors from overexposure to outside light that could have otherwise saturated the optodes (Pinti, Aichelburg, et al., 2018).

Participant	Age Range	fNIRS-Cap Size	Previous BCI Experience	Location	Motor Imagery Ability	fNIRS Data Analysis
P1	20-25	58	First time	Lab	13	Post-hoc
P2	20-25	56	3-4 times	Lab	14	Post-hoc
P3	25-30	58	First time	Lab	11	Post-hoc
P4	20-25	58	First time	Lab	19	Post-hoc
P5	45-50	56	> 10 times	Cafeteria	19	Real-time
P6	25-30	56	> 10 times	Cafeteria	19	Real-time

Table 1. **Participant Characteristics**. The table shows for each participant the age range (years), fNIRS capsize (cm), BCI experience, location of the fNIRS sessions, self-reported motor imagery ability (0-20) and time point of fNIRS data analysis.

Participant Preparation on Day 1

Motor Imagery Ability Questionnaire

Subjective reports of mental imagery ability have been found to correlate with objective measures of brain activation (Ahn, Cho, Ahn, & Jun, 2018; Cui, Jeter, Yang, Montague, & Eagleman, 2007; Lorey et al., 2011). In the current study, participants were asked to draw a rough sketch of a house, after which they were asked to imagine drawing the same sketch. They were encouraged to focus on the wrist and whole hand movements during the imagery period. Afterwards they were asked to rate the following five features on a 5-point Likert scale: (1) vividness of their imaginary sketch, (2) similarity of their imaginary sketch to their real sketch, (3) ease of imagination while mental drawing, (4) their imaginary skills in general and (5) enjoyment of the mental drawing task. This in-house questionnaire is based on existing questionnaires measuring related constructs (Barber & Wilson, 1978; Hall & Pongrac, 1983) and can be consulted in the Supplementary Material.

Autobiographical Questions

Autobiographical questions were created to ensure stability of answers over the three consecutive days. The six autobiographical questions can be consulted in the Supplementary Material. An example question is 'Which country were you born in?' with the answer options being 'The Netherlands', 'Germany', 'Belgium' or 'Other'. The page with the true answers of the participant was kept in a closed envelope until the fNIRS data was analyzed. Experimenters were thus blind to the reported answers during the fNIRS sessions and post-hoc analyses.

Participant Training

Participants were instructed to imagine drawing with their right hand with a comfortable and consistent speed for a duration of 10 s. We verbally suggested drawing simple contour images (*e.g.*, a house, boat, car) or small geometrical shapes (*e.g.*, cubes, triangles, circles). Participants chose their preferred image/shape, as the specific motor imagery content was not decoded by our BCI. If a mental image or shape was completed under 10 s, participants were instructed to recommence the mental drawing until they were cued to stop. During the rest periods (20 s), participants were instructed not to think about anything in particular and refrain from motor imagery. Participants were asked to practice mental drawing during three practice questions, with one question presented in each of the three sensory encoding modalities. The practice questions were selected from the autobiographical questions and followed an identical procedure to the answer-encoding runs elaborated on below (see Figure 1). The instructional part took around 15 min and the practice questions took around 5-10 min, depending on the participant. If the participant felt comfortable and had no

more questions, the fNIRS cap was placed on the participant's head and the first fNIRS run was conducted.

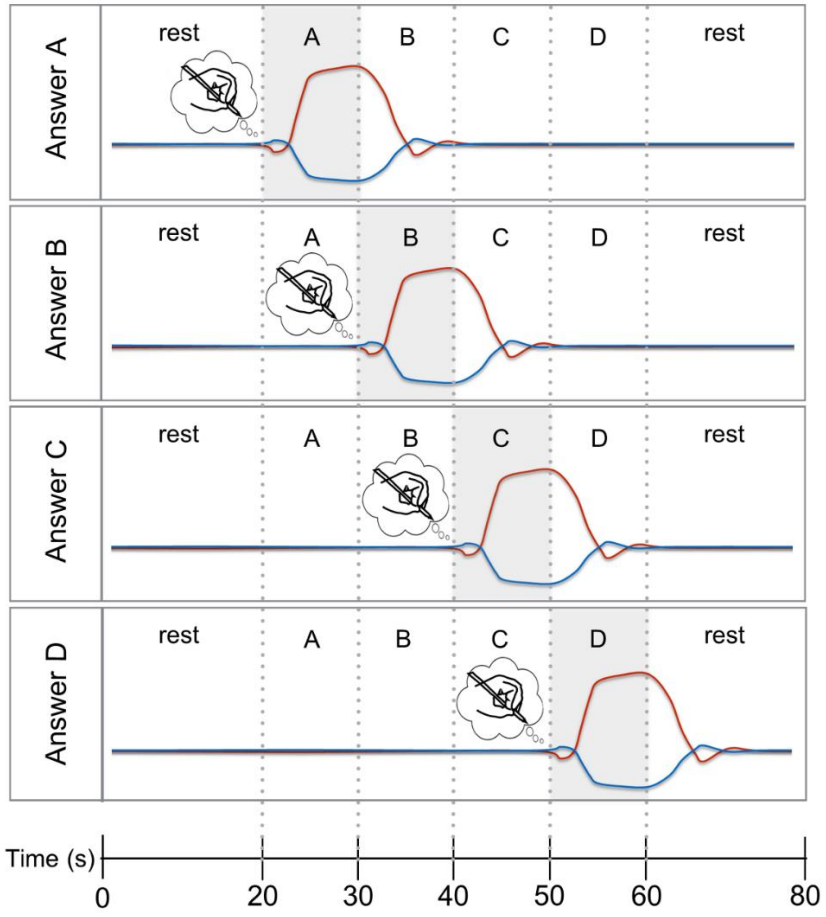


Figure 1. **Four-Choice Temporal Encoding Paradigm with Expected Time Courses.** Hypothesized HbO (red line) and HbR (blue line) responses for the four answer options "A", "B", "C" and "D". To chose answer option "A" (top panel), the participant had to start mental imagery upon the cue presented 20 s after trial onset and stop the mental imagery when answer option B was presented. For the remaining trial time, the participant had to rest and await the subsequent encoding trial. The other three panels show the hypothesized HbO and HbR response for answer options "B", "C" and "D".

fNIRS-Based Localization Procedure and Communication on Day 1, Day 2 and Day 3

Each fNIRS session consisted of seven functional runs: one localizer run and six answer-encoding runs. All fNIRS sessions were identical across the three testing days, with the questions and answer options presented in identical order, except for the sensory encoding modalities, which were counterbalanced across participants and sessions (see Figure 2). Software used for stimulus presentation were PsychoPy v.1.9 (Peirce, 2009) and NIRStim (v.3.0; NIRx Medical Technologies). Audio files were created using the text-to-speech function of NaturalReader (http://naturalreaders.com).

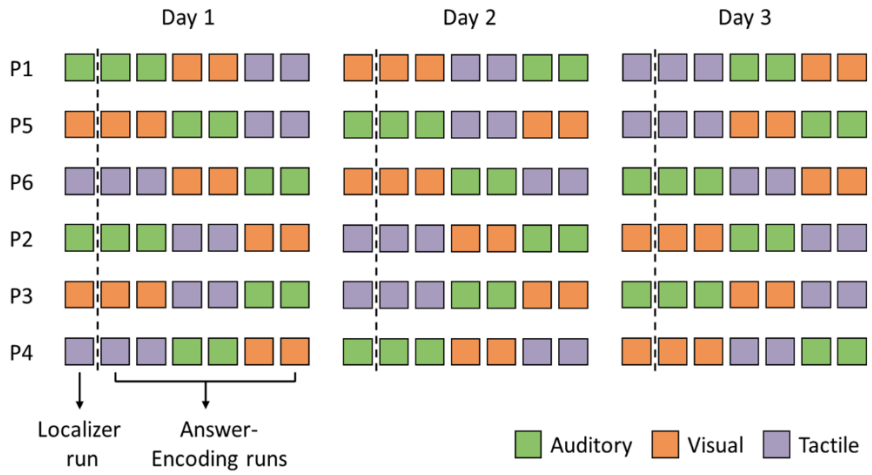


Figure 2. **Participant-Specific Experimental Protocols.** Each fNIRS session consisted of seven functional runs: one localizer run and six answer-encoding runs. Note that the three sensory encoding modalities, *i.e.,* auditory (green), visual (red) and tactile (purple), were counterbalanced across participants and sessions.

Localizer Run

The localizer run served to select a set of fNIRS channels for data analysis of the subsequently obtained answer-encoding data. After an initial 60 s rest period, the participant got the instruction to start mental drawing. After 10 s the participant got the instruction to stop mental drawing. After a rest period of 20 s, the participant was instructed to start the mental drawing again. Overall, 10 mental drawing trials with a duration of 10 s each were recorded. The total length of the localizer run was 6 min (60 s rest period + 10 x 10 s mental drawing + 10 x 20 s rest period). In the visual and auditory localizer, participants saw or heard the word 'draw' and 'rest'. In the tactile localizer, the experimenter touched the participant's hand to signal start and stop of the mental drawing. A stroke across the participant's hand signaled 'draw', whereas a soft tap on the hand signaled 'rest'.

Answer-Encoding Runs

The six four-choice questions were posed in six answer-encoding runs in every fNIRS session. At the beginning of each answer-encoding run, there was a 60 s rest period. Then, the participant heard or saw the question (7 s), after which the four answer options (10 s each) were presented serially. The participant started mental drawing when she saw/heard/felt the cue for the answer option of their choice. Presentation of the following answer option (in the case of answer A, B or C) or the cue for 'rest' (in the case of answer D), signaled to the participant to stop performing mental imagery (see Figure 1). The four answer options were serially presented five times, resulting in five trials per question/answer-encoding run. An answer-encoding run took 6 min 7 s (60 s rest period + 7 s question + 5 x 40 s mental drawing + 5 x 20 s rest period). In the visual and auditory answer-encoding runs, participants read or heard the question, answer options and

rest cue. In the tactile answer-encoding runs, the question and answer options were presented auditorily prior to the start of the run. The participant had to memorize the order of the answer options, as during the run no auditory instructions were given. The answer options were indicated by touching participant's fingers. Pinkie finger indicated answer option A, ring finger corresponded to option B, middle finger to C and index finger to D. The beginning of the resting period was communicated through a stroke over the full hand. The two participants in the university cafeteria received feedback during the fNIRS sessions, where the experimenter communicated the decoded answers to the participant after each answer-encoding run.

Questionnaire of Strategy and Comfort

After each fNIRS session, participants filled in a short questionnaire in which they were asked to shortly describe and/or draw what they imagined. They were also asked to describe how they experienced the fNIRS-BCI session. Lastly, participants were asked to rate their general level of comfort, cap comfortability and tiredness on a 10-point Likert scale (1 indicating 'uncomfortable/very tired' and 10 indicating 'very comfortable/not tired at all'). The questionnaire of strategy and comfort is provided in the Supplementary Material.

Questionnaire of General Study Impression on Day 3

On day 3, thus the last fNIRS session, participants filled in a final in-house questionnaire, which can be consulted in the Supplementary Material. This last questionnaire focused on participants' motivation, general impression, their prior BCI experience, their mental imagery experience throughout the study and their emotions while using the BCI. Participants' rated the easiness and pleasantness of the three sensory encoding modalities on a

10-point Likert scale (1 indicating 'not pleasant/easy at all' and 10 indicating 'very pleasant/easy'). Lastly, participants' rated the three encoding modalities according to their relative liking (1 = best, 2 = medium, 3 = worst).

fNIRS Data Acquisition

Data was obtained with the continuous-wave NIRScout-816 system (NIRx Medical Technologies; RRID: SCR_002491) and was recorded using NIRStar software (v14.2 & v15.2; NIRx Medical Technologies; RRID: SCR_014540). Eight light source and eight light detector optodes were installed. Sources emitted light at wavelengths 760 and 850 nm, while detectors recorded the near-infrared light, which was sampled at a frequency of 7.8125 Hz. The optodes were placed in spring loaded optode holders attached to the cap. They were positioned on known markers from the international 10- 20 EEG system (see Figure 3). The resulting 23 source-detector pairs, referred to as fNIRS channels, covered large parts of left-hemispheric fronto-parietal cortex. Frontal areas such as motor cortex (M1), supplementary motor area (SMA) and premotor cortex (PMC) are known for their activation during motor imagery (Abdalmalak, Milej, Diop, et al., 2017; Holper & Wolf, 2011; Kanoh, Murayama, Miyamoto, Yoshinobu, & Kawashima, 2009; Pfurtscheller, Scherer, Muller-Putz, & Lopes da Silva, 2008; Porro et al., 1996; Sitaram et al., 2007). Parietal areas, such as primary somatosensory cortex (S1) and intraparietal cortex, are also known to be activated by motor imagery (Aflalo et al., 2015; Fleming, Stinear, & Byblow, 2010; Lorey et al., 2011). In two participants, P1 and P2, optodes forming channels that were not selected for subsequent analyses were physically removed after the localizer run to reduce possible participant cap discomfort.

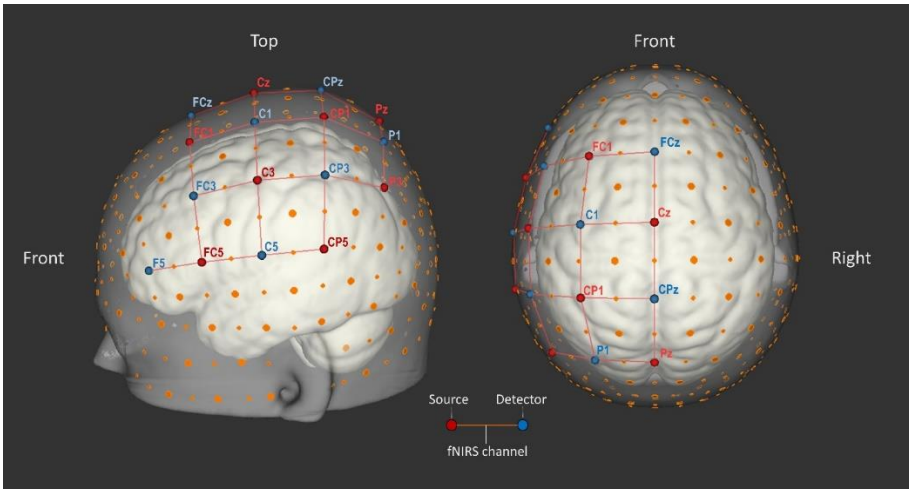


Figure 3. **Optode Layout.** Eight source (red) and eight detector (blue) optodes were placed on 16 points according to the international 10-20 EEG system. Large orange dots represent reference points of the 10-20 system, whereas small orange dots represent reference points of the extended 10-10 EEG system (Oostenveld & Praamstra, 2001). The red lines represent 23 source-detector pairs (each forming an fNIRS channel). Image created using NIRSite software (v.1; NIRx Medical Technologies; RRID: SCR_002491).

Data Analysis

fNIRS Signal Analyses

The main outcome of the current temporal encoding paradigm is communication accuracy, which was assessed as the percentage of correctly decoded answers. A set of signals-of-interest (SOIs), *i.*e., channel-by-chromophore combinations, were selected for each individual based on the participant's localizer run's data of that day. Answers were decoded from time courses of these SOIs with a univariate analysis using a General Linear Model (GLM) approach (Tak & Ye, 2014). The data of the four participants in the lab were analyzed *post hoc* in simulated real-time, whereas the data of the two participants in the cafeteria were analyzed online, *i.e.*, intra-session.

Raw Signal Processing

Firstly, signal quality was checked for each channel in each fNIRS session. A channel-wise coefficient of variance percentage (CV %; see Piper et al. (2014) for a more detailed description) was calculated using the localizer run data and an in-house Matlab script. Channels with a CV % above 15 were deemed to have poor signal-to-noise ratio and were excluded from further analysis (Pfeifer, Scholkmann, & Labruyère, 2018; Piper et al., 2014; Schmitz et al., 2005; Schneider et al., 2011).

The raw signal from the remaining channels was processed using Turbo-Satori software (v1.6.4, Brain Innovation B.V., Maastricht, Netherlands). Baseline calculations were performed on the data of the first minute of each run. Linear trend removal and moving average filtering (low-pass cut-off frequency: 0.25 Hz, filter order: 2; high-pass cut-off frequency: 0.01 Hz, filter order: 1) were applied. GLM analyses were performed on the preprocessed signal. A linear confound predictor and a high-pass confound predictor (sine + cosine) with a cutoff frequency of 0.0002 Hz were included in the GLM to account for any residual slow drifts. Residuals were corrected for serial correlations (Luhrs & Goebel, 2017).

Signal-of-Interest Selection

A participant-specific most-informative channel-by-chromophore combination was chosen based on the localizer data of that day. Two GLMs were fitted, one applied to HbO data and the other to HbR data, using a model including only a single predictor for mental drawing. The predictor was 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). The same amplitudes were used for the HbO and HbR task predictors. The contrast "mental drawing vs. rest" was computed for each channel and chromophore. The channel-by-chromophore combination revealing the highest t-value of this contrast was chosen as the SOI (Benitez-Andonegui et al., 2020). In other words, different chromophores could be selected for different participants. This subject-specific channel-by-chromophore was considered for the answer decoding in the context of the first three aims of this study. For the fourth aim (effect of signal averaging), the 2nd best SOI and 3rd best SOI were identified through selection of the 2nd and 3rd highest t-value for the chosen chromophore.

Answer Decoding

The first trial of each run was discarded from the analyses as it served as a practice ("warm-up") trial for the participant (Li et al., 2021; Moriguchi & Shinohara, 2019; Techayusukcharoen, Iida, & Aoki, 2019), resulting in four trials per answer-encoding run. Participants' answers were decoded from the time course of the SOI by judging either each trial individually (single-trial analysis) or joint analysis of the four trials per answer-encoding run (multi-trial analysis). Four GLMs were fitted per trial (single-trial analysis) or per run (multi-trial analysis) using four reference-time courses. The reference-time courses correspond to the four answer-encoding options in our design (see Figure 1). The default HRF from SPM12 was used (for details see above). The same amplitudes were used for the HbO and HbR task predictors. The contrast "mental drawing vs. rest" was computed for the SOI. This resulted in four t-values based on the four time course predictors for each of the four answer options. The answer option for which the highest t-value was obtained was chosen as the decoded answer. In the

context of our fourth research aim, *i.e.*, levels of signal averaging, four GLMs were also fitted to the 2nd and 3rd most-informative signal. The contrast "mental drawing vs. rest" was computed for each SOI. The four resulting t-values of SOI1 and SOI2 were averaged (SOI1-2), as well as the four t-values of SOI1, SOI2 and SOI3 (SOI1-2-3). The answer option for which the highest t-value was obtained was chosen as the decoded answer.

For each participant 72 single-trial answers (4 trials x 6 answer-encoding runs x 3 sessions) and 18 multi-trial answers (6 answer-encoding runs x 3 sessions) were decoded. These decoded answers were then compared to the true answers, *i.e*., the answers participants noted down before the first session. Our main outcome measure, decoding accuracy (in %), was calculated for each participant by dividing the number of correct answers by the total amount of answers, *i.e.*, 72 for the single-trial and 18 for the multi-trial approach. In the context of the research aims 2 and 3, *i.e.*, exploring sensory encoding modality and reliability over time, the decoded answers were split in three groups, *i.e*., per modality (auditory, visual and tactile) and per fNIRS session (day 1, day 2 and day 3). The number of correctly decoded answers was divided by the total amount of answers, *i.e.*, 24 for the single-trial and 6 for the multi-trial approach, to attain decoding accuracies. Lastly, the group mean was calculated together with the standard deviation. In the context of research aim 4, *i.e*., different levels of signal averaging, all 72 single- and 18 multi-trial decoded answers were considered. Decoding accuracies, were calculated for each participant and for each level of signal averaging (SOI1, SOI1-2 and SOI1-2-3) by dividing the number of correct answers by the total amount of answers. Also here the group mean was calculated together with the standard deviation.

Chance Level Definition

The theoretical chance level of our four-choice BCI is 25 %. However, given the limited amount of trials within a single participant, common in BCI studies, a threshold based on binomial distribution is considered more trustworthy and therefore more frequently used (Noirhomme et al., 2014). To assess the significance of each participants' decoding accuracy in the current study, chance levels were calculated based on a binomial distribution. The number of independent outcomes was four ($k = 4$) and the significance level was set at 5 % ($\alpha = 0.05$). For the single-trial results the number of independent trials was 72 ($n = 72$), resulting in the upper-bound chance level of 33.33 %. In other words, if 24 or more trials out of 72 were decoded correctly this was considered a significant result. For the multi-trial results the number of independent trials was 18 ($n = 18$), resulting in an upper-bound chance level of 44.44 %. If 8 or more trials out of 18 were decoded correctly this was considered a significant result. The chance levels of 33.33 % (single-trial) and 44.44 % (multi-trial) were used to evaluate the general decoding accuracies (aim 1) and the effect of signal averaging (aim 4). For evaluation of the participants' decoding accuracies per sensory encoding modality (aim 2) and per fNIRS session (aim 3), the chance level was 41.67 % (single-trial, $n = 24$) and 50 % (multi-trial, $n = 6$).

Subjective Measures

The ratings on the five features of the motor imagery ability questionnaire were summed to obtain a single motor imagery ability score, with a maximum score of 20. Two Pearson correlation coefficients ($\alpha = 0.05$) were computed to assess the relationship between the motor imagery ability score and single- and multi-trial decoding accuracies, both decoded from

the single most-informative channel-by-chromophore. All remaining in-house questionnaires are reported on a descriptive level, *i.e.*, sample average and standard deviation ($\bar{x} \pm SD$), given our small sample size.

Results

Signal of Interest Selection

All channels had sufficient signal quality, with a CV % below 15 across the three sessions. For each participant a single best-suited channel-by-chromophore combination was selected (see Supplementary Figure 1 and Supplementary Table 1). In two participants, an HbO channel was the most informative channel across all sessions. In another two participants, HbR was the most informative chromophore across all sessions. In the remaining two participants, either HbO or HbR was selected depending on the session. The event-related averages of the chosen channel-by-chromophore combinations are shown in Figure 4. The most informative fNIRS channels across all participants and sessions were FC5-FC3 and C3-C5, both chosen in five out of 18 cases (six participants × three fNIRS sessions). In the Supplementary Figure 2 and Supplementary Table 2, detailed information on the channel selection frequency for the 1st, 2nd and 3rd most informative channel selection is provided.

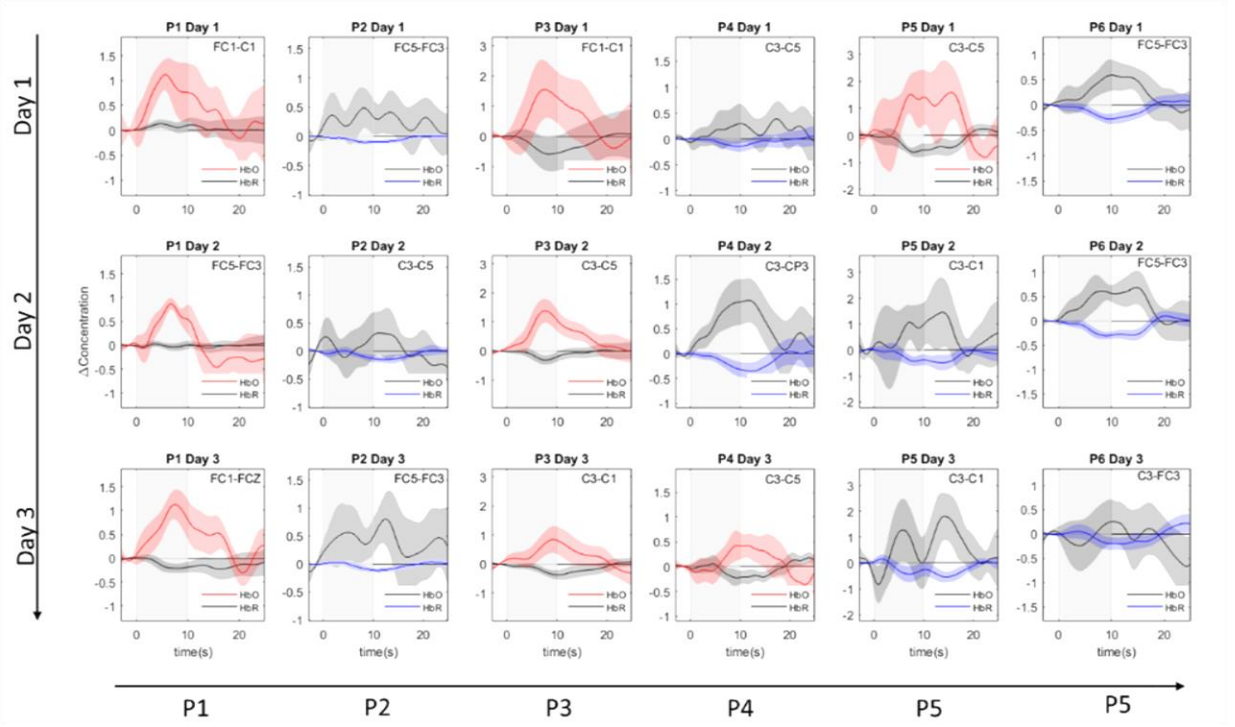


Figure 4. **Subject Specific Event-Related Averages.** Event-related averages for the most-informative channel-by-chromophore combination for each participant (columns) in each session (rows). The shaded rectangle represents the mental task duration (10 s). The event-related averages are depicted from 3 s before until 15 s after mental task performance. The selected channel can be read in the right upper corner. Colored lines depict the average concentration change of the selected chromophore: red for oxygenated hemoglobin (HbO) and blue for deoxygenated hemoglobin (HbR). For completeness, grey lines depict the chromophore counterpart belonging to the most-informative channel. The shaded area around the mean average line represents the 95% confidence interval of the mean.

Mean Answer-Decoding Accuracies

Each of the six individual participants reached a decoding accuracy significantly above the chance level for both single- and multi-trial analyses (see Figure 5). As expected, the multi-trial answer decoding outperformed the single-trial approach in each participant. Individual single-trial decoding accuracies ranged from 47.22 % to 77.78 %, whereas multi-trial decoding accuracies ranged from 72.22 % to 100.00 %. The group mean of the single-trial approach was 62.50 % (*SD* = 12.42), whereas the multi-trial group mean was 85.19 % (*SD* = 12.51). Note that all answers of participant 5 were decoded correctly across the three sessions using the multi-trial analysis, resulting in a 100 % accuracy. For participants 4 and 6, 17 out of 18 answers were decoded correctly using the multi-trial analysis, resulting in a 94.44 % accuracy.

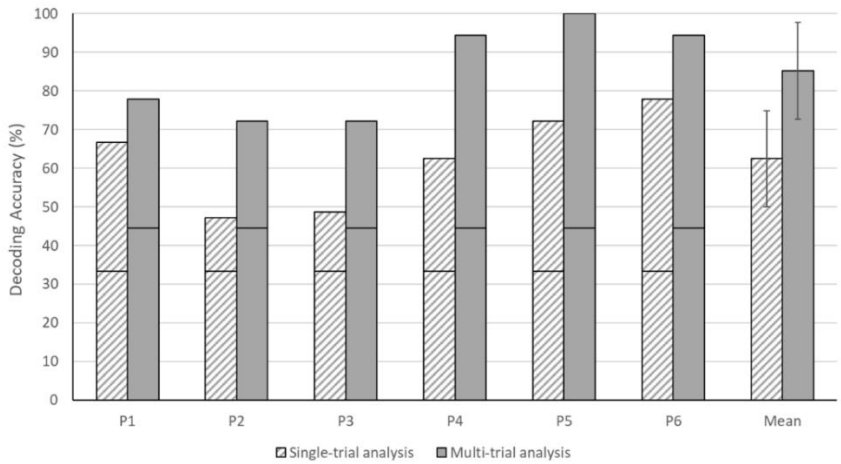


Figure 5. **Single- and Multi-trial Answer Decoding Accuracies for Individual Participants and the Group Mean.** The black horizontal stripe within each bar graph represents the chance level for single-trial (33.33 %) and multi-trial (44.44 %) accuracies. The error bars depict the standard deviation of the group mean. Note that all participants performed above the chance level in both analyses.

Answer-Decoding Accuracies across Sensory Encoding Modalities

In the single-trial approach, mean accuracies of 58.33 % (*SD* = 16.24) were obtained for the auditory, 65.97 % (*SD* = 20.14) for the visual and 63.19 % (*SD* = 11.91) for the tactile modality (see Figure 6). In four participants, decoding accuracies obtained with each of the three sensory encoding modalities were significant (chance level of 41.67 %). In two participants, one encoding modality did not reach significance (visual [P2], auditory [P3]; see Figure 7). In the multi-trial approach, mean accuracies increased to 80.56 % (*SD* = 19.48) for the auditory, 86.11 % (*SD* = 19.48) for the visual and 88.89 % (*SD* = 13.61) for the tactile modality (see Figure 6). In all participants, accuracies with respect to the three encoding modalities reached or surpassed the chance level of 50 % (see Figure 7). In one participant, *i.e.*, participant 5, all three encoding modalities reached 100 % accuracy.

Answer-Decoding Accuracies across Time

For the single-trial decoding accuracies, a slightly declining trend can be observed, with 68.75 % on day 1 (*SD* = 19.14), 63.89 % on day 2 (*SD* = 20.36) and 54.86 % on day 3 (*SD* = 19.26; see Figure 6). In three participants, accuracies were significant in all three fNIRS sessions (chance level of 41.67 %). In the three remaining participants, one fNIRS session did not reach significance (session 1 [P1], session 3 [P2 & P3]; see Figure 8). In the multi-trial approach, group mean decoding accuracies remained relatively stable across the three consecutive fNIRS sessions, with 86.11 % on day 1 (*SD* = 26.70), 86.11 % on day 2 (*SD* = 22.15) and 83.33 % on day 3 (*SD* = 21.08; see Figure 6). In all five participants, the three fNIRS sessions reached

or surpassed the empirical chance level of 50 % (see Figure 8). In one participant, one fNIRS session did not reach significance (session 1 [P1]).

Answer-Decoding Accuracies across Different Degrees of Channel Averaging

In the single-trial approach, decoding accuracies improved slightly when averaging two or three channels, from 62.50 % [SOI1; *SD* = 12.42] to 68.75 % [SOI1-2; *SD* = 8.77] and 65.74 % [SOI1-2-3; *SD* = 6.67], compared to when analyzing a single channel-by-chromophore (see Figure 6). In five participants, namely P1, P2, P3, P4 & P5, averaging across two or three channels resulted in an improved decoding accuracy (see Figure 9). In the multi-trial approach, decoding accuracies also increased slightly when averaging across two or three channels. from 85.19 % [SOI1; *SD* = 12.51] to 91.67 % [SOI1-2; *SD* = 13.03] and 91.67 % [SOI1-2-3; *SD* = 9.78]; see Figure 6). In four participants, namely P1, P3, P4 & P6 channel averaging with either two or three channels improved decoding accuracy (see Figure 9). In one participant, P5, the single channel multi-trial decoding accuracy was already perfect and hence channel averaging could not further improve this score.

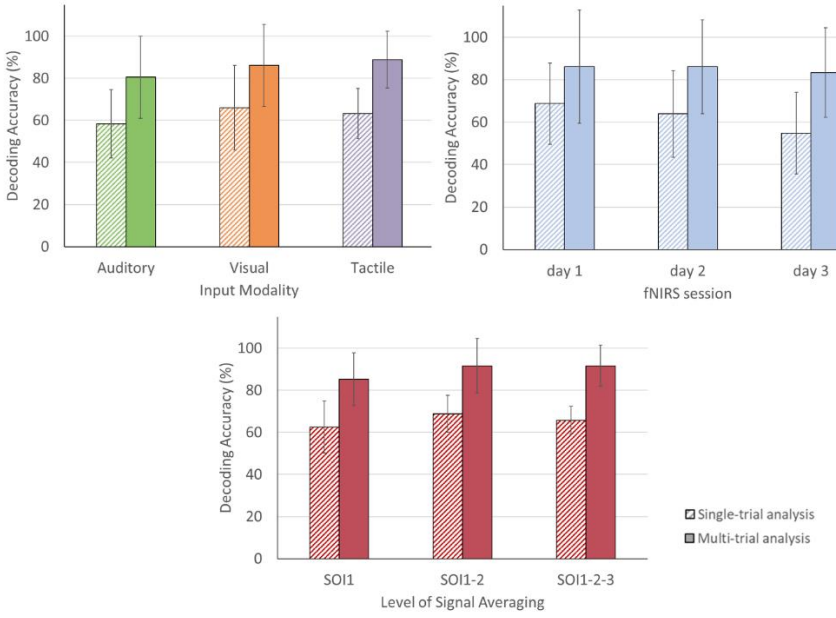


Figure 6. **Single- and Multi-trial Group Mean Answer Decoding Accuracy per Sensory Encoding Modality, fNIRS Session and Level of Signal Averaging.** Accuracies are depicted for the single-trial (striped bars) and multi-trial (solid bars) analysis. *Top left*: Accuracies according to sensory encoding modality. Note that all sensory encoding modalities were effective. *Top right*: Accuracies according to fNIRS session. Note that the multi-trial accuracies remained relatively stable over the three fNIRS sessions. *Bottom*: Accuracies according to level of signal averaging. Note that averaging across two (SOI1-2) or three (SOI1-2-3) signals slightly outperforms the single channel-by-chromophore approach (SOI1). The error bars depict the standard deviation of the group mean. *Abbreviations*: SOI = signal-of-interest.

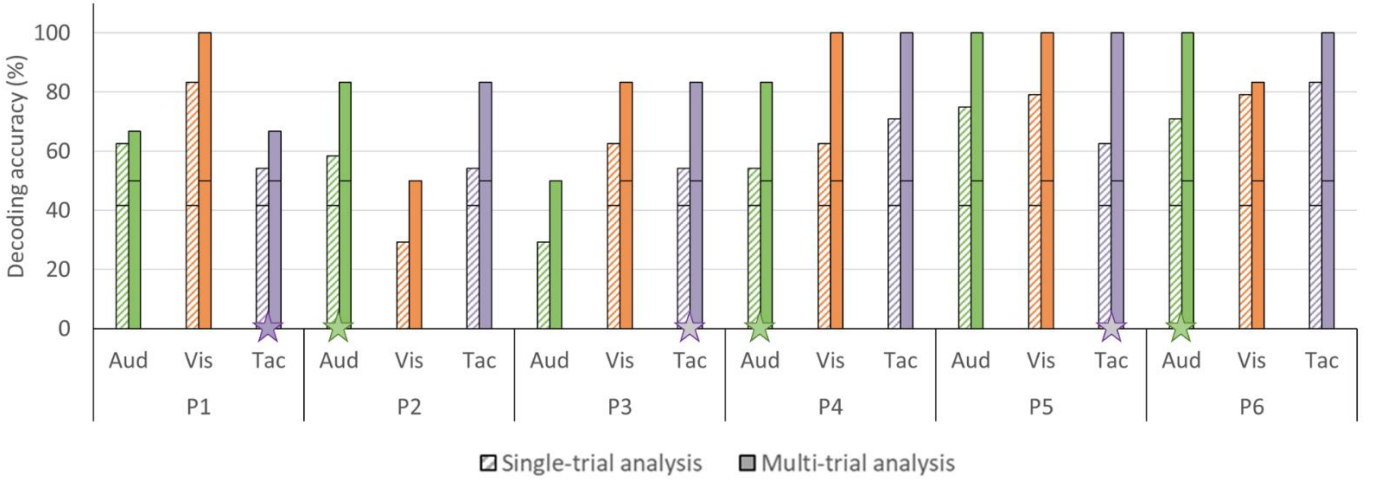


Figure 7. **Single- and Multi-trial Individual Decoding Accuracies per Sensory Encoding Modality.** Individual decoding accuracies for the auditory (green), visual (orange) and tactile (purple) encoding modality obtained with single-trial (striped bars) and multi-trial (solid bars) analysis. The black horizontal stripe within each bar graph represents the chance level for single-trial (41.67%) and multi-trial (50.00%) accuracies. The stars on the horizontal axis mark participants subjectively preferred sensory encoding modality. *Abbreviations:* Aud = auditory; Vis = visual; Tac = tactile.

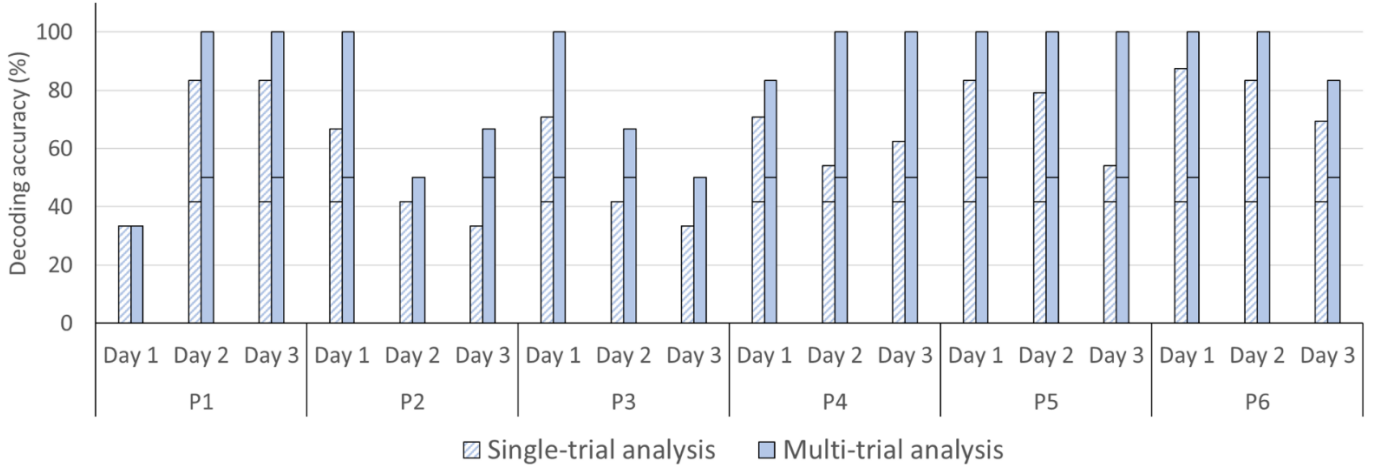


Figure 8. **Single- and Multi-trial Individual Decoding Accuracies across fNIRS Session.** Individual decoding accuracies for the 1st fNIRS session (day 1), 2nd fNIRS session (day 2) and 3rd fNIRS session (day 3) obtained with single-trial (striped bars) and multi-trial (solid bars) analysis. The black horizontal stripe within each bar graph represents the chance level for single-trial (41.67%) and multi-trial (50.00%) accuracies.

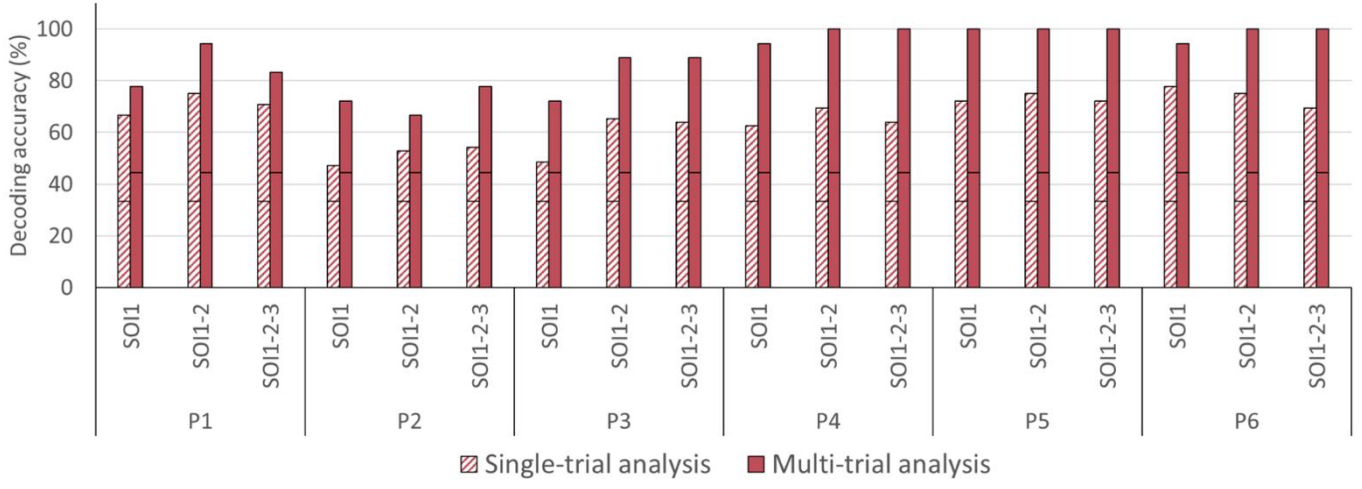


Figure 9. **Single- and Multi-trial Individual Decoding Accuracies across Level of Signal Averaging**. Individual decoding accuracies for the most informative channel-by-chromophore (SOI1), the average of the two most informative channel-by-chromophore (SOI1-2) and the average of the three most informative channel-by-chromophore (SOI1-2-3) obtained with single-trial (striped bars) and multi-trial (solid bars) analysis. The black horizontal stripe within each bar graph represents the chance level for single-trial (33.33%) and multi-trial (44.44%) accuracies.

BCI user experience

General BCI Experience

Four participants chose to mentally draw a house. One participant chose to mentally draw a house with a tree next to it and another participant imagined drawing small cubes. Participants felt generally comfortable during the fNIRS sessions (rating 7.72/10 ± 1.53). All participants reported feeling confident using the system. No participant reported feeling anxious. The fNIRS cap with spring-loaded optodes was experienced as reasonably comfortable (rating 6.72/10 ± 2.32), with 5 out of 6 participants reporting to have felt comfortable using the system. Two participants did report some discomfort during a single fNIRS session, with a few of the optodes causing noticeable pressure on the head. Participants did not experience significant fatigue (6.28/10 ± 1.93) during the experiment. Moreover, general comfort, cap comfort and fatigue remained relatively stable over the three fNIRS sessions (see Supplementary Figure 3). None of the participants reported a lowering motivation over the course of the fNIRS sessions.

General and Individual Preference of Sensory Encoding Modality

The auditory modality was judged as being the most pleasant (8.50/10 ± 0.55) and easy (9.00/10 ± 0.63) sensory encoding modality, followed by the tactile modality (pleasantness 7.83/10 ± 0.41; easiness 8.16/10 ± 1.33). Participants' judgement with respect to the visual modality were generally lower (pleasantness 5.60/10 ± 2.34; easiness 6.50/10 ± 1.38) and less in agreement, as reflected in a relatively large standard deviation (see Figure 10). Three participants preferred the auditory encoding modality, whereas the other three participants preferred the tactile encoding modality. No participant preferred the visual encoding guidance. Four participants

indicated in the remarks section that not being able to close their eyes hindered performing mental imagery. Participant 5 and 6 were measured in a naturalistic environment and both indicated that the auditory and tactile runs were more pleasant/relaxing than the visual runs because they could either look around or close their eyes, instead of having to fixate on the screen. P2 and P3 had identical multi-trial accuracies in the tactile modality (see Figure 7) but expressed differential subjective experiences. While P2 indicated that she became more uncomfortable during the tactile runs due to the presence of an experimenter, P3 felt more confident and reassured with the experimenter present.

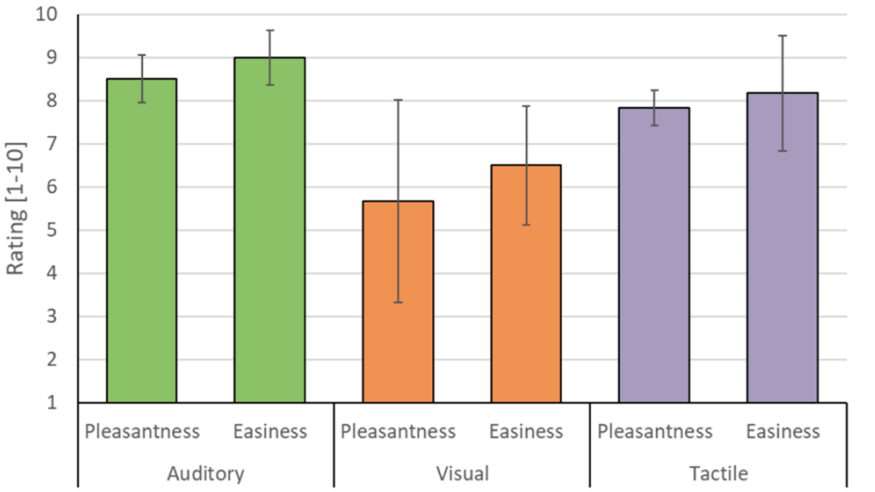


Figure 10. **Mean Participant Rating of Perceived Pleasantness and Easiness for Each of the Three Sensory Encoding Modalities**. Participants rated the auditory (green), visual (orange) and tactile modality (purple) on a scale from 1 (not pleasant/easy at all) to 10 (very pleasant/easy). Error bars depict the standard deviation of the group mean. Note that the auditory and tactile modality were rated as relatively more pleasant and easy compared to the visual modality.

Motor Imagery Ability Questionnaire

Participants' mental drawing was generally vivid (rating 3.33/4 ± 0.82) and judged similar to their sketch (3.17/4 ± 0.98). They found the mental

drawing task easy (3.33/4 ± 0.82) and enjoyable (2.83/4 ± 0.75). Participants judged their general imagination as being good (3.17/4 ± 0.98). The total scores on the motor imagery ability questionnaire (15.83/20 ± 3.60) are reported in Table 1. Self-reported motor imagery ability correlated significantly with the multi-trial decoding accuracies ($r(4)= 0.95$; $p < 0.01$), but not with the single-trial decoding accuracies ($r(4)= 0.73$; $p = 0.10$; see Supplementary Figure 4).

Discussion

The results show that the temporal answer-encoding paradigm, recently developed by our group (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017), is a an effective and convenient paradigm. Using a simple motor imagery task, relatively little preparation time and only a single fNIRS channel-by-chromophore combination, the paradigm enables effective and efficient four-choice BCI-based communication. Moreover, it is highly flexible as it allows for exploiting three different sensory encoding modalities (auditory, visual and tactile) for guiding answer encoding. Visual and auditory answer encoding in fNIRS-BCIs have been reported previously (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017; Naito et al., 2007; Naseer & Hong, 2015a) but tactile guidance was explored here for the first time, with encouraging results. Moreover, the results based on six participants demonstrate reliable communication over the course of three consecutive days. Note that two of the six participants were tested under more ecologically valid conditions in a university cafeteria (vs. in a laboratory). In the following sections, the implications of the current study

will be discussed in more detail, followed by limitations of the current and recommendations for future work.

Temporal Answer Encoding – an Effective and Convenient BCI Paradigm

Many fNIRS-BCI studies have exploited the differential spatial brain activation patterns associated with the execution of two or more mental imagery tasks (Batula et al., 2014; Li et al., 2021; Naseer & Hong, 2015a, 2015b). In previous work we combined the spatial features with a temporal component in the context of a binary fNIRS-BCI (Nagels-Coune et al., 2020). The decoding accuracy reached 66.67 % (HbO) and 58.33 % (HbR), with a subset of participants merely relying on the temporal aspect. Benitez-Andonegui et al. (2020) followed up with a six-choice fNIRS-BCI based on a purely temporal encoding, *i.e.*, using only one mental imagery task, reaching an accuracy of 73.96 %. In the current experiment, the temporal answer-encoding paradigm was tested in the context a four-choice fNIRS-BCI (see Figure 1). The single-trial decoding accuracy of 62.50 % (see Figure 5) obtained in this work is decent, given that other 4-choice fNIRS-BCI applications reached single-trial accuracies of 45.7 % (Batula et al., 2014) and 73.3 % (Naseer & Hong, 2015a). Note however that in both of these studies, large arrays of 18 (Batula et al., 2014) and 32 (Naseer & Hong, 2015a) fNIRS optodes were used to discern differentiable spatial brain activation patterns between four imagery tasks. In the current study, a single channel-by-chromophore was analyzed and participants performed a single imagery task. We found an average multi-trial decoding accuracy of 85.19 %, with each individual participant showing significant decoding accuracies (see Figure 5). One participant, P5, even reached 100 % decoding

accuracy across the three fNIRS sessions. A joined analysis of several encoding trials per answer (multi-trial analysis) substantially increased the decoding accuracy, as has been reported previously (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017).

The temporal answer-encoding paradigm presented here has many advantages due to its simplicity. Firstly, participants use a single mental imagery task, which reduces working memory load. Secondly, there is no need for a lengthy period for training a classifier, given that decoding analyses rely on straightforward GLM analysis (see Methods and Materials section). In the current experiment, 6 min localizer runs were performed by each participant to identify channels of interest. Note that in EEG-BCIs, users often need considerably longer training periods to be able to control their brain rhythms (Pires, Nunes, & Castelo-Branco, 2012), whereas in multivariate fNIRS-BCIs classifiers need extensive training datasets (Batula et al., 2014; Naseer & Hong, 2015a). However, a possible disadvantage of the temporal encoding paradigm, compared to multivariate classification methods, is that answer-encoding trials tend to take more time. For example, in the four-choice fNIRS-BCI study by Naseer and Hong (2015a) a single trial lasted only 10 s (compared to 40 s in the current study). Thirdly, we show here that, in principle, the information obtained from a single fNIRS channel-by-chromophore combination suffices for successfully using the developed fNIRS-BCI. Note that in two participants many of the optodes were removed after the localizer run that served to identify the most-informative channel. The possibility to rely on a single fNIRS channel increases the comfortability of the fNIRS-BCI and the overall aesthetics, factors often overlooked but being vital for the technology acceptance by users (Nijboer, 2015). Moreover, use of a small optode array could pave the

way to cost reduction of fNIRS hardware (Tsow, Kumar, Hosseini, & Bowden, 2021). Fourthly, encoded answers/commands can be decoded relatively easily in real-time with a basic GLM approach. In the current study, two participants received immediate feedback on their decoded answers. By using an existing commercially available software, here the Turbo-Satori software (Luhrs & Goebel, 2017) that particularly focuses on usability, we are one step closer to an fNIRS-BCI manageable by even caregivers and family members themselves. With this work, we further encourage fNIRS-BCI researchers to exploit the temporal features of the fNIRS signal for information encoding, next to using the spatial fNIRS-signal features that have been used so far (Batula et al., 2014; Hong et al., 2018; Naseer & Hong, 2015a; Weyand & Chau, 2015). The further exploration of a wide variety of paradigms might be necessary when taking into account the heterogeneous population of patients in need of a BCI.

The Alternative Use of Different Sensory Encoding Modalities – A Promise for Clinical Applications

Most fNIRS-BCIs using mental imagery have used either the visual or auditory modality to guide answer encoding (Abdalmalak, Milej, Norton, et al., 2017; Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017; Naito et al., 2007; Naseer & Hong, 2015a). However many of the target users have their vision affected (Gill-Thwaites & Munday, 2004; Riccio et al., 2012; Rousseau et al., 2012). Even target users with intact vision might prefer alternative encoding modalities, as a screen might exclude the user from ongoing social interactions (Nijboer, Plass-Oude Bos, Blokland, van Wijk, & Farquhar, 2014). The current work reported the first multimodal fNIRS-BCI that alternatively incorporated

auditory, visual and tactile sensory encoding within one experimental paradigm. Both the single- and multi-trial decoding accuracies were found to be above chance, being 58.33 % and 80.56 % for auditory, 65.97 % and 86.11 % for visual and, 63.19 % and 88.98 % for tactile encoding respectively (see Figure 6). These accuracies suggest that the fNIRS-BCI can work effectively with different sensory encoding modalities in healthy participants. Depending on the specific needs and preferences of potential patient BCI users, promising sensory encoding modalities can be selected. In the current work, three participants preferred the auditory modality, whereas the other three participants preferred the tactile modality (see Figure 7). Subjective preference can aid researchers to select a subject-specific optimal sensory encoding modality. For example, P2 had an identical multi-trial decoding accuracy using the auditory and tactile encoding modality, but subjectively preferred the auditory modality to guide motor imagery (see Figure 7). In the case of P2, choosing the auditory sensory encoding modality for future fNIRS-BCI use is an optimal decision.

To our knowledge, the current work is the first exploration of a tactile fNIRS-BCI. An experimenter stroked the BCI user's fingers and hand at specified times to cue possible on- and offsets of mental imagery. Using this basic approach, each individual participant reached significance in the multi-trial analysis (see Figure 7). Tactile stimulation provided by a person can be considered an advantageous technical simplification, but one could also easily use an electric stimulation device to administer the tactile guidance (Guger et al., 2017; Lugo et al., 2014). Such experimental decisions might also depend on the subjective experience of the BCI user. In our study, participants expressed differential subjective experiences with the tactile encoding modality. While P2 indicated feeling more uncomfortable

during the tactile runs due to the presence of an experimenter, P3 felt more confident and reassured with the experimenter in the room. A recent EEG-BCI study found that social presence and emotional support can enhance BCI accuracy for non-autonomous people, *i.e.*, people that prefer to work in group (Pillette et al., 2020).

Participants generally experienced the auditory sensory encoding modality as pleasant (8.50/10 ± 0.55) and easy (9.00/10 ± 0.63), followed by the tactile modality (pleasantness 7.83/10 ± 0.41; easiness 8.16/10 ± 1.33) and lastly the visual modality (pleasantness 5.60/10 ± 2.34; easiness 6.50/10 ± 1.38). Participants reported being hindered by the constraints of the visual encoding in terms of concentration/fixation on the screen. This could be due to visual fatigue, as well as general annoyance of feeling 'not socially present' (Nijboer et al., 2014). Another possible factor is the orthogonality of the sensory encoding modalities with respect to the mental task. The mental imagery task used here, *i.e.*, mental drawing, is partly based on visual imagination. Therefore, auditory or tactile instruction modalities might have been experienced as less hindering of the – partly visual - motor imagination.

A Reliable fNIRS-BCI over Time and Environments

Most fNIRS-BCI studies were performed in a single session (Abdalmalak, Milej, Norton, et al., 2017; Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017; Naito et al., 2007; Naseer & Hong, 2015a) but effectiveness over time is a crucial factor for end users. The findings here show that our fNIRS-BCI works reliably over the course of three consecutive days, with multi-trial accuracies of 86.11 % on day 1, 86.11 % on day 2 and 83.33 % on day 3 (see Figure 6). In the single-trial

decoding accuracies a slightly declining trend can be observed, with 68.75 % on day 1, 63.89 % on day 2 and 54.86 % on day 3 (see Figure 6). Although participants reported no decline in motivation across the fNIRS sessions, it is plausible that use of the fNIRS-BCI was less exciting on day 3. Therefore, participants might have been less focused on the task at hand in the final session. The only other longitudinal fNIRS-BCI study also reported no decline in BCI performance by an ALS patient (Borgheai et al., 2020).

Next to reliability over time, rehabilitation professionals have emphasized a need for BCIs to work reliably in different environments (Nijboer et al., 2014). Most fNIRS-BCIs that were tested outside the laboratory took place in a familiar and calm location such as the home or a care center (Abdalmalak, Milej, Norton, et al., 2017; Borgheai et al., 2020; Li et al., 2021). However, people with severe disabilities may leave their home and need to be able to communicate in varying contexts (Nijboer et al., 2014). Given the mobility of fNIRS hardware and its relative robustness against user head motion, fNIRS-BCIs may provide a useful opportunity in this context. In the current work, an fNIRS-BCI was tested in two healthy participants, P5 and P6, in a noisy and public place, which led to multi-trial accuracies of 100 % and 94.44 % (see Figure 5). These results are relatively high in the BCI field, where 70 % accuracy is a common criterion in binary studies (Kübler, Mushahwar, Hochberg, & Donoghue, 2006). Note, however, that both participants had ample prior BCI experience (see Table 1) which might have facilitated their high accuracies. In addition, these participants received online feedback on the decoded answer, which might have had a beneficial effect on the participants' general motivation. Participants that are more engaged in task performance are thought to produce more robust brain signals in a context of BCI (Nijboer, Birbaumer,

& Kubler, 2010; Nijboer et al., 2008). Given these encouraging results in two participants, future research may further explore the use of fNIRS-BCIs in more ecologically valid environments.

Decoding from a Single Channel or Multiple Channels? – An individual Matter

As a first approach, answer decoding was based on information obtained from a single fNIRS channel-by-chromophore combination. As in previous work from our group (Benitez-Andonegui et al., 2020; Nagels-Coune et al., 2020; Nagels-Coune et al., 2017), we found that the most-informative chromophore is subject-specific. While selection of the most-informative chromophore, *i.e*., HbO or HbR, was quite stable within four subjects, for two participants the selected chromophore varied across sessions. The latter might be caused by the fact that fNIRS-cap placement (although performed as precise and consistent as possible across fNIRS sessions) might still result in inevitable variation of optode location. Another cause for variation in the selected chromophore might be the presence of physiological noise, which might differ across participants and even days. Currently there is no consensus that one chromophore outperforms the other in terms of signal quality (Kohl et al., 2020). Considering both chromophores, which is rarely done in fNIRS-BCI's, seems the fair route until intensive investigation favors one chromophore over the other. This reasoning and our observations motivated to individually determine the best channel-by-chromophore combination per communication session.

We further investigated whether averaging two or three most informative fNIRS channels (compared to using a single channel-by-chromophore) improves answer-decoding accuracy. For participants

showing high decoding accuracies using the single most-informative channel-by-chromophore, decoding improvement was marginal, possibly reflecting a ceiling effect. However, in participants with initially lower accuracies, averaging across channels revealed to have benefits (see Figure 9). For example, in P3 accuracy rose from 48.61 % (SOI1) to 65.28 % (SOI1-2) and 63.89 % (SOI1-2-3). Averaging across a small number of channels in close proximity has been reported to result in more reliable measures (Wiggins et al., 2016). Future work should therefore investigate the accuracy benefit of adding a small number of channels in a systematic manner. We expect that channel averaging might be especially beneficial in cases where the single-channel fNIRS-BCI has low accuracy. A promising resource to ensure that the informative, here mental task sensitive, region is sampled by a small set of optodes is the Array Designer Toolbox (Brigadoi, Salvagnin, Fischetti, & Cooper, 2018). Through automated optode array design for a specific region-of-interest, there is an increased cortical sensitivity compared to manual optode placement. Alternatively, if anatomical fMRI data is available, probabilistic maps of fMRI-activation from an independent dataset can guide optode placement (Benitez-Andonegui et al., 2021).

BCI User Experience – A Factor Not to be Overlooked

In the developing field of fNIRS-BCI, much of the published work has focused on methodological/technical development. Yet, the success of an fNIRS-BCI also relies heavily on the ability of the participant to produce robust and reliable hemodynamic signals. We administered several in-house questionnaires to explore user skills and experience, as these factors may influence the quality of the evoked fNIRS signals (Holper, Shalom,

Wolf, & Sigman, 2011) and therewith BCI decoding accuracy (Cui et al., 2007; Jeunet, N'Kaoua, & Lotte, 2017; Sargent, Heiman-Patterson, Feldman, Shewokis, & Ayaz, 2018; Weyand & Chau, 2015). In addition, user experience affects the likelihood patients will actually use a BCI regularly (Nijboer, 2015). Participants generally felt comfortable and motivated in our study. Two participants did experience some discomfort in one session due to pressure induced by a few optodes. Discomfort is not uncommon in fNIRS studies (Cui et al., 2011; Rezazadeh Sereshkeh et al., 2018; Suzuki et al., 2010) and constitutes another motivation to move towards small-scaled fNIRS-optode setups. General comfort, cap comfort and fatigue scores remained relatively stable over the three fNIRS sessions (see Supplementary Figure 3). Participants that rated their motor imagery ability as high, tended to have a high multi-trial decoding accuracy ($r(4)= 0.95$; $p < 0.01$; see Supplementary Figure 4). In other words, participants that rated their imagination as vivid, similar to actual drawing, easy, enjoyable and generally good tended to achieve higher answer-decoding accuracies. This finding is in line with several BCI studies using EEG, fMRI and fNIRS neuroimaging techniques (Ahn et al., 2018; Jeunet, N'Kaoua, Subramanian, Hachet, & Lotte, 2015; Lorey et al., 2011; Weyand & Chau, 2015). This link between mental task ability and BCI accuracy paves the way to mental imagery user training, especially in users with low BCI accuracy (Kaiser et al., 2014).

Limitations and Future Work

A drawback of the current study is the absence of correction for physiological noise through the use of short-separation channels (Brigadoi & Cooper, 2015). Moreover, correction though spatial filtering was not

possible since these approaches require coverage of a larger area than the region of interest (Zhang, Noah, & Hirsch, 2016). Removal of systemic noise would likely have improved the reliability and accuracy of our BCI paradigm (Wiggins et al., 2016). However, through our focus on a participant-specific and daily-defined channel-by-chromophore, we did indirectly exclude "noisy" signals. For example, the event-related potential for P2 on day 1 (see Figure 4) shows a contaminated HbO signal and a clean HbR signal. Despite the relatively modest amplitude in HbR, compared to HbO, the HbR chromophore is chosen as the signal-of-interest.

Another drawback is the limited sample size in the current study. Generalization to the overall population is difficult based on the results of this sample. Nevertheless, the results are encouraging and show that four-choice fNIRS-based communication using different sensory encoding modalities is feasible. A more elaborate study with a larger sample size should be conducted following this proof-of-concept study.

Although our temporal encoding paradigm is effective, with 6 min 7 s per four-choice question, the information transfer rate is low. Three participants, P4, P5 and P6, had a significant single-trial decoding accuracy in each fNIRS session (see Figure 8). This finding suggest that robust communication is possible through joint analysis of less than four trials in some participants. Moreover, in these three subjects single-trial communication is already feasible with a decrease in decoding accuracy as the cost. Future fNIRS-BCI studies could improve the information transfer rate through shortening the mental task duration. In the temporal encoding six-choice fNIRS-BCI by Benitez-Andonegui et al. (2020) a mental task duration of 6 s yielded promising results. Another step towards drastically shortening encoding times could be to focus on the initial dip of the

hemodynamic response, rather than the full response. Khan and Hong (2017) reached a 76.5 % four-command decoding accuracy with their fNIRS-BCI with a post-stimulus window size of 2 s. Borgheai et al. (2020) also reported successful single-trial classification using a post-stimulus window size of under 4 s in ALS patients. Both studies highlight the efficacy of short event-related hemodynamic changes. Moreover, through such short post-stimulus windows, also the inter-stimulus interval can be shortened significantly. Future fNIRS-BCI development should further investigate and replicate these promising findings, as they would greatly enhance potential for daily use.

Furthermore, focusing on individualization of BCI procedures is highly recommended with respect to both the choice of the sensory encoding modality and the selection of a mental task to control the BCI. In the current study, all participants performed motor imagery, but other types of mental imagery should be explored as well, for example somatosensory imagery as recently applied in an fMRI-BCI context (Kaas, Goebel, Valente, & Sorger, 2019). In an ideal case, a mental task should be individually chosen according to the BCI user's preference from a compilation of proven BCI-control tasks (Weyand, Schudlo, Takehara-Nishiuchi, & Chau, 2015).

The fNIRS hardware used in the present study was rather bulky and transported on a cart, as is the case in most fNIRS studies (Scholkmann et al., 2014). However, recently developed mobile devices that can fit in a backpack (Pinti, Aichelburg, et al., 2018), combined with a limited optode setup as proposed here, can result in a small-scaled fNIRS-BCI. These simplifications in hardware might further stimulate exploration of fNIRS-BCIs in ecologically valid environments. This would increase the chance that

fNIRS-BCIs will be once indeed be used on a regular basis by patients, that are often already surrounded by bulky medical equipment (Nijboer et al., 2014).

Conclusion

In the current study, we tested a four-choice multimodal fNIRS-BCI in six healthy subjects. Using a temporal encoding paradigm and decoding the answers from a single channel-by-chromophore time course resulted in mean single- and multi-trial decoding accuracies of 62.50 % and 85.19 % respectively. Answer encoding was alternatively guided by three different sensory encoding modalities (visual, auditory or tactile). Decoding accuracies were found to be stable across three consecutive days. Moreover, decoding accuracies from two experienced BCI users were stable in an ecologically valid setting, *i.e.*, a cafeteria. Averaging of two or three most-informative channels further increased decoding accuracy compared to the single channel-by-chromophore approach. Future fNIRS-BCI studies should focus on increasing efficiency, *e.g.*, by decoding from quick-to-detect features of the hemodynamic response such as the initial dip, and on reporting relevant user experience.

Supplementary Material

Material and Methods

Autobiographical Questions

1. Which country were you born in?
   - ☐ The Netherlands
   - ☐ Germany
   - ☐ Belgium
   - ☐ Other

2. Which country are you currently living in?
   - ☐ The Netherlands
   - ☐ Germany
   - ☐ Belgium
   - ☐ Other

3. Do you have any siblings?
   - ☐ No, I do not
   - ☐ Yes, only brother(s)
   - ☐ Yes, only sister(s)
   - ☐ Brother(s) and sister(s)

4. Which colour was your first car?
   - ☐ I never owned a car
   - ☐ My first car was red
   - ☐ My first car was blue
   - ☐ It was neither red nor blue

5. What is your current housing situation?
   - ☐ Living with partner
   - ☐ Living in shared house
   - ☐ Living by myself
   - ☐ Living with parents

6. Do you have a godchild/godchildren?
   - ☐ Yes, only girl(s)
   - ☐ Yes, only boy(s)
   - ☐ Yes, only boy(s) and girl(s)
   - ☐ No, I do not

Motor Imagery Abilities Questionnaire

1. With your dominant hand, please draw a rough sketch of a house.

2. Now imagine drawing the same sketch without actually doing so. Try imagining movements most similar to those used when actually drawing (e.g., wrist and whole hand movements).

3. How vivid was your imagination of drawing the sketch? (Please circle one of the numbers)

0	1	2	3	4
Not very vivid				Very vivid

4. How similar was your imagination of drawing the sketch compared to the actual drawing? (Please circle one of the numbers)

0	1	2	3	4
Not similar at all				Almost identical

5. How easy did you find it to imagine drawing the sketch? (Please circle one of the numbers)

0	1	2	3	4
Not easy at all				Very easy

6. How would you rate your imagination in general? (Please circle one of the numbers)

0	1	2	3	4
Not good at all				Very good

7. How much do you enjoy this task? (Please circle one of the numbers)

0	1	2	3	4
Not at all				Very much

Questionnaire of Strategy and Comfort

1. Please shortly describe what exactly you imagined during the "mental drawing" task. Draw here what objects/images you drew in your mind.

2. How well did it work in general? Were there any problems? Did you realize any differences between the different trials/runs? Do you have any remarks/suggestions?

3. How comfortable did you feel during the session? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not comfortable at all									Very comfortable

4. How comfortable was the cap? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not comfortable at all									Very comfortable

5. How tired did you become throughout the session? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Very Tired									Not tired at all

Questionnaire of General Study Impression

Motivation and General Impression						
		Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1.	I found the study interesting.	☐	☐	☐	☐	☐
2.	I enjoyed the task.	☐	☐	☐	☐	☐
3.	I was motivated to perform the study.	☐	☐	☐	☐	☐
4.	My motivation got lower throughout the study.	☐	☐	☐	☐	☐
5.	My motivation got higher throughout the study.	☐	☐	☐	☐	☐
6.	I got bored throughout the study.	☐	☐	☐	☐	☐
7.	I got tired throughout the study.	☐	☐	☐	☐	☐

Prior Experience						
		No	Once	Twice	3-4	>4
8.	I have participated in experiments Measuring brain-activity (EEG, fMRI, fNIRS, MEG, PET).	☐	☐	☐	☐	☐
9.	Have you participated in BCI experiments?	☐	☐	☐	☐	☐
10.	Have you participated in neurofeedback experiments?	☐	☐	☐	☐	☐

If you have answered question 9 with **yes** (otherwise skip):

		No	Once	Twice	3-4	>4
11.	Have you participated in EEG BCI experiments?	☐	☐	☐	☐	☐
12.	Have you participated in fMRI BCI experiments?	☐	☐	☐	☐	☐
13.	Have you participated in fNIRS BCI experiments?	☐	☐	☐	☐	☐

If you have answered question 10 with **yes** (otherwise skip):

		No	Once	Twice	3-4	>4
14.	Have you participated in EEG neurofeedback experiments?	☐	☐	☐	☐	☐
15.	Have you participated in fMRI neurofeedback experiments?	☐	☐	☐	☐	☐
16.	Have you participated in fNIRS neurofeedback experiments?	☐	☐	☐	☐	☐

Mental Imagery

		Strongly disagree	Disagree	Neutral	Agree	Strongly agree
17.	My imagination of mental drawing was well throughout the whole study.	☐	☐	☐	☐	☐
18.	My imagination was similar to real drawing.	☐	☐	☐	☐	☐
19.	My imagination got more realistic throughout the study.	☐	☐	☐	☐	☐
20.	My imagination got less realistic throughout the study.	☐	☐	☐	☐	☐
21.	My imagination of drawing was very vivid.	☐	☐	☐	☐	☐
22.	My imagination got more vivid throughout the experiment.	☐	☐	☐	☐	☐
23.	My imagination got less vivid throughout the experiment.	☐	☐	☐	☐	☐

Emotions

		Strongly disagree	Disagree	Neutral	Agree	Strongly agree
24.	I felt confident using the system.	☐	☐	☐	☐	☐
25.	I felt comfortable using the system.	☐	☐	☐	☐	☐
26.	I felt anxious using the system.	☐	☐	☐	☐	☐
27.	I felt stressed using the system.	☐	☐	☐	☐	☐
28.	I felt excited using the system.	☐	☐	☐	☐	☐
29.	I felt natural using the system.	☐	☐	☐	☐	☐
30.	I am satisfied with my performance.	☐	☐	☐	☐	☐
31.	I am satisfied with the performance of the system.	☐	☐	☐	☐	☐
32.	I got frustrated throughout the experiment.	☐	☐	☐	☐	☐

Modalities

1. How pleasant did you find the **auditory** guidance? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not pleasant at all									Very pleasant

2. How easy did you find the **auditory** guidance? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not easy at all									Very easy

3. How pleasant did you find the **visual** guidance? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not pleasant at all									Very pleasant

4. How easy did you find the **visual** guidance? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not easy at all									Very easy

5. How pleasant did you find the **tactile** guidance? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not pleasant at all									Very pleasant

6. How <u>easy</u> did you find the **tactile** guidance? (Please circle one number)

1	2	3	4	5	6	7	8	9	10
Not easy at all									Very easy

7. Rate your liking of the three modalities overall (1 = best, 2 = medium, 3 = worst). If you liked two modalities equally, rate them with the same number.

Auditory ☐ Visual ☐ Tactile ☐

8. Please give a brief explanation why.

_____

_____

Other

9. Was there any question that was ambiguous to you? (Unclear which answer to choose)

☐ yes ☐ no

If so, which one(s) _____

10. Was there any question that elicited strong emotions?

☐ yes ☐ no

If so, which one(s) _____

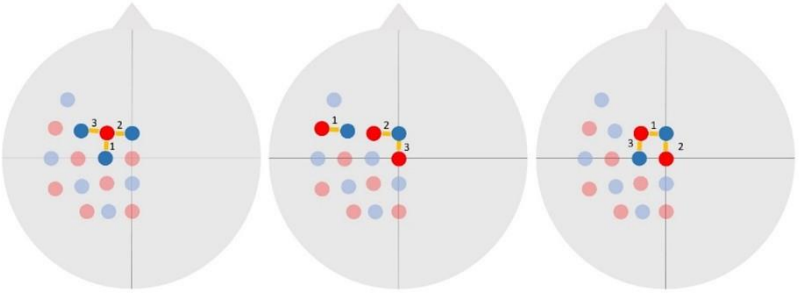
11. Do you have any other remarks on the study?

Results

Subject-Specific Channel Selection

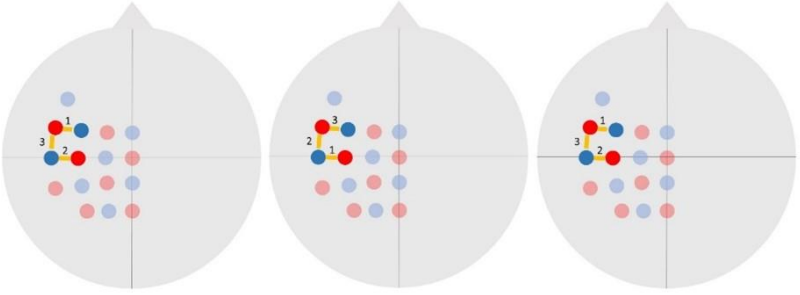
Based on the localizer data, three channels were selected for each participant in each session. The channel selection for each of the six participants can be gauged in Supplementary Figure 1. The EEG coordinates of these channels are displayed in Supplementary Table 1. The channel selection frequency across the six participants is partly depicted in Supplementary Figure 2. All absolute frequencies can be read from Supplementary Table 2.

P1



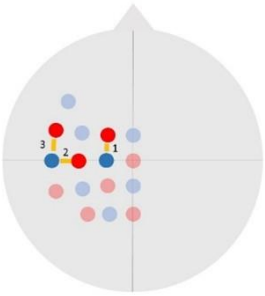
Session 1: auditory localizer, HbO | Session 2: visual localizer, HbO | Session 3: tactile localizer, HbO

P2

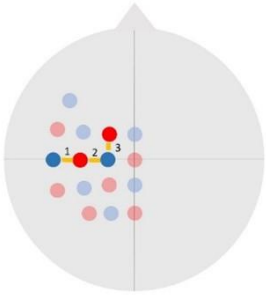


Session 1: auditory localizer, HbR | Session 2: tactile localizer, HbR | Session 3: visual localizer, HbR

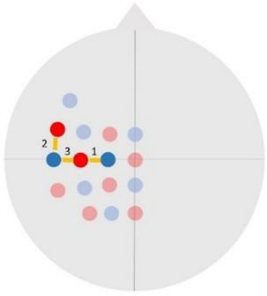
P3



Session 1: visual localizer, HbO

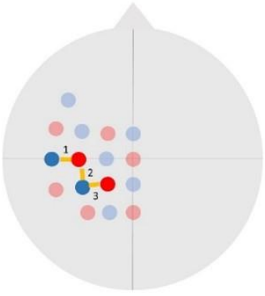


Session 2: tactile localizer, HbO

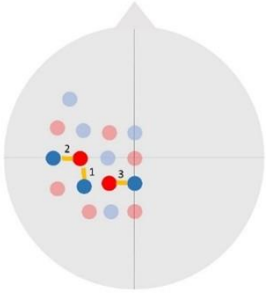


Session 3: auditory localizer, HbO

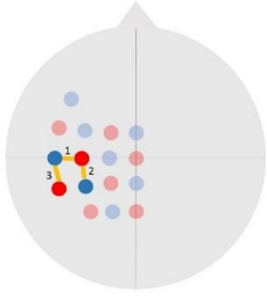
P4



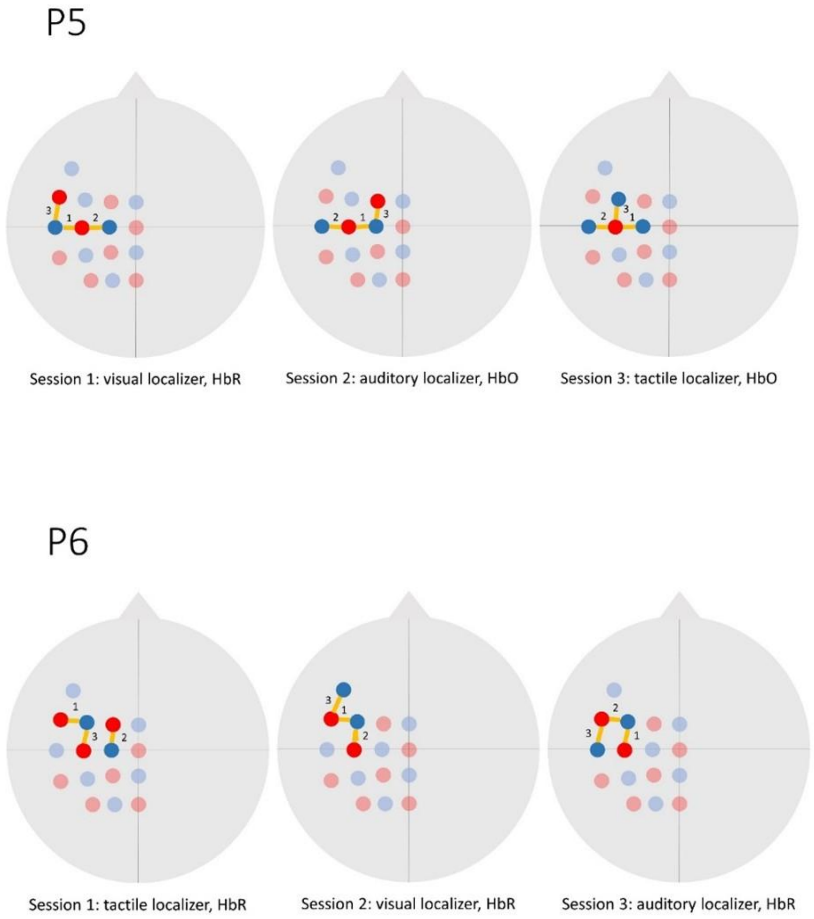
Session 1: tactile localizer, HbR



Session 2: auditory localizer, HbR



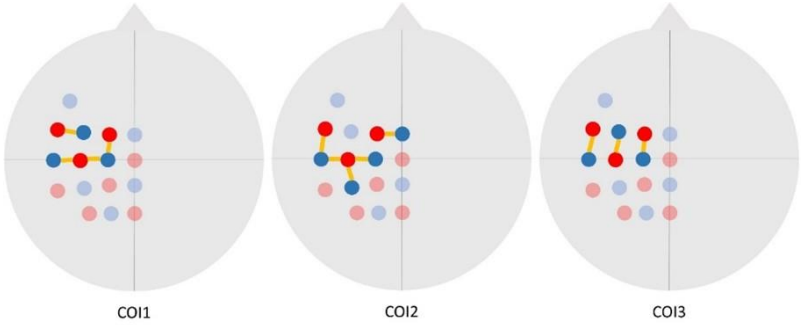
Session 1: visual localizer, HbO



Supplementary Figure 1. **Individual Participant's Channel Selection**. For each participant the most informative channels are displayed for each fNIRS session. The yellow lines between a source (red) and detector (blue) optode indicate the channel-by-chromophore that were chosen as the most informative channel (1), the 2nd most informative channel (2) and the 3rd most informative channel (3). *Abbreviations:* HbO, oxygenated hemoglobin; HbR, deoxygenated hemoglobin.

PARTICIPANT	SESSION	CHROMOPHORE	SOI1	SOI2	SOI3
P1	Session 1	HbO	FC1-C1	FC1-FCZ	FC1-FC3
	Session 2		FC5-FC3	FC1-FCZ	CZ-FCZ
	Session 3		FC1-FCZ	CZ-FCZ	FC1-C1
P2	Session 1	HbR	FC5-FC3	C3-C5	FC5-C5
	Session 2		C3-C5	FC5-C5	FC5-FC3
	Session 3		FC5-FC3	C3-C5	FC5-C5
P3	Session 1	HbO	FC1-C1	C3-C5	FC5-C5
	Session 2		C3-C5	C3-C1	FC1-C1
	Session 3		C3-C1	FC5-C5	C3-C5
P4	Session 1	HbR	C3-C5	C3-CP3	CP1-CP3
	Session 2	HbR	C3-CP3	C3-C5	CP1-Cpz
	Session 3	HbO	C3-C5	C3-CP3	CP5-C5
P5	Session 1	HbR	C3-C5	C3-C1	FC5-C5
	Session 2	HbO	C3-C1	C3-C5	FC1-C1
	Session 3	HbO	C3-C1	C3-C5	C3-FC3
P6	Session 1	HbR	FC5-FC3	FC1-C1	C3-FC3
	Session 2		FC5-FC3	C3-FC3	FC5-F5
	Session 3		C3-FC3	FC5-FC3	FC5-C5

Supplementary Table 1. **Individual Channel × Chromophore Selection.** In each session, the most promising channel-by-chromophore combination was selected for every participant. The last three columns show the channels-of-interest (SOI). *Abbreviations:* HbO, oxygenated hemoglobin; HbR, deoxygenated hemoglobin; COI1, most informative channel; COI2, 2nd most informative channel; COI3, 3rd most informative channel.



Supplementary Figure 2. **Channel Selection Frequency.** Channel selection frequency (n=18; 6 participants x 3 fNIRS sessions) of the most informative channel (COI1), the 2nd most informative channel (COI2) and the 3rd most informative channel (COI3). The yellow lines between a source (red) and detector (blue) optode indicate informative channels that were chosen more than once as informative out of 18 cases.

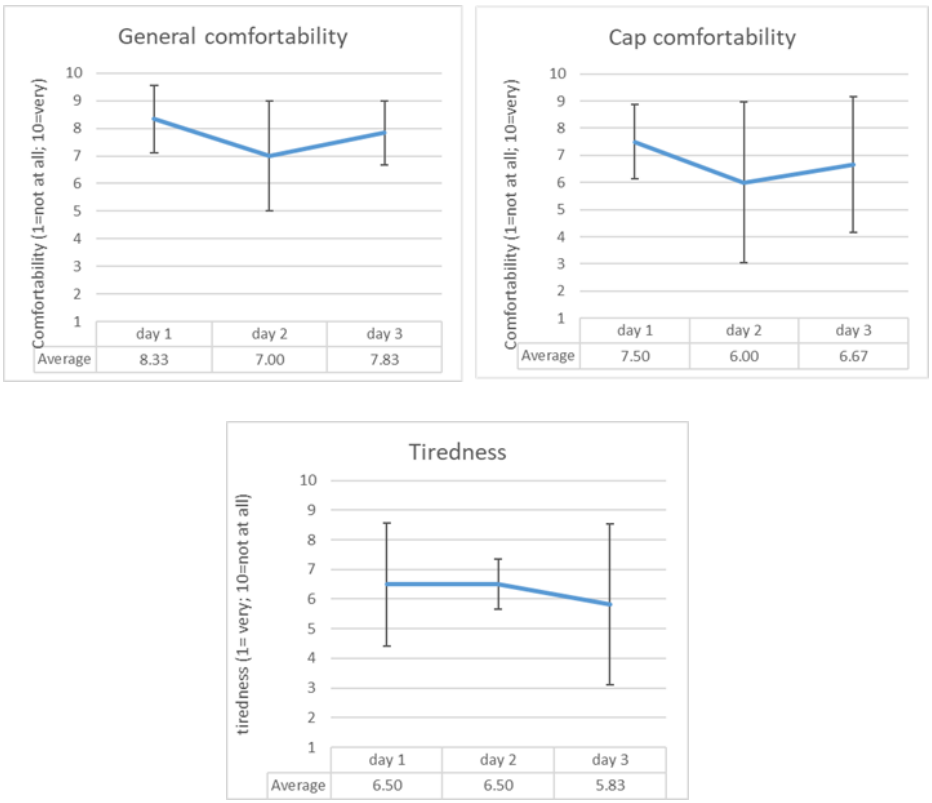
FNIRS CHANNEL	FREQUENCY		
	COI1	COI2	COI3
FC5-F5	0	0	1
FC5-C5	0	2	5
FC5-FC3	5	1	1
C3-C5	5	6	1
C3-FC3	1	1	2
C3-CP3	1	2	0
C3-C1	3	2	0
CP5-C5	0	0	1
CP5-CP3	0	0	0
P3-CP3	0	0	0
P3-P1	0	0	0
FC1-FC3	0	0	1
FC1-FCZ	1	2	0
FC1-C1	2	1	3
CZ-FCZ	0	1	1
CZ-C1	0	0	0
CZ-CPZ	0	0	0
CP1-CP3	0	0	1
CP1-C1	0	0	0
CP1-CPZ	0	0	1
CP1-P1	0	0	0
PZ-CPZ	0	0	0
PZ-P1	0	0	0
SUM	18	18	18

Supplementary Table 2. **Absolute Channel Selection Frequency.** The fNIRS channels identified by their EEG coordinates (left column) and the absolute selection frequency of the most informative channel (COI1), the 2nd most informative channel (COI2) and the 3rd most informative channel (COI3). The sum of absolute frequency is 18 (6 participants and 3 fNIRS sessions).

BCI user experience

Experienced Comfort and Tiredness across fNIRS Sessions

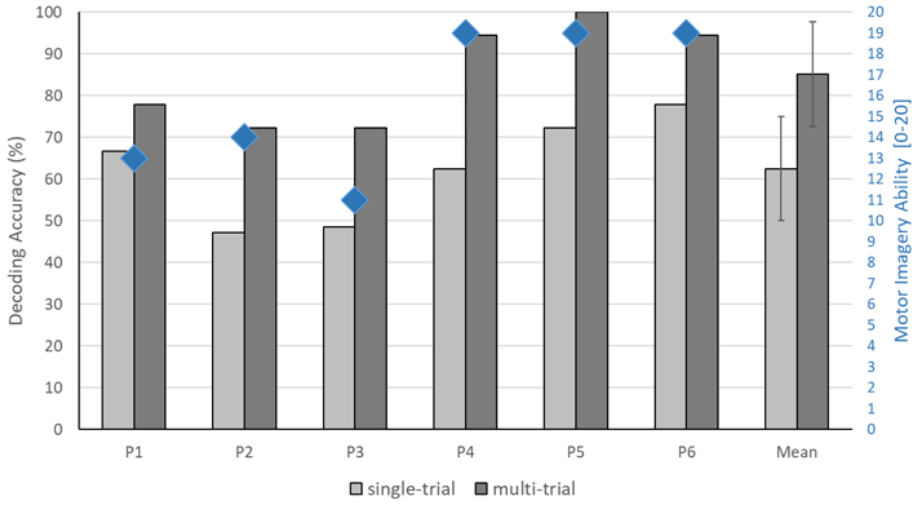
General comfortability, cap comfortability and tiredness scores remained relatively stable over the three fNIRS sessions (see Supplementary Figure 3).



Supplementary Figure 3. **Mean Comfortability, Cap Comfortability and Fatigue across fNIRS Sessions.** Participants rated each aspect on a 10-point Likert scale (1 indicating 'uncomfortable/very tired' and 10 indicating 'very comfortable/not tired at all'). The error bars depict the standard deviation of the group mean. Note that all ratings remained relatively stable across the sessions.

Motion Imagery Questionnaire

The self-reported motor imagery ability scores (0-20) correlated significantly with the multi-trial decoding accuracies ($r(4)= 0.95$; $p < 0.01$), but not with the single-trial decoding accuracies ($r(4)= 0.73$; $p = 0.10$). Participants that rated their motor imagery ability as high, tended to have a high multi- trial decoding accuracy (see Supplementary Figure 4).



Supplementary Figure 4. **Individual and Sample Mean Decoding Accuracies and Motor Imagery Ability Score.** The single- (light grey) and multi-trial (dark grey) decoding accuracies can be interpreted on the primary axis (left). Error bars depict the standard deviation of the group mean. Motor imagery ability scores are depicted with blue diamonds and can be interpreted using the secondary y-axis (right). Note the association between the participants' self-reported motor imagery ability and their communication success.

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5 Summary and Discussion

Patients with complete LIS are in need of muscle-independent communication means. BCIs circumvent the muscular system by recording brain signals and employing them for communication and control (Wolpaw et al., 2000). The most commonly used BCI systems are based on neuroelectric brain activity, namely EEG (Kübler et al., 2009; Lazarou, Nikolopoulos, Petrantonakis, Kompatsiaris, & Tsolaki, 2018; Marchetti et al., 2013; Won, Kwon, Jang, Ahn, & Jun, 2019). For a considerable portion of participants/patients an EEG-BCI does not enable functional communication. (Allison & Neuper, 2010; Dickhaus, Sannelli, Müller, Curio, & Blankertz, 2009). Given the large patient heterogeneity, a wide range of neuroscientific recording techniques should be investigated with respect to their suitability as BCI-input modality. Recently hemodynamic neuroimaging methods were explored in the context of BCI. Following successful communication paradigms using fMRI (Bardin et al., 2011; Monti et al., 2010; Sorger et al., 2009; Sorger, Reithler, Dahmen, & Goebel, 2012), the current work focused on the hemodynamic method of fNIRS. FNIRS is a portable functional neuroimaging method with a myriad of other advantages, in that it is easy to operate, safe, relatively inexpensive and relatively robust against motion artifacts (Cutini, Moro, & Bisconti, 2012; Irani, Platek, Bunce, Ruocco, & Chute, 2007; León-Carrión & León-Domínguez, 2012; Naci et al., 2012; Pinti et al., 2018; Scholkmann et al., 2014). The current work aimed at transference of fMRI-BCI paradigms to the flexible fNIRS method. The overarching research aim being the development and validation of straightforward, robust, efficient, and cost-effective fNIRS-based communication paradigms that can be tailored to individual patients' situations and eventually be used in daily life. Several answer encoding paradigms and multiple analysis pipelines were explored

in this thesis. All developments were designed to enable future clinical use. In the following, the three empirical chapters of this thesis will be summarized and discussed. Recommendations for future studies are presented. Limitations of the three studies performed are discussed, together with general issues regarding BCI research. Lastly, a main conclusion is drawn.

Summary

In **chapter 2**, a novel yes/no fNIRS-BCI paradigm was tested in a controlled laboratory setting. Twenty healthy participants were auditorily instructed to perform motor imagery for encoding a yes-answer. They were instructed to rest for encoding a no-answer. Participants performed two localizer runs, consisting of 20 trials of motor imagery with resting periods in between, and six answer encoding runs, consisting of five trials each. The paradigm enables communication, *i.e.*, answering a binary question, in the order of 30 min (±15 min training; ±10 min localizer, ±6 min encoding). Nine optodes (three sources, six detectors) were placed on the left fronto-parietal region. FNIRS data were analyzed *post-hoc*. Two analysis pipelines, using both univariate and multivariate procedures, and participants' subjective experience were explored:

(1) Univariate data analysis. For each individual participant, a COI was determined based on general linear model analysis of HbO and HbR time series obtained from the first localizer run. Participants' answers could be decoded from this single COI with an accuracy of 64.25 % on a single-trial and 65.00 % on a multi-trial basis (the latter using majority voting). In eight participants, single-trial accuracies were significantly above

chance level. For the group of nine participants with individual single-trial accuracies of 70 % or higher – with 70 % being considered a sufficient accuracy for a BCI (Kübler, Mushahwar, Hochberg, & Donoghue, 2006) – the average single- and multi-trial accuracy were 79.44 % and 84.09 % respectively.

(2) Multivariate data analysis. A support vector-machine was trained on all 14 fNIRS channels using data obtained in the two localizer runs. Participants' answers could be decoded with an accuracy of 62.33 % on a single-trial basis and 63.33 % on a multi-trial basis (the latter using majority voting). In eleven participants, single-trial accuracies reached statistical significance. For the group of ten participants with individual single-trial accuracies of 70 % or above, the average single- and multi-trial accuracy were 72.33 % and 85.71 % respectively.

(3) Participant experience. Participants rated the mental drawing task as pleasant and easy to perform. Comfortability decreased slightly across the runs, with a large drop in the last run.

This first study confirmed the high potential of fNIRS for binary communication. The encoding paradigm implementing a single mental imagery task required relatively little cognitive effort and minimal pre-training (± 30 min). It enabled binary communication for a substantial number of participants in a single session, even implementing information obtained from a single fNIRS channel only.

In **chapter 3**, an alternative auditory yes/no fNIRS-BCI paradigm was explored in eighteen participants. In this paradigm, both answer options correspond to the performance of a unique mental imagery task. Participants were asked to perform mental drawing for a "yes" answer or

spatial navigation for a “no” answer. Each mental imagery task results in spatially distinct brain activation, which can be analyzed to infer the performed task and thus encoded answer. In addition to this spatial differentiation, the two mental imagery tasks had to be performed in distinct auditorily cued time windows. This paradigm thus exploits both spatial and temporal characteristics of fNIRS signals. Participants performed four localizer runs, consisting of 40 trials for each condition, and six answer encoding runs, consisting of five trials per mental imagery condition. Nine optodes (three sources, six detectors) were placed on the left fronto-parietal region. Answers were decoded in simulated real-time, as to make realistic predictions of future real-world applications. The main analysis pipeline employed general linear model analysis (univariate analysis). Analyses for HbO and HbR data were performed separately, resulting in a maximum of four SOI’s (2 mental tasks x 2 chromophores). Multivariate data analysis was performed to explore the differentiability of the two mental tasks. Participants’ subjective experience and physical features (such as hair color and density) were registered. The latter, being a potential indicator of fNIRS signal quality and obtained using an in-house fNIRS suitability questionnaire. The main results were the following:

(1) Communication (univariate data analysis). The average single-trial decoding accuracy was 56.85 % (HbO) and 54.81 % (HbR), with five individual participants reaching significance (empirical chance level at 63.33 %). An average multi-trial decoding accuracy of 66.67 % (HbO) and 58.33 % (HbR) was found, with nine participants reaching significance (empirical chance level at 83.33 %). In four out of these nine participants a 100 % effective communication was established through use of the HbO or HbR signal.

(2) Multivariate data analysis. The spatial differentiability of the two mental tasks was explored using multivariate pattern analysis (MVPA). An average single-trial accuracy of 58.33% (using 20 training trials per task) and 60.56% (using 40 training trials per task) was found, with four (SVM20-20) and seven (SVM40-40) individual participants reaching significance through permutation testing. A majority voting approach was used to obtain multi-trial accuracy. Combining the outcomes of the five trials within each run, heightened the accuracies to 62.04% (SVM20-20) and 75% (SVM40-40).

(3) Participant experience. The comfortability of the participants decreased over time, from 8.03 ± 1.27 (run 1) to 6.53 ± 1.55 (run 10). The spatial navigation task was considered more difficult to execute compared to the mental drawing task ($t = 4.70$, $p < 0.001$). No significant difference between both tasks was found in terms of pleasantness ($t = 1.86$, $p = 0.081$).

(4) fNIRS suitability questionnaire. Questionnaire scores, obtained by adding scores related to physical features of a participant, correlated significantly with the signal-to-noise ratio of the raw light intensities ($r = -0.499$).

This second empirical chapter constituted the first binary fNIRS-BCI study for communication using two active mental imagery tasks to differentiate two answer options. Previous fNIRS-BCIs for communication had not yet explored the use of two active tasks. Moreover, imaginary spatial navigation – a task used in the seminal fMRI work in DoC patients (Monti et al., 2010) – was explored for the first time using fNIRS. The encoding paradigm, with both spatial and temporal features, enabled effective

communication in half of our participants (multi-trial, both HbO and HbR). The use of both spatial (different mental tasks activate differential brain areas) and temporal (unique time windows for each mental task) encoding ensured differentiation of the two answer options.

In **chapter 4**, a four-choice fNIRS-BCI was investigated in six participants over three consecutive days. The four answers were presented serially to the participants. When participants were presented with their chosen answer, they were asked to perform mental drawing. Answer encoding was guided by either the visual, auditory, or tactile sensory modality. For the tactile modality, the questions and answer options were reviewed with the participant beforehand. The four answer options and rest cue were indicated by touching a participant´s fingers. A localizer run was performed to select the participant-specific most informative fNIRS channel-by-chromophore constellation. Six four-choice questions, with five trials each, were then posed to each participant. Sixteen optodes (eight sources, eight detectors) were placed on the left fronto-parietal region. In two participants, only the most-informative optodes were retained after the localizer run. Answers were decoded using univariate analysis of the participant-specific most informative fNIRS channel-by-chromophore. Data were analyzed post-hoc in simulated real-time in four participants. Two participants used the fNIRS-BCI in a cafeteria instead of a laboratory, their answers were decoded in real-time. The trade-off between number of optodes and decoding accuracy was post-hoc explored. Lastly, participants' subjective experience was obtained using several in-house questionnaires.

(1) Communication. Answer decoding was accurate with 62.5 % (single-trial) and 85.19 % (multi-trial). Communication success was 86.11 % for visual, 80.56 % for auditory, and 88.89 % for tactile sensory

encoding. Communication was reliable over three days with mean multi-trial accuracies of 86.11 % on day 1, 86.11 % on day 2, and 83.33 % on day 3. The two participants using the fNIRS-BCI in real-time and in a cafeteria obtained excellent single-trial (72.22 % and 77.78 %) and multi-trial (100 % and 94.44 %) communication accuracies.

(2) Number of optodes/accuracy trade-off. Multi-trial accuracy increased from 85.19 % (one-channel approach) to 91.67 % (two/three-channel approach).

(3) Participant experience. Participants generally felt comfortable and confident using the fNIRS-BCI. The auditory modality was rated the most pleasant and easy encoding modality, followed by the tactile modality. Not a single participant preferred the visual modality to the auditory or tactile modality. Participants' own estimations of their motor imagery ability correlated significantly with the multi-trial accuracies [$r(4) = 0.95$; $p < 0.01$].

The third study extended our two-choice fNIRS-BCI to a four-choice fNIRS-BCI with a temporal encoding paradigm. This work was the first report of a fNIRS-BCI enabling auditory, visual and tactile sensory encoding within a session. Moreover, tactile encoding was explored in an fNIRS-BCI for the first time. Communication was significant and robust in every participant. Moreover, fNIRS-BCI communication was stable across three consecutive days. Longitudinal data of an fNIRS-BCI have only been reported in a single patient previously (Borgheai et al., 2020). Lastly, two participants were able to successfully use the fNIRS-BCI in real-time and in a real-world environment, *i.e.*, a cafeteria. The fNIRS-BCI thus demonstrated robustness across participants, modalities, time and environments.

Implications and Future Directions

In the following, the implications of the empirical chapters are discussed in the order of the BCI cycle (see Figure 1 in **chapter 1**): (1) answer encoding, (2) data collection and (3) answer decoding. Lastly, the participant's subjective experience is discussed.

Flexible Answer Encoding

In the current work, three unique answer-encoding paradigms were explored. In **chapter 2**, the binary answers were encoded by the simple absence or presence of mental imagery (spatial encoding paradigm). In **chapter 3**, two differently timed mental imagery tasks were used to encode the two answers (spatiotemporal encoding paradigm). In **chapter 4**, a four-choice fNIRS-BCI enabled communication using a single mental imagery task (temporal encoding paradigm). All paradigms focused on simple yet effective answer encoding that have the potential for communication within a single session. A purely temporal encoding paradigm, as presented in **chapter 4**, was found to be particularly suitable for multiple-choice fNIRS-BCIs. Benitez-Andonegui et al. (2020) even extended the temporal encoding paradigm to a six-choice fNIRS-BCI. In the fNIRS-BCI literature, answer encoding is generally based on differential spatial features of mental tasks. Spatial paradigms are in need of multiple mental imagery tasks (Batula, Ayaz, & Kim, 2014; Naseer & Hong, 2015; Weyand & Chau, 2015) and classifiers require extensive training (Batula et al., 2014; Naseer & Hong, 2015). For participants it requires substantial attention, working memory and abstract thinking to link mental tasks with a specific answer option. An assumption often made in BCI research is that LIS patients have relatively normal cognitive functioning (Nijboer, Plass-Oude Bos, Blokland, van Wijk,

& Farquhar, 2014). As with all brain disorders, the level of cognitive functioning varies greatly depending on the etiology. Nevertheless even an infarction of the pons, without additional brain damage, commonly results in symptoms such as fatigue, headache and disturbed attention (Hong, Khan, & Hong, 2018). Relatively simple encoding paradigms, as presented in **chapter 2, 3 and 4**, require little cognitive effort from the BCI-user and, thus, heighten the probability of clinical use[14]. We encourage the fNIRS-BCI community to not lock-in on spatial paradigms and multivariate classification only and explore/apply a wide variety of potential encoding paradigms based on both spatial and temporal fNIRS-signal features.

Next to basic design of an encoding paradigm, fNIRS-BCI should be flexible in terms of the implemented sensory-encoding modality. LIS patients frequently have impaired vision (Gill-Thwaites & Munday, 2004; Riccio, Mattia, Simione, Belardinelli, & Cincotti, 2012; Rousseau, Pietra, & Nadji, 2012). Therefore, the encoding paradigms presented in **chapters 2 and 3** employed auditory instructions. In **chapter 4**, a multimodal fNIRS-BCI was explored for the first time. Four-choice answers could be encoded through either visual, auditory or tactile guidance in the same session. This crucial development is another step towards clinical studies, given the varying degrees of sensory functioning in LIS patients (Nijboer et al., 2014). We recommend the fNIRS-BCI field to continue exploring several sensory encoding modalities, specifically the under-researched tactile encoding.

Lastly, a usable BCI needs to function reliably across time and environments. EEG-BCIs very rarely allow sustained communication at their

[14] Keep in mind that learning a new skill is possible for patients with severe cognitive disorders, given enough guidance, practice and internal motivation. For example, a severely brain-injured patient with amnesia, tetraplegia and anarthria was able to learn to use an eye-tracking device (Trojano, Moretta, & Estraneo, 2009).

initial accuracy (Allison & Neuper, 2010). In the field of fNIRS-BCI, a single study has reported longitudinal BCI performance (Borgheai et al., 2020). The few studies that took place outside the laboratory were performed at participants home (Abdalmalak et al., 2017; Borgheai et al., 2020; Li, Yang, & Cheng, 2021). In **chapter 4**, we showed that our fNIRS-BCI performance was stable across three consecutive days. Two participants used the fNIRS-BCI to successfully communicate in a cafeteria. It is recommended that future fNIRS studies continue to test BCI performance across time and environments to ensure a robust fNIRS-BCI.

Capturing Brain Data with fNIRS

In **chapter 2 and 3**, nine optodes were mounted in non-spring loaded optode holders. In **chapter 4**, 16 optodes were mounted in spring-loaded optode holders. Compared to previous fNIRS-BCI research, relatively few optodes were employed in this work[15]. For example, Naseer and Hong (2015) explored the possibility of a four-choice fNIRS-BCI using 32 optodes. Previous fNIRS studies have reported frequent participant drop-out due to cap discomfort (Cui, Bray, Bryant, Glover, & Reiss, 2011; Rezazadeh Sereshkeh, Yousefi, Wong, & Chau, 2018; Suzuki, Harashima, & Furuta, 2010). The limited amount of optodes used in the current work might have contributed to our zero drop-out rate, due to discomfort, across **chapters 2-4.**

In **all empirical chapters**, a substantial number of participants were able to communicate using the data from a single channel. In **chapter 4**, we

[15] Due to our encoding paradigms enabling straightforward univariate analysis using information from participant-specific informative fNIRS channels.

even physically removed non-informative optodes after the localizer run in two participants. Despite the initial success of a single channel approach in LIS patients by Naito et al. (2007), fNIRS-BCI studies rarely decode answers from a single channel. As mentioned above, the trend in fNIRS-BCI research is to measure many channels and perform multivariate analyses (Batula et al., 2014; Hong et al., 2018; Naseer & Hong, 2015; Weyand & Chau, 2015). In **chapter 4**, we found that averaging two or three most informative fNIRS channels improves decoding accuracy in participants with a low single channel accuracy. In participants with already functional communication, however, the benefits were marginal. Hereby we showed it is possible to reduce optodes and obtain sufficiently high decoding accuracies for functional communication. Using merely one or a few optodes heightens the likelihood of technology acceptance by end-users, given that patients are often already surrounded by bulky medical material (Nijboer et al., 2014). Next to comfortability, esthetics play a vital role in technology acceptance. BCI development should not only focus on functionality, but also on human values such as self-esteem (Nijboer, 2015). The work in this thesis demonstrates there is a participant-specific optimum to be found in the number of optodes/accuracy trade-off. Future experiments should continue to reduce the number of optodes whenever possible to heighten potential clinical use.

When only a few optodes are mounted, it is evidently of utmost importance that these optodes have a good signal-to-noise ratio. A good signal requires good optical contact between optodes and skin. In **chapter 3**, a straightforward in-house questionnaire – capturing fNIRS-relevant participants' physical features – had predictive value for the signal-to-noise ratio of the raw light intensities. Note that in **chapter 3**, common

optode holders were used. These common optode holders are more comfortable than spring-loaded holders (Lloyd-Fox, Blasi, & Elwell, 2010), as they are not pressing the optodes against the skin, and will likely continue to be used when testing vulnerable populations. Future studies might explore the use of spring-loaded optode holders, as used in **chapter 4**, only in those participants with a negative predictive questionnaire score. Moreover, more research on the influence of participants' physical features, such as hair, skin and head size, is needed. Lastly, we encourage fNIRS researchers to report the type of optode holders used in their empirical studies.

Answer Decoding – The Land of Many Choices

In fMRI literature there are widely recognized data processing pipelines (Lindquist, Meng Loh, Atlas, & Wager, 2009; Poldrack, 2007; Worsley et al., 2002). Analysis of fNIRS data is not yet as standardized. There is no consensus on fNIRS signal processing and guidelines have not yet been published (Pfeifer, Scholkmann, & Labruyère, 2018). Therefore, there are many processing and analyses choices to be made.

In **chapters 3 and 4**, the data quality was checked using the unfiltered raw data. The signal-to-noise ratio was calculated for each channel using the coefficient of variance (Piper et al., 2014). In **chapter 3**, we found 37 % of channels to contain substantial amounts of noise. Univariate results were reported with and without exclusion of these noisy channels. BCI accuracy was higher when noisy channels were excluded. In **chapter 4**, all channels had a sufficient signal-to-noise ratio and none were excluded. The crucial difference between these two studies is the use of either "normal" or spring-loaded optode holders. We therefore recommend

fNIRS researchers, especially those using “normal” optode holders, to report the data quality and exclude/correct noisy channels before further analysis.

Satori (**chapter 2**) or TurboSatori (**chapter 3 and 4**) software was used to convert the raw light intensities to oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR). Subsequently linear trend removal and moving average filtering were applied to the data. At this point, a researcher can choose to focus on either HbO, HbR data or both. In **chapter 2**, the HbO and HbR data were taken together for both uni- and multivariate analyses. In **chapter 3**, the univariate analysis included separate HbO and HbR analyses. Decoding accuracies were significant in six participants for each chromophore. In **chapter 4**, about half of the participants performed best using HbO and the other half using HbR. These roughly comparable amounts of participants were also found in a six-choice fNIRS-BCI performed in our lab (Benitez-Andonegui et al., 2020). In the fNIRS literature, the debate is still ongoing on which is the preferred chromophore in the context of fNIRS-BCI. HbO has been historically preferred with mention of a relatively better signal-to-noise ratio, robustness and discriminative power (Hwang et al., 2016; Leff et al., 2011; Mihara et al., 2012; Rezazadeh Sereshkeh et al., 2018). However, there is no consensus on a superior chromophore in terms of signal quality (Kohl et al., 2020). Reporting results for both chromophores, which currently is still a rare practice in fNIRS-BCI, should be encouraged.

When measurements include several optodes, one can choose to focus on one to a few channels (univariate analysis) or look for spatial patterns using all channels (multivariate analysis). In the current work, the focus was on using a single channel in combination with univariate analysis,

as such an approach fits with our limited optode set-up and designs that take into account the temporal aspect of the hemodynamic response. In **all empirical chapters**, a channel or even signal of interest was selected based on a localizer run, a run in which participants were instructed to perform the mental task in cued time windows. A general linear model analysis was ran for all channels, resulting in t-values per channel. Using this method, several participants could use the BCI successfully. Next to our focus on univariate analysis, the differentiability of the answers using a multivariate approach was explored in the two binary fNIRS-BCI studies. In **chapter 2**, a support vector-machine was trained to distinguish mental task performance from rest, with a result of 62.33 %. In **chapter 3**, a support vector machine was trained to distinguish mental drawing from spatial navigation imagery, with a result of 58.33 % (20 training trials) and 60.59 % (40 training trials). The results of these binary paradigms are rather low compared to previous binary fNIRS-BCIs (Naseer & Hong, 2013; Naseer, Hong, & Hong, 2014), which is probably due the low data quality. In general, we recommend to not merely focus on spatial differentiation of mental tasks in fNIRS-BCI development, as it requires a substantial number of optodes, cognitive effort from the BCI-user, time investment (training the classifier) and more complex data analysis techniques. We encourage alternative BCI paradigms, such as those presented in this thesis, to be explored further.

When taking a broad perspective on fNIRS-BCI answer decoding, open science practices will aid establishment of recognized fNIRS data processing pipelines (Klein, Kohl, Lührs, Mehler, & Sorger, 2024). Firstly, preregistration of hypotheses, methodology and analysis pipelines will enable researchers to learn from all fNIRS studies (Schroeder et al., 2023), not merely a “significant” subset of studies. Hereby also counteracting

publication bias, *i.e.*, publishing mainly studies with a significant finding (Kicinski, Springate, & Kontopantelis, 2015). Secondly, sharing data and analysis codes will enable validation and replication of fNIRS-BCI findings (Poline et al., 2022). Hereby advancing and consolidating fNIRS-BCI knowledge. We therefore recommend researchers to adhere to open science practices, as they will undoubtably contribute to the development of fNIRS signal analyses guidelines and the advancement of neuroscience in general (Kohrs et al., 2023; Niso et al., 2022).

Participants' Experiences

For fNIRS-BCIs to be accepted by end-users there is more needed than merely a high BCI accuracy. As with all technology, users need to feel confident – or even enjoy – using it. **All three empirical studies** in this thesis recorded the subjective experience of the involved participants.

The comfortability of wearing the fNIRS cap dropped across the measurement session in **chapters 2 and 3**, indicating that prolonged use of an fNIRS-BCI, *i.e.*, over several hours, is not pleasant using currently available hardware. Optode reduction and improvements in hardware can pave the way forward.

In **chapter 2**, participants considered the mental drawing pleasant and easy. In **chapter 3**, participants experienced spatial imagery as more difficult than mental drawing but as pleasant. In **chapter 4**, participants self-assessed their general motor imagery ability. These scores correlated significantly with their BCI accuracy, *i.e.*, multi-trial decoding accuracy. These finding highlight the need for individualizable BCIs, in which participants can select their favorite mental tasks. Weyand, Schudlo, Takehara-Nishiuchi, and Chau (2015) successfully personalized selection of

mental tasks in an fNIRS-BCI. In line with this work, we recommend further research to offer participants several mental imagery tasks, so that a participant-specific imagery task can be selected.

In **chapter 4,** participants indicated a clear preference for auditory and tactile encoding compared to visual encoding. Participants remarked that the visual modality required more attention/concentration, although the tactile encoding modality objectively required most working memory, as participants had to memorize the order of the four answer options. Participant-informed selection of encoding modality seems the way forward.

Next to the evident advantage of a BCI being pleasant in itself, there is an added gain in terms of accuracy. Psychological state and motivation have been found to influence EEG-BCI performance in individual subjects (Nijboer, Birbaumer, & Kubler, 2010). Also with respect to fNIRS-BCIs, ease and enjoyment have been found to correlate with accuracy (Weyand & Chau, 2015). In line with this research, we found that participants' ratings of ease and pleasantness correlated significantly with multivariate answer-decoding in **chapter 3**.

Limitations

The main drawback of **all three empirical studies** is the relatively crude correction for physiological noise. The fNIRS signal has been shown to be influenced by blood pressure, heart rate, respiration, etc. (Bauernfeind, Wriessnegger, Daly, & Müller-Putz, 2014; Zhang, Brown, & Strangman, 2007). In all chapters, low- and high-pass filters were employed to filter out physiological noise. However, this approach is inferior to direct measurement of extra-cerebral factors by, *e.g.,* implementing short-

seperation channels. True functional brain activation can be obtained when the extra-cerebral hemodynamics are regressed out (Brigadoi & Cooper, 2015). The hardware to reliably measure extra-cerebral hemodynamic signals, *i.e.*, short-seperation channels, was not yet available at the time of data collection of the **three studies**. Alternative correction methods, not requiring additional hardware, are principal component analysis (Zhang, Noah, & Hirsch, 2016), independent component analysis (Santosa, Jiyoun Hong, Kim, & Hong, 2013) or multi-channel corrections (Pfeifer et al., 2018). In **all three empirical chapters**, these kind of corrections could not be applied due to limited amount of optodes in each study.

Secondly, the information transfer rate in the three fNIRS-BCIs is relatively slow. In **chapter 2 and 3**, answering a binary question took roughly 3 min. In **chapter 4**, it took roughly 6 min to encode a four-choice answer. These relatively long encoding times are caused by the need of several trials in fNIRS. In contrast, fMRI-BCI paradigms are robust enough so that a single trial often suffice to decode an answer. In three individual participants in **chapter 4**, we did find significant single-trial results that were sustained for three consecutive days. Thus at least in some individual cases, the fNIRS signal is robust enough to deduce the answer encoding time to 80 s in a four-choice BCI paradigm. Future fNIRS-BCI research might additionally shorten the mental task duration needed to encode an answer. Benitez-Andonegui et al. (2020) used a 6 s – compared to our 10 s – mental task duration successfully in a six-choice fNIRS-BCI. A promising development is the use of the initial dip of the hemodynamic response, reducing the mental task duration further to 2/4 s (Borgheai et al., 2020; Khan & Hong, 2017).

Thirdly, in **all empirical chapters** large interindividual differences with respect to the achieved communication accuracy were found. In a portion of participants, the fNIRS-BCI performed exceptionally well yet for others the fNIRS-BCI could not enable functional communication. This is not a unique finding. A general limitation to all BCI systems is that it simply does not work for everyone. A "universal BCI" that anyone can successfully use does not – and might not in the future – exist (Allison & Neuper, 2010). Even in healthy individuals, some BCIs do not reach accuracies required for functional communication. An estimated 20 % of subjects do not reach desirable levels of control using an EEG-BCI (Allison & Neuper, 2010; Dickhaus et al., 2009). In EEG literature, this recurring issue was coined "BCI illiteracy" (Blankertz et al., 2008; Dickhaus et al., 2009; Kübler & Muller, 2007; Nijholt et al., 2008). In the hemodynamic literature, non-functional BCI performance has also been reported (Bardin et al., 2011; Holper, Shalom, Wolf, & Sigman, 2011). BCI illiteracy is an unfortunate term in two manners. Firstly, the term inherently implies that the BCI user, through physiological or functional traits, is at fault (Thompson, 2019). Secondly, the term hinders the methodological investigation of the various reasons why a BCI might not perform adequately for a certain person (Thompson, 2019). Reasons for a lack of BCI accuracy are multifold. Possible causes include: (1) Mistakes in BCI setup or a noisy environment (Allison & Neuper, 2010), *i.e.,* an external source of electricity or light in the case of EEG and fNIRS respectively. (2) Users are tested at the wrong time of day (fatigue) or phase in their recovery process. (3) The sensory encoding modality or display/instructions are not suitable for the individual participant (Allison & Neuper, 2010). (4) The BCI classifiers need more training. (5) The cut-off point is too strict. For example the common 70 % threshold in binary

paradigms (Kübler et al., 2006). (6) Patients suffer from cognitive impairment (Ringholz et al., 2005). (7) Participants need more training (Thompson, 2019). (8) A small percentage of people suffer from aphantasia, *i.e.*, the inability to have visual experiences by mere thinking (Zeman, Dewar, & Della Sala, 2015). (9) The mental imagery task does not invoke the typical brain activation or is not detected by neuroimaging (Bardin et al., 2011; Holper et al., 2011). (10) Participants are not motivated or involved enough and need more absorbing feedback, such as virtual reality (Allison & Neuper, 2010; Benitez-Andonegui et al., 2020).

Development of fNIRS-BCIs is highly relevant in the discussion on BCI illiteracy. Exploration of an alternative, non-invasive method such as fNIRS that relies on hemodynamic instead of electrophysiological activation can constitute a valuable alternative. For example, patients that have involuntary movement or suffer from seizures of spasms[16] can often not benefit from EEG-based BCIs (Nijboer et al., 2014).

Fourthly and lastly, in **all three empirical chapters** healthy participants, mostly young and eager neuroscience students or the researchers themselves, were tested. Next to these necessary proof-of-concepts studies, there are just a handful of fNIRS-BCI studies conducted in patients (Abdalmalak et al., 2017; Borgheai et al., 2020; Naito et al., 2007). Transference of BCIs from healthy participants to patients is not trivial. FNIRS-BCI accuracies might be worse due to a multitude of reasons. For example, patients' hemodynamic responses might be atypical due to their brain injury, medication etc. (Phillips, Chan, Zheng, Krassioukov, & Ainslie, 2016). There is a clear need for more studies directly involving patients. In the context of the current PhD work, a clinical study was planned and

[16] Such as those patients with Duchenne disease, Rett syndrome or cerebral palsy.

ethical approval was granted. Unfortunately the restrictions related to the COVID-19 pandemic prevented data collection. In addition to more clinical studies, future fNIRS-BCIs might choose an alternative rationale than the basic research approach of testing of a single BCI in a homogenous group. In user-centered research, a patient in need of a BCI is the starting point. Given the patient-specific needs and clinical profile, several BCI systems and encoding modalities are tested and even adapted to his/her needs (Käthner, Kübler, & Halder, 2015; Schreuder et al., 2013). Such a user-centered design approach might be the antidote to BCI illiteracy.

Conclusion

Patients suffering from locked-in syndrome are in need of muscle-independent communication means. A brain-computer interface circumvents the muscular system by translating voluntary brain activation into their intended meaning. The most commonly used neuroimaging method is EEG, yet not all users are able to control an EEG-BCI. An fNIRS-BCI can constitute a valuable alternative, as it relies on hemodynamic rather than neuroelectric signals. In this dissertation three fNIRS-BCI paradigms were developed and tested in healthy participants. In chapter 2, a binary fNIRS-BCI was tested with mental drawing for “yes” and resting for “no”. In chapter 3, a binary fNIRS-BCI with spatiotemporal encoding was tested. Participants had to perform mental drawing or spatial navigation imagery in distinct cued time windows. In chapter 4, a four-choice fNIRS-BCI employing different sensory encoding modalities and based on a single mental task and temporal encoding was tested on three consecutive days. Individual participants could use our two- and four-choice fNIRS-BCIs successfully. Across all chapters, several analysis pipelines were explored with a specific

focus on participant-specific selection of informative channels. Many novel elements were investigated in this thesis. Chapter 3 constituted the first binary fNIRS-BCI using two mental tasks. Moreover, it was the first fNIRS study exploring spatial navigation imagery in an fNIRS-BCI context. Chapter 4 presented the first fNIRS-BCI enabling auditory, visual or tactile answer encoding within one encoding paradigm. Moreover, it included the first testing of an fNIRS-BCI in real-time in an ecologically valid environment, a cafeteria. Finally, it constituted one of the few studies to look into reliability across time. The functional communication results in all three chapters show that fNIRS-BCIs are promising and worth further development and investigation in clinical contexts.

Short Summary (English)

Shedding Light on Motor-Independent Communication:
fNIRS-based Brain-Computer Interfacing for Everyday Life

Patients with locked-in syndrome are almost completely paralyzed while at the same time being fully awake and aware. These fully conscious humans are in need of motor-independent communication. A brain-computer interface (BCI) circumvents normal output pathways through use of voluntarily evoked brain signals. A BCI thus translates brain activation into intended meaning. In this thesis, functional near-infrared spectroscopy (fNIRS) is used to measure hemodynamic brain signal changes in the context of a BCI. The three studies in this thesis aimed to develop and validate straightforward, robust, efficient and cost-effective communication paradigms that can be tailored to individual users and eventually be used in daily life. In **chapter 2,** a binary fNIRS-BCI was tested with mental drawing for "yes" and resting for "no". In **chapter 3**, a binary fNIRS-BCI with spatiotemporal encoding was tested, *i.e.*, unique imagery tasks and time windows for each answer option. In both studies, roughly half of the participants were able to communicate using the binary fNIRS-BCI. In **chapter 4**, participants used a four-choice BCI with a single mental task. All six participants could communicate using the fNIRS-BCI via three sensory modalities (visual, auditory and tactile) across three consecutive days. Two participants even communicated using the fNIRS-BCI in a cafeteria. The results in all three chapters show that fNIRS-BCIs are promising and worth further development and investigation in clinical contexts.

Short Summary (Dutch)

Motor-Onafhankelijke Communicatie Belicht:

fNIRS-gebaseerde Brein-Computer Interface voor het Alledaags Leven

Patiënten met het locked-in syndroom zijn bijna volledig verlamd maar behouden hun bewustzijn. Zij hebben nood aan motor-onafhankelijke communicatie mogelijkheden. Een brein-computer interface (BCI) omzeilt de perifere spieren en zenuwen door gebruik te maken van bewust opgewekte hersensignalen. Een BCI vertaalt dus hersenactiviteit naar betekenis. In deze scriptie wordt de methode functional near-infrared spectroscopy (fNIRS) gebruikt om hemodynamische fluctuaties in hersenactiviteit te meten. De drie studies in deze scriptie hadden tot doel eenvoudige, robuuste en efficiënte communicatie-paradigma's, die kunnen worden afgestemd op individuele gebruikers en uiteindelijk in het alledaagse leven kunnen worden gebruikt, te ontwikkelen en te valideren. In **hoofdstuk 2** werd een binaire fNIRS-BCI getest met imaginair tekenen voor "ja" en rusten voor "nee". In **hoofdstuk 3** werd een binaire fNIRS-BCI met spatiotemporele codering getest, d.w.z. met unieke verbeeldingstaken en tijdsvensters voor elke antwoordoptie. In beide studies kon ongeveer de helft van de deelnemers communiceren met behulp van de binaire fNIRS-BCI. In **hoofdstuk 4** gebruikten deelnemers een vierkeuze BCI met één mentale taak. Alle zes deelnemers konden communiceren met behulp van deze fNIRS-BCI via drie zintuiglijke modaliteiten (visueel, auditief en tactiel) gedurende drie opeenvolgende dagen. Twee deelnemers gebruikten de BCI zelfs in een cafetaria. De resultaten in alle drie hoofdstukken tonen aan dat fNIRS-BCI's veelbelovend zijn voor verder onderzoek en ontwikkeling in een klinische context.

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6 Knowledge Valorization

Communication with others through speech is fundamental to our human experience and general well-being. The overarching goal of the field of research, in which this thesis is situated, is development of alternative means of communication for patients who have lost the means to communicate naturally. Patients suffering from the so-called 'locked-in' syndrome (LIS) are almost completely paralyzed while at the same time being awake and aware. One possible solution to this clinical problem can be found in motor-independent communication through a brain-computer interface (BCI). A BCI uses voluntarily evoked brain signals for communication, without relying on peripheral nerves and muscles to produce speech (Wolpaw et al., 2000).

The three studies in this thesis aimed to develop and validate straightforward, robust, efficient and cost-effective communication paradigms that can be tailored to individual users and eventually be used in daily life. A relatively new neuroimaging method, namely functional near-infrared spectroscopy (fNIRS) was used to measure signal changes in the brain. FNIRS is a relatively easy-to-apply, inexpensive, safe and portable technology (Irani, Platek, Bunce, Ruocco, & Chute, 2007; Scholkmann et al., 2014). In **chapter 2**, participants imagined drawing to answer "yes" or merely rested to answer "no". In **chapter 3**, participants imagined drawing to answer "yes" or imagined walking through their house to answer "no". In both studies, roughly half of the participants were able to communicate using the binary BCI. In **chapter 4**, a small group of participants used a four-choice BCI with a single mental task (mental drawing). All six participants could communicate using the fNIRS-BCI via three sensory modalities (visual, auditory and tactile) across three consecutive days.

The scientific impact on the short-term is clear as **all three empirical chapters** were peer-reviewed and published in scientific journals. **Chapters 2 and 3** were presented to a scientific audience via oral and/or poster presentation (see conference contributions). Many methodological novelties – with the aim of improving fNIRS-BCI methodology, especially increasing fNIRS-signal quality or enhancing decoding accuracy – were explored in these works. For example, in **all chapters** novel temporal and spatiotemporal answer-encoding paradigms were developed and tested. Furthermore single-channel answer decoding and the effect of different types of optode-holders were explored as well as the influence of participants' physical features on signal quality. In **chapter 3**, spatial navigation imagery was used for the first time in the context of fNIRS-based motor-independent communication. Each of these separate innovations can influence communication BCI's in the short- and long-term. Outside the field of communication BCI's, such as brain-robot or neurofeedback applications, the three novel answer encoding paradigms (**chapter 2-4**) have a clear applicability. For the whole field of fNIRS, the methodological developments presented in this thesis, such as the use of an fNIRS suitability questionnaire in **chapter 3**, pave the way for more robust data collection. Lastly, this work has potential to inspire other disciplines, such as neuroenhancement, neurofeedback or brain-based gaming applications, as well as influence industrial and technical developments, such as advancements in fNIRS hard- and software.

Given that the field of research of this thesis is relatively applied, the societal implications for healthcare and quality of life of affected patients are obvious. Restoration of the possibility to interact with one's surrounding is essential to LIS patients psychological well-being. Despite

losing all physical autonomy, appropriate assistive technology can enable cognitive/mental autonomy (Lulé et al., 2009). Although the work in this thesis involved healthy participants, the potential clinical application has been a topic of focus. In **all empirical chapters,** participants' subjective experience was recorded, as a BCI should be comfortable and easy to use. In **chapter 4,** the performance of the BCI was tested over three consecutive days, as patients need a BCI that works not only once but continuously. A BCI should also perform outside the laboratory, *i.e.*, in the real world, so two participants used the BCI in a cafeteria. Moreover, three sensory encoding modalities were explored to include potential users with modality-specific disabilities (*e.g.*, blindness). In the short-term, clinical studies involving affected patients can use the knowledge obtained in this thesis to further improve usability of clinical fNIRS-BCIs. In the long-term, use of fNIRS-BCIs to communicate in daily life can hopefully become a reality, with the **three chapters** being a step in this direction. Establishing fNIRS-BCIs as a viable option for patients implicates more patients could find a suitable BCI, as the group of LIS patients is heterogenous. For example, patients that have involuntary movement or suffer from seizures of spasms can often not benefit from EEG-based BCIs (Nijboer, Plass-Oude Bos, Blokland, van Wijk, & Farquhar, 2014). Moreover, the knowledge obtained in this work is not merely potentially beneficial to LIS patients. Several patients groups can directly benefit from the current work. An fNIRS-BCI can be a valuable option for patients who have some remaining muscle control (*e.g.*, vascular or traumatic brain injury) but in which motor function is easily exhausted. As discussed in **chapter 2**, a simple yet robust binary BCI could serve as a diagnostic tool in patients with a disorder of consciousness (*i.e.*, unresponsive wakefulness syndrome or minimally conscious state). Even

patients without motor dysfunction could benefit from the knowledge obtained. For example, neurofeedback therapy aims to put brain activity related to behavior, emotion and/or cognition under volitional control of the subject, to then change/adapt said behavior, emotion and/or cognition. Neurofeedback is typically performed using electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) but use of fNIRS as neurofeedback signal is on the rise. The knowledge in this work, for example our focus on channel-of-interest and/or signal-of-interest and reports on the location of mental task-related brain activity, can be directly applied to fNIRS-neurofeedback research. In the long term, it might become possible that fNIRS-neurofeedback ameliorates symptoms in patients who had a stroke (through modulation of motor regions) or suffer from ADHD, autism or social anxiety (through modulation of prefrontal regions) (Kohl et al., 2020).

To inform and involve future target groups about the research findings, BCI information sessions and workshops can be organized. Possible end-users could be invited via existing patient organizations. The approach being ideally user-centered, meaning a patient in need of a BCI is the starting point. Given the patient-specific needs and clinical profile, several BCI systems and encoding modalities are tested and even adapted to his/her needs (Käthner, Kübler, & Halder, 2015; Schreuder et al., 2013).

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L`Enfer, c`est le Manque des Autres.

Paraphrase of Sartre by Dirk de Wachter

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Photograph of female students at the KU Leuven (Belgium) from the academic year 1927-28.

Female students were permitted to study in Leuven from 1920 onwards. In other Belgian cities, such as Gent, Liège and Brussels, female students were welcomed 40 years earlier. In the Netherlands, the first female was permitted to study in 1871.

Curriculum Vitae

Laurien was born on September 21st, 1990 in Sint-Truiden, Belgium. She attended Sint-Aloysius Middelbaar Onderwijs and Katholieke Centrum-scholen Sint-Truiden until 2008. After high school, Laurien studied psychology at the University of Leuven (KU Leuven, Belgium), were she completed a Bachelor of Science in Psychology (Magna cum Laude) in 2011. She attended classes at the University of Stirling (Scotland) in the context of the Erasmus exchange program. In 2013 Laurien graduated as a Master of Science in Psychology (Magna cum Laude) at the University of Leuven. Laurien further specialized in the field of neuroscience by completing a Research Master in Clinical and Cognitive Neuroscience (Cum Laude) at Maastricht University, the Netherlands, in 2015. During this Master, she was a visiting graduate student at the University of California Los Angeles, USA, with a focus on fNIRS for the detection of consciousness. She returned to the Netherlands in 2015 after receiving a Research Talent grant by the Netherlands Organization for Scientific Research (NWO) and started her PhD under supervision of Dr. Sorger, Dr. Riecke and Prof. Dr. Goebel. During the course of her PhD trajectory Laurien devoted herself to research, as well as teaching activities in the psychology bachelor program. After two years working as a full-time PhD candidate, Laurien continued her research half-time while working as a neuropsychologist at the University Psychiatric Hospital Sint-Kamillus (Belgium). There Laurien worked in highly specialized inpatient and outpatient treatment divisions for patients with noncongenital brain damage.

Publications

Peer-Reviewed Articles

Nagels-Coune, L., Riecke, L., Benitez-Andonegui, A., Klinkhammer, S., Goebel, R., De Weerd, P., Lührs, M., & Sorger, B. (2021). *See, Hear, or Feel - to Speak: A Versatile Multiple-Choice Functional Near-Infrared Spectroscopy-Brain-Computer Interface Feasible With Visual, Auditory, or Tactile Instructions.* Frontiers in Human Neuroscience, 15, 784522. doi:10.3389/fnhum.2021.784522

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