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APPLICATIONS OF FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (fNIRS) TO NEUROREHABILITATION OF COGNITIVE DISABILITIES

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Functional Near-Infrared Spectroscopy (fNIRS) is a neuroimaging technique that utilizes light in the near-infrared spectrum (between 700 and 1000 nm) to detect hemodynamic changes within the cortex when sensory, motor, or cognitive activation occurs. FNIRS principles have been used to study brain oxygenation for several decades, but have more recently been applied to study cognitive processes. This paper provides a description of basic fNIRS techniques, and provides a review of the rehabilitation-related literature. The authors discuss strengths and weaknesses of this technique, assert that fNIRS may be particularly beneficial to neurorehabilitation of cognitive disabilities, and suggest future applications.

INTRODUCTION AND GOALS

The aim of this paper is to describe a neuroimaging technique that appears to hold unique promise for utilization within the area of neurorehabilitation. This technique, functional Near-Infrared Spectroscopy (fNIRS), relies on optical techniques to detect changes in the hemodynamic response within the cortex when sensory, motor, or cognitive activation occurs. While optical techniques (i.e., those that are derived from the physical principles of light absorption and reflectance) have been applied to the study of brain oxygenation and metabolism for several decades (Hill & Keynes, 1949; Jobsis, 1977), the earnest use of fNIRS to study cognitive processes and neurorehabilitation began only within the last 10 to 15 years. In the following sections we aim to provide a description of this novel technique, a review of the rehabilitation-related fNIRS studies that have been published up to this point, and a discussion of strengths and limitations of this method. In addition, we hope...
DESCRIPTION OF FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (fNIRS)

fNIRS detects brain responses in a manner similar to that of PET and fMRI. That is, increases in metabolic demand as a consequence of cognitive activation leads to the well-known hemodynamic response, which ultimately increases total blood flow, regional blood volume, and regional blood oxygenation (Roy & Sherrington, 1890). The imaging data acquired in fMRI are achieved through recording of the blood oxygen level dependent (BOLD) signal, which relies on differences in the magnetic properties of oxyhemoglobin (oxy-Hb) and deoxyhemoglobin (deoxy-Hb).

Like fMRI, fNIRS also depends on the ratio of oxy-Hb and deoxy-Hb, but the optical properties—rather than paramagnetic properties—of this ratio are the focus of concern: Oxy-Hb and deoxy-Hb are the primary light-absorbing constituents in the brain, and each absorbs near-infrared light in a different manner. To capture data regarding changes in the oxy-Hb and deoxy-Hb ratio, the fNIRS procedure involves the placement of light sources and detectors on the scalp. Near infrared light (defined as non-ionizing electromagnetic radiation with wavelengths between 700 and 1000 nm) is projected through the scalp and skull, and ultimately penetrates into the first several millimeters of brain tissue. An array of photodiode detectors records the wavelengths of light reflected and absorbed.

The basic brain-dedicated fNIRS instrumentation is composed of three modules: a simple headpiece that holds the fNIRS emitters and sensors, the data acquisition board which hosts the electronic system to control the light sources and collect the reflected light, and the host server (Danen, Wang, Thayer, & Yodh, 1998) (see Figure 1).

This fairly simple and relatively inexpensive method allows for the quantification of changes in oxy-Hb and deoxy-Hb and, by summation, total blood volume (total-Hb) that are related to changes in brain activity during motor or cognitive tasks (Villringer & Chance, 1997). In addition, because fNIRS data is processed in the same manner as fMRI data and, as in fMRI, these outputs can be used to generate brain maps of activation, direct comparison between the two methods is possible through the use of standard brain-mapping software such as SPM or other similar programs.

Although investigational, in addition to measuring some of the same physiological parameters as conventional brain-imaging procedures, fNIRS possesses several potential advantages over these techniques that are particularly relevant to rehabilitation applications. For example, within the rehabilitation population, it is not unusual for individuals to have a history of multiple exposures to ionizing radiation associated with x-ray or other imaging procedures due to complicated and often long-term issues related to injury or illness. As near-infrared light sources are non-ionizing and do not exceed the energy accumulated by the brain on a sunny day, they are not harmful to tissue and repeated monitoring via fNIRS is considered to be safe. FNIRS procedures are non-invasive and are safe for use with individuals who have plates, pins, or other metallic implants that might preclude the use of magnetic imaging techniques, such as fMRI. As such medical hardware is not at all uncommon for

to suggest ways in which fNIRS may be particularly applicable to some of the unique research problems associated with neurorehabilitation.
individuals in the rehabilitation population, the use of fNIRS may provide an opportunity to safely study individuals who may otherwise be ineligible to be evaluated using other methods. In addition, when compared to the large, expensive equipment and dedicated space needed for other imaging techniques, the “simplicity” of the equipment required for fNIRS allows it to be less expensive and ultimately more usable for more frequent and repeated studies of the same subject.

The size and configuration of this equipment also make it potentially possible to conduct fNIRS in an office setting, at bedside, in therapy, or even potentially in a home setting, making this method more convenient and less intimidating for the patients or subjects, and decreasing the likelihood that they would experience the claustrophobic or fearful reactions often associated with fMRI.

With the potential portability of systems and the lack of sensitivity to movement during data acquisition, perhaps the greatest advantage of all is the ability to use fNIRS equipment in “real-life” situations. As the true purpose of rehabilitation is to assist individuals in the return to the highest possible levels of functional independence, the opportunity to monitor brain activity while individuals are engaged in actual functional activities may prove to be an invaluable resource for guiding therapeutic treatments and measuring or even predicting the brain’s response in the context of progress towards goals. This technique, therefore, has the potential to significantly impact standards of care and eventual outcomes for
individuals who are engaging in rehabilitation following significantly disabilitating injuries or illness.

Despite the advantages suggested above, it should be noted that there are currently some limitations and needs for further development of this technique. For example, to date there has not been consistency in the development of fNIRS probes or instrumentation, and there has been significant variability in the measurements (i.e., oxy-Hb, deoxy-Hb, total Hb) and methods reported in the literature. As a result, there is a need for increased standardization in order to establish the reliability and validity of fNIRS. In addition there are also limitations in spatial resolution (limited to approximately 1 inch depth), which may make fNRS inappropriate for studying some brain regions or types of function, thus limiting its applicability to some degree. While full descriptions of the various types of instrumentation and design are beyond the scope of this paper, it is important to consider these issues as the current literature is discussed, and as the development of fNIRS techniques moves forward. Through the following review of the literature, we hope to provide information about the work that has been done up to this point, and to fuel additional discussion about the strengths and limitations of this technique, as well as potential future directions for study.

fNIRS RESEARCH

fNIRS has been in used in various research and industrial contexts for several decades, however its utilization in research on cognitive processes and neurorehabilitation has been a very recent development. Prior to the 1990s, most fNIRS studies had been of neonates. In the early 1990s, Villringer and colleagues (Villringer, Planck, Hock, Schleinkofer, & Dirnagl, 1993) introduced fNIRS as a “new tool” for studying hemodynamic changes in the brain during cognitive activity. Through their study of 16 healthy adult subjects participating in visual stimulation and picture observation tasks, they found a pattern of increases in oxy-Hb and corresponding decreases in deoxy-Hb associated with cognitive activity. They were able to demonstrate that these changes were not due to alterations in skin blood flow, but rather due to hemodynamic changes in the brain. They asserted that this technique could be developed into a viable bedside method for collecting data regarding cerebral hemodynamics related to brain activity. Similar conclusions were drawn by simultaneous investigations by Chance and colleagues (i.e., Chance, Zhwang, Lipton, Alter & Rachofsky, 1992). These initial studies served to demonstrate the potential assets offered by fNIRS and provided an initial framework for future studies, that to date have covered a variety of behaviors.

Motor and Visual Tasks

Perhaps due to a need to establish baseline studies of cortical applications of fNIRS technology in the literature, several studies have focused on observations of areas of the brain where the localization of function has been more established, such as in visual and motor regions of cortex. For example, in motor studies, a common finding regarding hemodynamic response during finger opposition tasks has been an increase in oxy-Hb and a decrease in deoxy-Hb, with greatest changes noted in the sensorimotor cortex, contralateral to the hand performing the task.
(i.e., Francescini, Fantini, Thompson, Culver, & Boas, 2003; Maki, Yamashite, Yoshitoshi, Watanabe, Mayanagi, & Koizumi, 1995; Obrig et al., 1996; Watanabe, Yamashita, Maki, Ito, & Koizumi, 1996). These findings have generally been consistent with previous fMRI findings (i.e., Allison, Meador, Loring, Figueroa, & Wright, 2000; Cramer, Finkelstein, Schaechter, Bush, & Rosen, 1999).

Additional common findings have focused on the differences in timing of changes in oxy-Hb and deoxy-Hb, with increases in oxy-Hb occurring prior to decreases in deoxy-Hb in the contralateral motor cortex following performance of a hand opening/closing task (Jadzewski, Strangman, Wagner, Kwong, Poldrack, & Boas, 2003) and a sequential finger opposition task (Obrig et al., 1996).

fNIRS studies of motor tasks have also demonstrated more detailed basic activation patterns in gait: For example, Miyai and colleagues (2001) found bilaterally increased levels of oxy-Hb and total Hb in the medial primary sensorimotor cortices and supplementary motor areas with walking activity. When subjects were asked to engage in alternating foot movement without actual walking, activation fell into a similar pattern, but was reduced. When an alternating arm swing (as if walking) was performed without gait, oxy-Hb increases were noted only in the lateral portion of the primary sensorimotor regions. In comparison, when subjects were asked to imagine walking without doing so, activation was noted caudally in the bilateral supplementary motor areas. Two of eight subjects then completed the imagery and alternating foot movements during fMRI. The activation patterns were found to be consistent between fNIRS and fMRI for these two tasks. The general findings were consistent with the previous work mapping motor movement, however fNIRS allowed for greater description due to the ability to study active movement.

In an additional fNIRS study of active versus passive motor movement, Francescini and colleagues (2003) compared the strength and patterns of activation for a finger opposition task (active movement) and a passive tactile stimulation condition as well as a condition in which electrical stimulation was applied to the hand. Their findings regarding patterns of activation were consistent with previous PET and fMRI findings (i.e., an increase in oxy-Hb and decrease in deoxy-Hb in the sensorimotor cortex contralateral to the stimulated hand). They also found stronger hemodynamic response to be associated with the active voluntary task (finger opposition) as compared to the passive tactile and electrical stimulation conditions. In an additional study, which will be described later in this paper, Okamoto and colleagues (2004) also found differences in activation associated with performance of actual versus “mock” performance of motor tasks. Differences such as these may speak to the limitations of studying functional activities while utilizing methods such as fMRI, which significantly limit movement during imaging, and suggest that fNIRS may be a more useful technique for studying the cortical hemodynamics associated with active motor function.

Similar to findings of studies utilizing motor-related paradigms, evaluations of hemodynamic response in the occipital cortex following visual stimulation have also shown patterns indicating an increase in oxy-Hb mirrored by a decrease of deoxy-Hb (Heekeren et al., 1997; Jadzweski et al., 2003; Kato, Kamei, Takashima, & Ozaki, 1993; Obrig et al., 2002). Despite such similarities, some differences in the timing of motor and visual hemodynamic response have been noted. For example, Jadzweski and colleagues (2003) found that while visual data were qualitatively similar to motor
data, there was some difference in the initial pattern of the oxy-HB and deoxy-HB ratio change, as well as a simultaneous peak for oxy-Hb, deoxy-HB, and total Hb. This finding was consistent with the findings of other visual cortex studies, but varied from response in the motor cortex. The authors suggested that such differences may be due to different capillary transit times within the motor and visual cortices.

Visual studies have also been used to attempt to evaluate whether a linear relationship exists between neuronal and hemodynamic activity in the brain upon visual stimulation (Gratton, Goodman-Wood, & Fabiani, 2001; Obrig et al., 2002; Wolf et al., 2003). Findings of these studies have generally supported the model of such a relationship within the visual cortex. Additional fNIRS studies using a visual paradigms have shown localization of function to the visual cortex, consistent with other types of neuroimaging results (Meek et al., 1995). Two other fNIRS visual studies of note found differences in activation using various levels of stimulus intensity (Wolf et al., 2003), and evidence of decreased hemodynamic response following habituation using a visual paradigm (Obrig et al., 2002).

**Cognition**

Initial studies applying fNIRS for assessing different types of cognitive ability often included less standardized tasks. For example, Chance, Zhuang, UnAh, Alter, and Lipton (1993) measured changes in cerebral hemodynamics associated with subjects’ performance of visually presented abstract thinking tasks. Hoshi and Tamura (1993) studied subjects during visual and auditory stimulation, as well as during conduct of mental tasks, such as mentally solving a mathematical problem. That same year, Hoshi and Tamura (1993) also found differences in hemodynamic response between an older and younger group of subjects performing a mental problem-solving task, and Okada, Tokumitsu, Hoshi, and Tamura (1993) observed gender and handedness differences in hemodynamic response in subjects completing a mirror drawing task.

From the late 1990s through to the present, there has been an increase in the number of fNIRS studies related to higher-level cognitive functioning. In their 2003 review article, Obrig and Villringer suggested, however, that there is a gap in the literature between studies of basic functions, such as the motor and visual studies noted above, and the complexity of such functions as language and higher-level cognitive tasks. Not surprisingly, as compared to the studies of motor and visual functioning, fNIRS findings of higher-level cognitive functions are more complex and varied, with less consistency in patterns of oxy-Hb and deoxy-Hb reported. In fact, as previously suggested, some of the greatest limiting factors in our ability to establish the reliability and validity of fNIRS, and to discuss trends in the literature, are the variability of the functions studied, the methods used, and the measurements reported.

fNIRS studies of language provide an example of these challenges: Language paradigms have included comparisons of semantic anomalies versus a regular reading task (Horovitz & Gore, 2004), syntactic versus semantic decision tasks (Noguchi, Takeuchi, & Sakai, 2002), and performance by aphasic versus non-aphasic subjects (Sakatani, Yuxiao, Lichty, Li, & Zuo, 1998). While in each of these studies, differences in localization of hemodynamic response were evident when within-study paradigm tasks were compared, the variability between language tasks across studies and variations in protocols limits direct comparison.
As an additional example, Cannestra and colleagues (Cannestra, Watenburge, Obrig, Villringer, & Toga, 2003) conducted a localization study of language functioning using fNIRS. They assessed hemodynamics related to covert visual object naming versus motor movement of the tongue and hand (right finger opposition). Using an fNIRS system with light-emitting optodes located over the precentral sulcus and light-detecting optodes placed both 3 cm anterior (over the prefrontal cortex) and 3 cm posterior (over the pericentral region), they were able to distinguish Broca’s area from motor areas. The overall findings were therefore consistent with what is known about cortical areas associated with language and motor functioning. However, they also found an overlap in oxy-Hb changes, with increases noted in both anterior and posterior optode positions across all tasks for all subjects. In contrast, changes in deoxy-Hb were more pronounced, more localized and varied in location with each task. For example, deoxy-Hb decreases were noted during both motor tasks in the posterior position, with no significant deoxy-Hb change in the anterior position noted during a finger opposition task, while deoxy-Hb decreases were noted in the anterior position during a tongue movement task, but at a lower magnitude as compared to the posterior. In comparison, during the covert visual naming task, oxy-Hb increases were noted in both the anterior and posterior positions, with greater significance in the anterior position. Decreases in deoxy-Hb were noted only in the anterior position, with increases in deoxy-Hb actually noted in the posterior position. Based on these findings, the authors concluded that deoxy-Hb may be the best parameter for mapping language cortices using fNIRS.

Statements of Obrig and Villringer (2003) were in agreement with Cannestra and colleagues. They noted that, based on the physiological basis of the BOLD signal, a decrease in deoxy-Hb is indeed the most valid parameter indicating cortical “activation.” They also point out, however, that that one of the problems in the fNIRS literature, is that oxy-Hb changes are often used as the parameter of choice, and deoxy-Hb changes are only sometimes reported. Unfortunately, this is case in several other language studies (e.g., Kennan, Horovitz, Maki, Yamashita, Koizumi, & Gore, 2002; Noguchi et al., 2002; Saki, Hashimoto, & Homae, 2001), making direct comparison in the fNIRS language literature additionally complicated.

Comparison of other studies of higher-level cognitive processes pose similar challenges. As an example, Fallgatter and Strick conducted two separate studies utilizing fNIRS with different tasks associated with frontal lobe functioning. In 1997, the authors observed hemodynamic patterns during subject performance of the Continuous Performance Test (CPT). Their findings indicated primarily right frontal activation. Statistically, they observed significant differences between hemispheric hemodynamics, with significant differences noted in deoxy-Hb during task performance as compared to baseline, but no significant changes in oxy-Hb in the right, as compared to the left hemisphere. In a 1998 study by these same authors, healthy subjects performed the Wisconsin Card Sorting Test during fNIRS. Compared to baseline at rest, findings indicated a significant oxy-Hb increase bilaterally in the frontal brain regions.

Studies focusing on the prefrontal cortex have also yielded varying results: For example, in a study of 14 healthy subjects, Schroeter and colleagues (Schroeter, Zysset, Kupka, Kruggel, & von Cramon, 2002) utilized an event-related design in which fNIRS was used to measure changes in oxy-hemoglobin, deoxy-hemoglobin, total
hemoglobin, and the redox state of cytochrome-c-oxidase (Cyt-Ox) in 14 healthy subjects completing a color–word matching Stroop task. They found patterns of increased oxy-Hb and total Hb, and decreased deoxy-Hb concentrations indicating brain activation patterns similar to what has been observed in other studies. Stronger hemodynamic response was noted in the lateral prefrontal cortex bilaterally for incongruent as compared to neutral or congruent trials, suggesting that the interference during the incongruent trials induced stronger brain activation. The authors concluded that it is feasible to use an event-related design in fNIRS studies of cognition.

Another study of prefrontal cortex functioning conducted by Toichi and colleagues (2004) used fNIRS to investigate changes in hemodynamic response for simple attention versus higher cognitive processing tasks with 10 Japanese and 10 American healthy adult subjects. Results of this study found increases in oxy-HB and decreases in deoxy-HB in the prefrontal cortex during higher-level cognitive tasks (both verbal and visual), with increases in tissue hemoglobin saturation (THS) noted as well. In comparison, increases in both oxy-HB and deoxy-HB were observed during basic attention tasks, with no significant changes in THS noted. The patterns of hemodynamic response were found not to be affected by either task difficulty or language. The authors suggested that differing patterns in changes in deoxy-Hb might be a distinguishing marker in studying prefrontal cortex activation during attention versus higher-level cognitive tasks.

In addition to the studies mentioned above, in recent years, Dr. Britton Chance and his colleagues at the University of Pennsylvania have spearheaded development and testing of fNIRS technology for other cognitive applications. The collaboration of the applicant team of biomedical engineers from Drexel University with Dr. Chance has focused on functional optical brain imaging as a means to assess cognitive workload during attention and working memory tasks as well as complex tasks such as war games performed by healthy volunteers under operational conditions (Izzetoglu, Bunce, Izzetoglu, Onaral, & Pourrezaei, 2003; Izzetoglu, Bunce, Onoral, Pourrezaei, & Chance, 2004).

While, overall, fNIRS studies of cognitive functioning have found activation in brain regions that are generally consistent with fMRI and other brain-mapping techniques, the variability of results reported in the literature needs to be evaluated further. It is possible that further validation of fNIRS techniques on more basic functions may assist in the application of fNIRS to more complex functions. In addition, the development of consistent instrumentation, methods, and measurement reporting will be important for establishment of reliability and validity to occur.

Aging and Psychiatric Populations

While most earlier baseline studies utilized healthy subject groups, more recently studies of groups with psychiatric or neurological diagnoses have also begun to appear. For example, Fallgatter and Strik (1997) used fNIRS to study elderly healthy controls in comparison to subjects with probable Dementia of the Alzheimer’s Type (DAT) during performance of verbal fluency tasks (both letter and category). While both groups performed better on the category task, healthy subjects performed significantly better on both tasks, as compared to subjects with DAT. In addition, reduced baseline oxygenation was noted for DAT subjects. During
performance of the verbal fluency tasks, an expected oxy-HB increase was noted in
the left hemisphere for controls, as compared to the right hemisphere. A loss of
hemispheric laterization was noted for DAT subjects. Other fNIRS studies have
also shown evidence of a decrease in hemodynamic response associated with Alzhei-
mér’s disease (Hock et al., 1996; Hock et al., 1997) and normal aging (Hock, Muller-
Spahn, Schuh-Hofer, Hofmann, Dirnagle, & Villringer, 1995; Hock et al., 1996;
Hoshi & Tamura, 1993; Kwee & Nakada, 2003; Mehagnoul-Schipper et al., 2002;
Schroeter, Zysset, Kruggel, & von Cramon, 2003). Decreases in activation within
regions of interest and alterations in hemodynamic patterns have also been noted
in individuals with diagnoses such as schizophrenia (Shinba et al., 2004; Suto,
Fukada, Ito, Uehara, & Mikuni, 2004) and mood disorders (Matsuo, Kato, Fukuda,
& Kato, 2000; Matsuo, Kato, & Kato, 2002) as compared to healthy controls. Pre-
vious fMRI, PET, and SPECT studies have commonly found reductions or altera-
tions in hemodynamic response with aging, neurological disease, and psychiatric
diagnoses (Mehagnoul-Schipper et al., 2002; Weinberger et al., 2001). Therefore
the findings of these studies are consistent, and suggest that as fNIRS techniques
continue to be developed, the study of various population groups using this method
will be beneficial.

fNIRS AND REHABILITATION

While limited fNIRS studies have been conducted within the rehabilitation
population, we argue that this is an area where this technology may be most appli-
cable. As the focus of rehabilitation is on increasing functional capacity through
therapeutic interventions, it seems possible that Obrig and Villringer’s (2003) call
for additional studies of basic paradigms with cortical regions that have been well
defined, such as primary and secondary sensory areas, may be addressed readily
within this population. In addition, the opportunity to compare healthy controls
with those who have acquired brain injury may actually aid in clarifying what has
been found regarding the hemodynamics associated with cortical functioning for
both basic paradigms, as well as more complex cognitive processes, such as language
and memory. It seems possible that the more basic components of functions, which
could be duplicated in fMRI paradigms where movement is limited, could be
assessed using both fMRI and fNIRS for comparison, after which studies could
be extended to examine actual functional activities, and could be compared to the
basic information acquired through both imaging methods. Consider the study by
Miyai and colleagues, which was described earlier in this paper: In this study, sub-
jects engaged in active walking, foot movements only, arm swing only, and motor
imaging. Although basic localization of motor functioning has been established
using other techniques, because movement in this study was broken down and could
be studied actively using fNIRS, the results of this study provided new information
about the cortical mapping of various components of gait activity. In addition, fNIRS
allowed for the study of actual gait, which is not possible using fMRI. By designing
the study to include the assessment of some gait components using both fMRI and
fNIRS, similar activation patterns could be observed, helping to validate the findings.
Based on their findings suggesting that it is possible to map dynamic activities, such as
gait, using fNIRS, the authors suggest that this technique may be useful in evaluating
pathological gait and as part of rehabilitative therapy. This study presents a design that is ideally suited to study functional activity in rehabilitation, and which would not be possible utilizing other neuroimaging techniques alone.

In yet another study that speaks to the need to assess dynamic activities with methods that allow for performance of actual functional tasks, Okamoto and colleagues (2004) found significant differences in areas of cortical activation when subjects performed an actual functional task (apple peeling) during fNIRS, and when the same task was performed in a mock fashion during simultaneous fMRI and fNIRS (actual apple peeling caused activation of the prefrontal cortex, while mock apple peeling did not). The authors argued that studying tasks in a simplified manner, as may be required by fMRI and similar neuroimaging methods, may not provide an accurate picture of cortical activation that occurs during actual activities. We would argue that the ability to map activation accurately during activity has the potential to greatly enhance our knowledge of healthy function, but also to learn how about the correlations between the restoration of function and altered hemodynamic patterns following injury or during rehabilitation. Ultimately, increased accuracy in brain mapping during rehabilitation has the potential to allow us to watch changes in hemodynamics as function returns and design treatments to optimize recovery.

To date there have been only a few studies reported in the literature actually utilizing fNIRS within neurorehabilitation populations, with most of these studies being conducted with individuals who experienced stroke. Of the published studies in this area, the majority have primarily focused on fNIRS measurements recorded during motor exercises. The following sections review the literature available in these areas and point to the need for further application of fNIRS technology for the study of individuals in rehabilitation.

Stroke

In 2002, Miyai and colleagues assessed 6 nonambulatory patients with severe hemiplegia following stroke. Study of these patients was conducted at 3 months following stroke, on average. An fNIRS imaging system was implemented during a treadmill-walking task under partial body weight support. Support was provided either with mechanical assistance in swinging the paretic leg, or through use of a technique provided by physical therapists that enhanced swinging of the paretic leg. Performance of the gait activity was associated with increases in oxy-Hb in the medial primary sensorimotor cortex, with greater increases noted in the unaffected hemisphere, as compared to the affected hemisphere. Data indicated that, during hemiplegic gait, there was enhancement of premotor activation in the affected hemisphere, and activation of the presupplementary motor area was also noted. The facilitation technique provided by the physical therapist was shown to induce increased cortical activations as well as gait performance, as compared to the use of mechanical assistance. The authors concluded that multiple motor areas, including the premotor cortex (PMC) and presupplementary motor area (PSMA) might be involved in the restoration of gait function in patients with severe stroke.
In an additional study, Mayai and colleagues (Mayai, Yagura, Hatakenaka, Oda, Konishi, & Kubota, 2003) conducted an fNIRS gait study of eight patients with stroke. Cortical activities were measured during hemiparetic gait activities on a treadmill both before and after 2 months of inpatient rehabilitation. They found initial asymmetries in activation in the medial primary sensory cortex (SMC), pre-motor cortex, and supplementary motor area (SMA), with increased oxygenated hemoglobin levels in the unaffected hemisphere, as compared to the affected hemisphere, during gait activities. Improvement in asymmetrical SMC activation correlated with improvement on gait tasks. They concluded that recovery of locomotion after stroke may be associated with improved asymmetry in SMC activation and enhanced premotor cortex activation in the affected hemisphere.

Another study of stroke patients (Kato et al., 2002) compared fNIRS and FMRI to examine six patients who experienced stroke, specifically within the distribution of the middle cerebral artery (MCA), exhibited left hemiparesis, and recovered to the point that they had minimal or mild residual hemiparesis. Subjects were studied during a hand movement task of both the unaffected and affected hand. Results of both fMRI and fNIRS studies found evidence suggesting that compensation or reorganization of the hemisphere ipsilateral to the affected hand may contribute to recovery from hemiparesis. The authors concluded that fNIRS was useful for the study of poststroke alterations in motor functioning.

In 1998, Sakatani and colleagues conducted a study of cerebral blood oxygenation and hemodynamic response differences in the left prefrontal cortex of 29 subjects engaged in a confrontational naming task. The sample consisted of 10 post-stroke nonfluent (Broca’s) aphasia patients, 6 post-stroke non-aphasic patients, and 13 age-matched healthy controls. Results indicated differences between the aphasic and non-aphasic groups in patterns of change in the fNIRS parameters induced by the language tasks, although results within groups were variable. For example, in both the healthy control group and the nonaphasic stroke patients, oxygen metabolism and hemodynamics of the left prefrontal cortex changed significantly with performance of the language task. The most common pattern of change noted for both of these groups was an increase in oxy-Hb and total-Hb with a slight decrease or no change in deoxy-Hb, with some within group variations of this pattern noted. In contrast, for the aphasic group who had some difficulty in performing the language task, the most common pattern observed was an increase in deoxy-Hb with an increase of oxy-Hb and total-Hb. Statistical analysis demonstrated a significant difference in deoxy-Hb between the aphasic and non-aphasic groups, with no significant differences found between the healthy controls and non-aphasic stroke subject groups. The authors asserted that the significantly different pattern observed in the aphasic group as they engaged in language tasks suggested that the left prefrontal cortex of aphasic patients utilized more oxygen during such tasks as compared to nonaphasics. The multiple activation patterns observed within groups suggested some individual differences in activation associated with the performance of language-based tasks.

Saitou, Yanagi, Hara, Tsuchiya and Tomura (2000) conducted a study of 44 post-stroke patients with hemiplegia and 24 healthy controls. They asked subjects to perform several physical and occupational therapy related tasks. Healthy control subjects performed a head up tilt (HUT) task, as well as calculations and an erg-
ometer task. Stroke patients performed these same tasks as well as tasks involving reading aloud, listening to music, reciprocal extension, non-paralyzed extension, passive range of motion, pulley, bridge, facilitation, stand-up, and gait activities. Changes in cerebral blood volume (CBV) and cerebral oxygen volume (COV) were measured with an fNIRS apparatus placed at mid-forehead in healthy controls and over the impaired cerebral hemisphere among hemiplegic patients. In healthy controls, results indicated that the change patterns of CBV and COV differed between tasks: A decrease in COV was noted with HUT, a limited increase in both COV and CBV was observed with the calculation task, and a gradual increase in both measures was noted with ergometer tasks. In hemiplegic patients, results indicated significant (positive) CBV changes with performance of ergometer, facilitation, stand-up, and gait tasks. Significant (negative) changes were noted with use of a passive movement device to produce finger extension. Significant (positive) changes in COV were noted in ergometer and facilitation tasks, and (negative) in HUT. The authors concluded that fNIRS was useful for observing changes in hemodynamics and oxygenation in various types of rehabilitation interventions. It was also noted that some tasks increased both COV and CBV (ergometer and facilitation) in the affected prefrontal cortex of hemiplegic patients.

Murata, Sakatani, Katayama, and Fukaya (2002) used fNIRS to observe concentration changes of deoxy-Hb, oxy-Hb, and Total-Hb in a group of six patients with cerebral ischemia as compared to six healthy controls. FNIRS results were compared with BOLD-fMRI findings. Their results indicated differences in cerebral blood oxygenation between the two groups during performance of a hand-grasping task, which at the behavioral level all patients could perform in a manner similar to controls. Specifically, within the control group, decreases in deoxy-Hb and associated increases in oxy-Hb and total-Hb in the primary sensory cortex were observed during the task performance. In comparison, the patient group results indicated a significant deoxy-Hb increase from baseline, as well as an increase in oxy-Hb and total-Hb, indicating cerebral blood flow increases in response to neuronal activity. In comparison to the fNIRS findings, BOLD-fMRI findings indicated only limited activation areas in the affected primarily sensorimotor cortex of patients. The authors suggest that BOLD-fMRI may overlook activation areas unless both increases and decreases of signal are taken into consideration.

In another comparison study of fMRI and fNIRS (Kato, Izumiyama, Koizumi, Takahashi, & Itoyama, 2002), six right-handed patients who suffered MCA territory cerebral infarction with minimal or mild residual left hemiparesis were evaluated. The focus was on evaluation of compensatory motor activation of cortical regions using fMRI and fNIRS during a hand movement task at chronic stages. Five healthy controls were also examined. Activation patterns between fMRI and fNIRS were consistent, however it was noted that fNIRS detected only superficial activation. In addition it was reported that while fMRI had superior spatial resolution, fNIRS provided a dynamic profile of activation. fMRI and fNIRS activation patterns of healthy controls during each hand movement were noted predominantly in the contralateral primary sensorimotor cortex and supplementary motor areas. Stroke patients exhibited this same pattern with movement of the unaffected hand. With movement of the affected hand, however, the activation patterns of stroke patients revealed extended activation in the contralateral motor cortex, as
well as in the primary motor cortex and supplementary motor areas of the ipsilateral motor cortex. The authors suggested that the fMRI and fNIRS findings of this study provided evidence that compensation or reorganization of the ipsilateral motor cortex contributes to the recovery from poststroke hemiparesis. As a result, the authors concluded that fNIRS might be a useful tool for studying cerebral reorganization following stroke.

Overall, most of these studies involved evaluation of motor functioning. Those using direct comparison to fMRI, found consistent activation patterns. In studies where more complex cognitive processes were included, results were somewhat more variable, which is consistent with the previous discussion of the literature. Taken as a whole these studies demonstrate the usefulness of fNIRS for evaluating hemodynamic patterns associated with active function following stroke.

**Traumatic Brain Injury**

The current authors are aware of no published studies directly evaluating the use of fNIRS with traumatic brain injury (TBI) patients during the course of rehabilitation. fNIRS studies involving individuals with TBI have generally examined patients in acute care, particularly in intensive care units. For example, Gopinath and colleagues (Gopinath, Robertson, Grossman, & Chance, 1993) applied fNIRS to detect the presence of intracranial hematoma in 46 patients with head injury. Of the 40 patients with intracranial hematomas identified by CT, fNIRS demonstrated greater absorption of light on the side of the hematoma in all 40 cases. fNIRS was then used to follow up patients post-operatively in the ICU where differences in optical density of tissue on the injured versus non-injured hemispheres were measured. In 36 of the 40 patients with hematoma, the previously observed asymmetry resolved following surgical evacuation, or after natural reabsorption of the hematoma. In four patients who developed delayed or postoperative hematomas, asymmetry (as demonstrated with fNIRS) persisted. The authors concluded that fNIRS was a useful tool for this type of assessment in head-injured patients.

Robertson, Gopinath, and Chance (1995) first applied fNIRS serially over the course of 3 days in the detection of delayed intracranial hematomas in 167 patients with head injury. They concluded that early diagnosis using fNIRS might reduce secondary injury by allowing for early identification and treatment of delayed hematomas. In another study, Kirkpatrick and colleagues (Kirkpatrick, Smeilewski, Czosnyka, Menon, & Pickard, 1996) assessed the potential use of fNIRS in a neurointensive care unit with 14 ventilated patients with head injury. They used a multimodality recording system and recorded fNIRS-derived changes in oxy-Hb and deoxy-Hb, as well as signals derived from intracranial pressure, cerebral perfusion pressure, peripheral oxygen saturation, and jugular venous saturation. Evaluation of the recorded data indicated that fNIRS showed correlated changes in 97% of events recorded that showed clear changes in cerebral perfusion pressure accompanied by hemodynamic changes in the middle cerebral artery flow velocity and cortical perfusion as measured by other methods.

In another study of patients in intensive care, Kampfl and colleagues (Kampfl, Pfaueler, Denchev, Jaring, & Schmutzard, 1997) used fNIRS to evaluate changes in regional cerebral oxygen saturation (rSO2) in eight patients with severe head injury.
They assessed four patients with intracranial pressure (ICP) higher than 25 mmHg, and four with ICP lower than 25 mmHg. At baseline, they found fNIRS values to be significantly higher in the low ICP group as compared to the high ICP group, despite the fact that other measures (i.e., arterial PO2, pCO2, peripheral oxygen saturation, and transcranial Doppler sonography) did not detect significant differences between groups. Patients in both groups were then given 50% O2 for a period of 3 minutes, followed by follow-up measurement. Again, similar values in peripheral oxygen saturation, arterial PO2, and TCD velocities were found. Using fNIRS, however, rSO2 values were found to be significantly increased in the low ICP group after the hyperoxygenation period, but no detectable change was noted in the high ICP group, and rSO2 values in the high ICP group were significantly lower than in patients in the low ICP group. The authors suggested that fNIRS might be useful as a monitoring tool for the non-invasive evaluation of impaired cerebral microcirculation in head-injury patients who have increased ICP. In contrast, Buchner and colleagues (Buchner, Meizensberger, Dings, & Roosen, 2000) monitored 31 patients with severe brain injury during acute intensive care. fNIRS was compared with invasive ICP, CCP, and regional brain tissue PO2 monitoring. They found a high failure rate and limited sensitivity of fNIRS as compared to other measures, and determined the fNIRS is not suitable for clinical use for neuromonitoring following brain injury.

In a preliminary study of children who had experienced traumatic brain injury (Adelson, Nemoto, Colak, & Painter, 1998), fNIRS monitoring was used to continuously monitor 10 patients and was found to reliably detect changes in cerebral hemodynamics. The authors suggested that FNIRS may be a useful tool to gain an improved understanding of the diffuse cerebral swelling seen in children following severe TBI.

Brawanski, Faltermeier, Rothoerl, and Woertgen (2002) compared the measure of local hemoglobin oxygen saturation (rSO2) by fNIRS and a slightly more invasive measure of local oxygen pressure in white matter of the brain (tipO2), to assess whether tipO2 and rSO2 signals provide similar information for monitoring patients in neurosurgical intensive care units. A tipO2 probe and an fNIRS sensor were positioned over the frontal lobe area of most significant injury (as indicated by CT scan) in 12 patients, 9 with severe TBI and 3 with aneurismal subarachnoid hemorrhage. By means of fNIRS-derived spectral analysis, the authors determined that tipO2 and rSO2 signals contain similar information, despite the fact that different registration methodologies are used.

Despite the paucity of fNIRS studies of individuals with TBI to date, we would argue that, based on the available rehabilitation literature and the results of the work conducted with stroke patients, the development of paradigms to study those undergoing rehabilitation following TBI is both appropriate and important. It seems likely that designing studies to utilize fNIRS findings in conjunction with the serial neuroimaging and neuropsychological testing protocols, which are often used to assess recovery from injury, could be useful both to validate fNIRS techniques, and, ultimately, to provide data about functional recovery not possible with the currently used neuroimaging methods. We are currently conducting pilot studies utilizing fNIRS with this population and see the potential for growth in this area of study in the future.
fNIRS: ASSETS AND CONSIDERATIONS

In sum, the research to date has begun to examine numerous applications of fNIRS and has helped to establish some of the unique assets offered by this technology. Although most studies seem to generally conclude that fNIRS technology is applicable to functional brain mapping, we have described some limitations and needs for further development throughout this paper. Table 1 provides a summary of some of the strengths and limitations that may be important to consider when designing and implementing fNIRS studies.

Regarding limitations: In evaluating the available literature, there are currently differences in the reporting of oxy-Hb, deoxy-Hb, and total-Hb as parameters of choice for indicating cortical activation. Also, many of the studies in the literature utilize different instrumentation with varied configurations, numbers, and placements of optodes. In addition, as previously mentioned, there is tremendous variability in the types of tasks assessed, especially when looking at the literature regarding higher-level cognitive functioning. Due to differences such as these, as well as factors such as limited spatial resolution, differences in skull and hair thickness at various places on the head, and differences in statistical analysis, some difficulty in direct comparison between studies needs to be considered.

Table 1 Summary of pros and cons of fNIRS application to rehabilitation

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td><strong>1. Portability</strong></td>
<td>• Instrumentation for system is typically limited to a laptop and head unit</td>
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<tr>
<td><strong>2. Availability</strong></td>
<td>• Lack of standardized fNIRS measurements</td>
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<td><strong>3. Non-invasive</strong></td>
<td>• Much variability in studies to date, regarding what measurement (deoxy-hb, oxy-hb, total Hb) is reported</td>
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<tr>
<td><strong>4. Allows observation of “actual” not “mock” tasks performance</strong></td>
<td>• Variability in instrumentation</td>
</tr>
<tr>
<td><strong>5. Allows observation of dynamic tasks performance</strong></td>
<td>• Many systems have been independently developed and subsequently may have variability in capacity</td>
</tr>
</tbody>
</table>

**Table 1** Summary of pros and cons of fNIRS application to rehabilitation

- **Advantages**
  - Portability: Instrumentation for system is typically limited to a laptop and head unit
  - Availability: Low cost systems
  - Non-invasive: Does not require intravenous administration of radioisotopes
  - Allows observation of “actual” not “mock” tasks performance
  - Allows observation of dynamic tasks performance

- **Disadvantages**
  - Lack of standardized fNIRS measurements
  - Variability in instrumentation
  - Limited spatial resolution
  - Appropriateness

- **Limitations**
  - Differences in the reporting of oxy-Hb, deoxy-Hb, and total-Hb as parameters of choice for indicating cortical activation.
  - Variability in instrumentation with varied configurations, numbers, and placements of optodes.
  - Tremendous variability in the types of tasks assessed.

- **Needs for further development**
  - Establish further reliability and validity of fNIRS measurement.
  - Establish which aspects of rehabilitation may most benefit from fNIRS.
Despite limitations, however, we have argued that fNIRS has several advantages over other methods, especially for the study of functional activity: The size, cost, and portability are major advantages regarding the actual imaging equipment. The safety and non-invasiveness of the procedure provides improved patient comfort and convenience. Most importantly, the ability to collect data while individuals are engaged in everyday activities has the potential to provide more accurate data regarding hemodynamic changes associated with functional activity.

FUTURE DIRECTIONS

The present array of imaging technologies provides researchers and, to a lesser degree, clinicians with an arsenal of ways to measure changes in the brain. Yet it is likely that emerging technologies such as fNIRS will hold even greater promise for neurorehabilitation by bringing the imaging lab into the rehabilitation clinic. Obrig and Villringer (2003) suggest the need for further methodological and technical developments, further studies to define spatial resolution, and more standardized statistical/data analysis as some issues for the future development of fNIRS in order to provide increased standardization and comparability within the literature. Based in this review, the current authors are in agreement with this assessment. While it is unlikely that fNIRS will replace fMRI or other neuroimaging methods, it appears that, with development, it has the potential to provide superior data regarding functional activity in rehabilitation. While further reliability and validity may need to be established for more basic functions and then applied to more complex cognitive functions, a review of the literature suggests that the ability to do so is promising. Ultimately, this may allow for the development of more accurate and effective therapeutic interventions and improved outcomes for individuals recovering from both physically and cognitively disabling illnesses or injuries.

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REFERENCES


