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# Hemoglobin (Hb) - Oxyhemoglobin (HbO) Variation in Rehabilitation Processes Involving Prefrontal Cortex

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Additional information is available at the end of the chapter

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## Abstract

The prefrontal cortex is the anterior part of the frontal lobe, situated before the primary motor cortex and the premotor cortex and plays a role in the regulation of complex cognitive, emotional and behavioral functioning. It includes various Brodmann areas, such as 9, 10, 11, 12, 46, 47. The basic function of this region is guiding thoughts and actions toward one's goals. The goal of the study is using functional near-infrared spectroscopy (fNIRS) to identify the most suitable rehabilitation model in subacute post-ischemic pathologies and impairments involving directly or indirectly the prefrontal cortex. The aim is to measure threshold parameters for neural fatigue through Hb-HbO<sub>2</sub> variation. The overall purpose is the ongoing evaluation of Hb-HbO<sub>2</sub> variation throughout the entire tailored rehabilitation program with the observation of patient's clinical changes, which represents the heart of the Cerebro rehabilitation model.

**Keywords:** rehabilitation, PFC damage, fNIRS, Hb-HbO<sub>2</sub> variation, cerebro rehabilitation model

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## 1. Introduction

Although not yet widely used, probably because of lacking clinical education, near-infrared spectroscopy (NIRS) shows several methodological advantages if compared with other non-invasive measurements of neural activation.

NIRS specific and unique features make it a prospective tool for studying stimulus-based responses to emotion processing in the prefrontal cortex (PFC). However, there are obstacles for the implementation of NIRS on emotional research that must be considered.

This study focuses on NIRS ability to express suitable measures for the most adequate rehabilitation process with results that permit to evaluate the effects of PFC activation over emotions. Specifically, the neural mechanism underlying these processes is based on a bidirectional interaction between emotion and action, excellent to be measured using NIRS technique.

The Cerebro procedure aims at setting the fundamentals for NIRS application in those fields whose aim is to evaluate suitable rehabilitation models in prefrontal cortex related disorders by analyzing task-related stimuli that are mediated by pathways involving sensory processing, memory and emotion. To do so, NIRS parameters during recording will be considered along with the NIRS level of criticality in order to determine the good practice for functional processing of the required result.

When talking about prefrontal cortex (PFC), we need to remember that the associative cortex in the frontal lobe has a lagging development in the neocortical regions. PFC is one of the cortical regions which undergoes a major expansion during personal maturation and evolution. In human adults, PFC represents approximately one-third of the whole neocortex. The PFC ongoing and wide development is demonstrated by its impeccable structure.

In developing brains, like infants', PFC's delayed maturation is marked by a late myelination of axonal connections.

Prefrontal cortex in primates is necessary not only for keeping relevant information in mind to complete a task but also for the active suppression of the irrelevant stimuli. Patients with ictus or pathological aging, affecting the lateral portion of the PFC, can discriminate between auditory tasks but fail when irrelevant auditory stimuli are included [1].

This information is important in order to define the NIRS-fNIRS ratio (fNIRS: functional near-infrared spectroscopy since this is used when a stimulus is given, and the outcome is a measurement of how the stimulus affects brain activity; if not it is a resting state registration that we call NIRS) where inhibitory responses or noise can influence the assessment of the result. Noise is the key point for the identification of an optimal functional assessment; therefore, in the following paragraph, we focus on specific measurements, precautions to be taken and the right procedure to follow, step by step, in the preliminary phase of testing.

## 2. NIRS and fundamentals of measurements

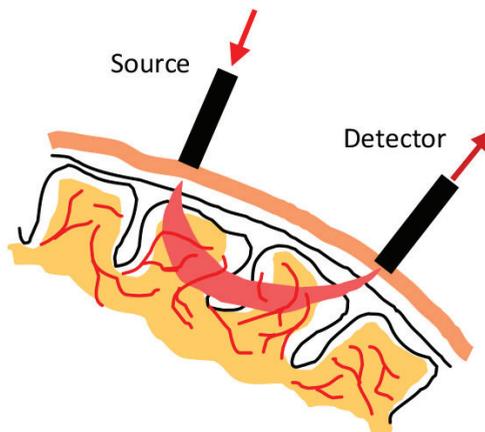
For the evaluation of rehabilitative activity that involve prefrontal cortex (PFC), we used the NIRS functional detector systems: near-infrared spectroscopy uses low-intensity optical radiations to measure changes in light absorption by the cortical vascular tissues in order to detect changes in local concentration of oxy- and deoxyhemoglobin as a correlate of functional brain activity.

Each measurement channel is formed by an optic emitter (source) and a receiver (detector) placed on the subject's head. Due to the scattering (light diffusion) properties of the tissue, a portion of the received light will deeply pierce in the tissue structure, where it interacts with chromophores like hemoglobin. The degree of penetration and the shape

of the probing volume are determined by the source-detector distance and by the optical properties of local tissues. Cortical NIRS signals are estimated to originate from an area that is placed between source and detector and from a tissue depth that is no more than the half of the source-detector distance (see **Figure 1**). Optical signals are weakened by biological tissues; intensity will decrease in terms of centimeters, therefore the optimal distance between source and detector is a compromise that must be verified in order to reach the maximum depth while maintaining a sufficient signal quality (signal-to-noise ratio). The optimal distance used in this study is the verified one of 30 mm and the cortical detection depth is around 25 mm.

To achieve spatial imaging of the PFC, we used the NIRX imaging equipment that employs matrixes of paired source-detectors arranged on the area of interest, where each source channel forms a measurement channel with each detector channel. Therefore, a setup with X sources (S) and Y detectors (D) will produce an X\*Y measurement channel. This is true despite the position and the source-detector distance although only those channels whose distance is within a certain limit will produce signals with usable amplitudes and noise levels. Due to this model, there are no restrictions on how to set up sources and detectors, thus allowing us the maximum flexibility and freedom in realizing this functional study. At the same time, we focused on the experimental design ensuring signal quality during the set up and consequent optimal signal values data analysis. Meanwhile, we aimed at a perfect positioning which could guarantee signal quality and consequently adequate data analysis.

In order to achieve the abovementioned goals, calibration procedures were made for each functional assessment in which each source-detector combination was optimized. According to the quantity of light emitted by the source and received by the detector, the system predicts the optimal amplification signal, that is, the best signal quality that can be achieved. This process is automatically run by the control system during the calibration phase.



**Figure 1.** (Courtesy of NIRx Medical Technologies) Each measurement channel is formed by an optic emitter (source) and a receiver (detector) placed on the tissue surface. Cortical NIRS signals are estimated to originate from an area that is placed between source and detector and from a tissue depth that is no more than half of the source-detector distance.

One-year effort was needed in order to gain familiarity and competence with this system, and this amount of time is largely recommended in order to avoid hardware failure resulting in variations of the identified values.

The NIRS model used in this study is named NIRSport (**Figure 2**,  $8 \times 8$  imaging system ( $8 \times 8$  mean 8 sources and 8 detectors). This NIRS hardware is attached to a pre-configured tablet or PC throughout a USB 2.0 cable. Every NIRS montage cap, on which sources and detectors are attached, follows the 128 standard EEG positions (known as the 10/20 international system).

### 2.1. Optimal system check

Before running the system, sources and detectors must be placed on subject's head. The montage, in this case the Prefrontal Cortex (PFC) one, was chosen among a wide selection of different montages provided by NIRX. By starting the program, a system data sheet is displayed with a typical configuration setup for data acquisition.

Signal quality is the pre-requisite for a good functional recording; thus, before starting to record, it is necessary to run a source-detector calibration to verify it.

NIRS provides quality signal for each channel, classified by color (**Table 1**):

- Excellent (green): this quality level allows a clear view of heart fluctuation in the HBO signal and is appropriate for highest demands such as single-trial/single-subject evaluation. Cardiac signal may not be discernible on the display due to physiological reasons, but the output allows to detect the current noise and pull out neural activity with a suitable statistical analysis (filtering, SPM event-related mean, group mean).

If signal quality is low (red or white), neural activation may not be visible and blocked by noise signal. The most probable reason is the optical quality of the tissue itself. Losing the signal and consequently losing a channel information data are mostly due to the erroneous location of sources and detectors.



**Figure 2.** (Courtesy of NIRx Medical Technologies) NIRSport  $8 \times 8$  imaging system; detectors and sources must be placed in the corresponding slot, equally for triggers sent to the software through a specific equipment (if necessary), the connection USB cable and, on the other side, the power supply connector.

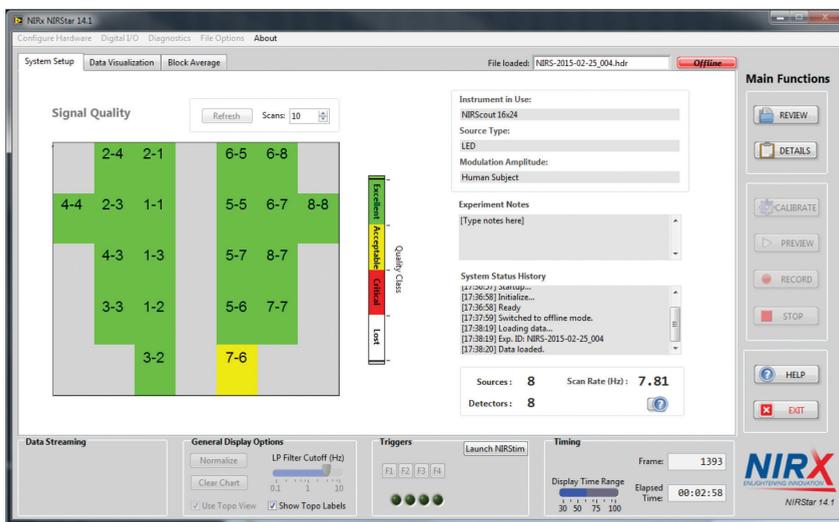
**Table 1** shows signals criterion that are considered from right to left; algorithm quality scale checks if optimal level is reached for each channel, then evaluates signal strengths for each wavelength (760–850 nm) and estimates the detected noise level. The final signal quality classification for a given channel depends on the worst marker obtained.

**Figure 3** shows a signal quality map where every channel has been judged to be “excellent” (in green) or “acceptable” (in yellow); this means that each channel achieved amplification gain intervals from 1 to 6. Levels ranged from 0.09 to 1.40 and the corresponding noise level is <2.5%. These values are shown in an appropriate software window.

The button “Refresh” allows us to update quality assessment without running a new calibration. It is important to keep in mind that a quick and well-done montage setup will shorten this calibration phase in order not to stress out the subject emotionally. The topographic layout helps to locate each channel and to act on a specific channel to set optimal signal quality.

Signal Quality	NScout Gain [10 <sup>^</sup> x]	NSport Gain [10 <sup>^</sup> x]	Level [V]	Noise [%]
Excellent	1 - 6	0 - 2	0.09 - 1.40	< 2.5
Acceptable	7	3	0.03 - 0.09	2.5 - 7.5
Critical	0	-	0.01 - 0.03	> 7.5
Lost	-	-	< 0.01	-

**Table 1.** (Courtesy of NIRx Medical Technologies) shows signals criterion that are considered from right to left; the final signal quality classification for a given channel depends on the worst marker obtained.



**Figure 3.** (Courtesy of NIRx Medical Technologies) shows a topographic layout in which excellent signal quality are displayed for each channel except for one that is acceptable.

By clicking on the “Details” button, a detailed calibration window will open with individual maps of gain, level and noise. Gain map: an inverse relationship exists between gain and intensity of the received light, intensity of light must be more amplified if the light signal is weak. If the outdistance between sources and detectors is between 2.5 and 3.0 cm, we expect a gain of 4, if lower than 4 there is a low level of light attenuation. If channels do not reach a maximum gain level of 7, the signal levels will be marked red and a new calibration phase needs to be run after having improved the contact between optodes and skin. Important is that the displayed layout is qualitatively reproducible across different subjects attending the experiment.

Signal level: Signal levels and noise ratios can be examined for each wavelength differently to the gain levels. Signal levels are mapped according to a logarithmic scale and expressed in voltage units.

Noise: In order to quantify the noise level, the system uses coefficient of variation ( $CV = \text{standard deviation}/\text{mean} \times 100$ ) of those recorded data used to assess signal levels.

Dark noise: high levels of dark noise may be due to environmental light disturbance or if the NIRS system is connected to power.

As default, the color combination is set according with the traffic light colors (excellent, acceptable, critical and lost). If “Quality Scale” button is deactivated, the older color scheme is displayed as shown in **Figure 4**.

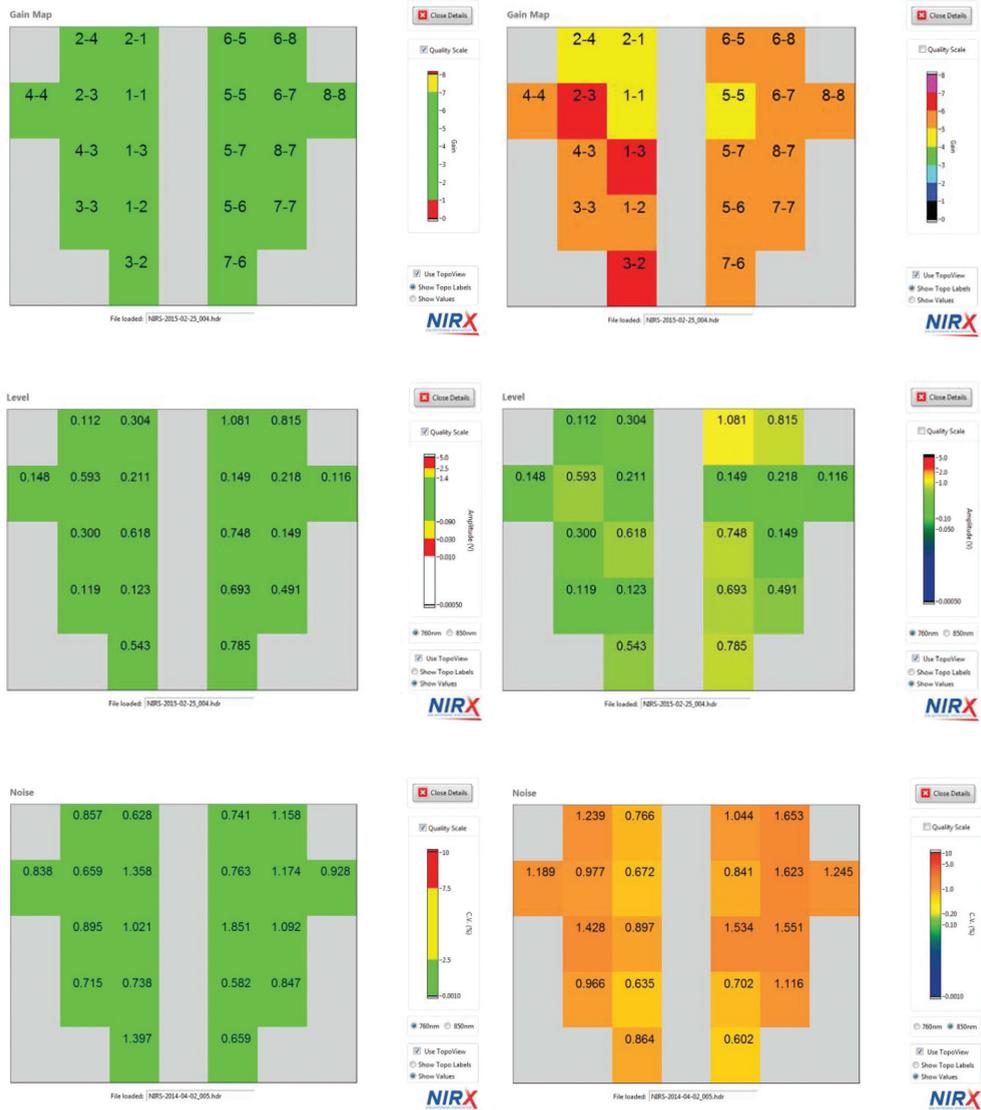
## 2.2. Data visualization and recording

If the configuration phases and the calibration have been followed correctly, real-time data are displayed in a preview or can be directly recorded. Side-by-side there is a trace display and a topographic map for Hb and HbO concentration (**Figure 5**). Data presented in the topographic map represent estimated changes of oxy and deoxyhemoglobin concentration. The recorded data are raw signals of individual wavelengths.

The estimated data of oxy and deoxyhemoglobin concentration vary for each channel and are shown on the left side of the data visualization panel. In order to set an appropriate rehabilitation approach this allows us to visually inspect the ongoing fluctuations and verify them according to a given stimulus. For a clinical assessment, being able to analyze temporal sequences of each channel by selecting them individually is important. Amplifying the signal level (**Figure 6**) allows us to enlarge the fluctuations in order to better inspect the recording data. If no scale factor is applied, the unit of Hb state is mmol/L but may be scaled up to a factor of 2000 mmol/L.

Before starting the recording, in the preview data visualization, it is important to apply the low-pass frequency filter to remove high-frequency noise or the heartbeat component (**Figure 7**).

Despite the trace display, the Hb-HbO concentration is shown as a 2D map where channels are depicted (**Figure 8**).



**Figure 4.** (Courtesy of NIRx Medical Technologies) shows gain map, signal level and noise in a topographic layout for each channel. In the left column, the option “quality scale” is activated; in the right column, the option “quality scale” is deactivated, where the only thing changing is the color scheme.

In order to enhance Hb dynamics on the display, the Hb gain can be scaled up for better clinical observations purposes. The trace display in **Figure 8** has been filtered to remove high frequency and 1 Hz heartbeat frequency.



Figure 5. (Courtesy of NIRx Medical Technologies) Data visualization with a trace display on the left side of the screen, topographic layout on the right side of the screen expressing changes in Hb-HbO concentration. Remember that the recorded data are raw data, based on individual wavelengths.

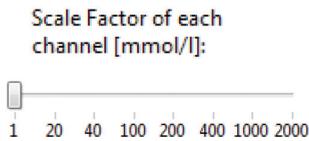


Figure 6. (Courtesy of NIRx Medical Technologies) This scale factor allows signal levels to be increased from 1 to 2000 mmol/L.

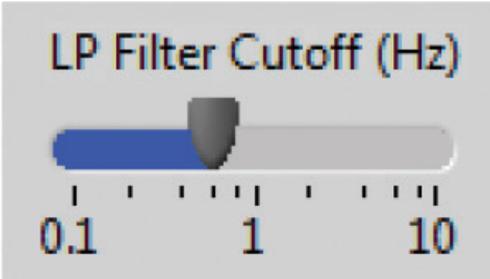


Figure 7. (Courtesy of NIRx Medical Technologies) shows the low-pass filter; in this case, the 1 Hz heartbeat frequency is filtered out.

In clinical assessment, responses to psycho-physiological stimuli (audio, visual, tactile, etc.) are interesting to examine; therefore, NIRS signal must be correlated to event-related stimuli. Markers are necessary to set the beginning and the end of a task or subjects response. NIRS can be provided with internal or external trigger signals (Figure 9) coming from other equipment that allows stimulus presentations.

The software allows to set markers manually during the experiment in case of unexpected experimental event such as motion artifacts or subject distraction.

A block average feature allows to visualize real-time topographic areas in multiple conditions (Figure 10).

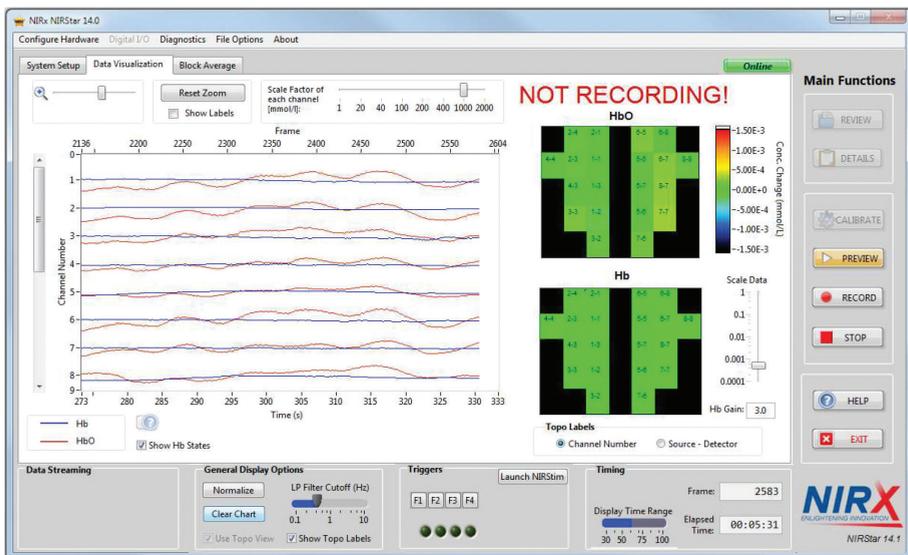


Figure 8. (Courtesy of NIRx Medical Technologies) shows the data visualization panel. On the right side of the screen, Hb and HbO concentration are represented for each channel, and on the topographic map, there are channel numbers or source-detector labels.



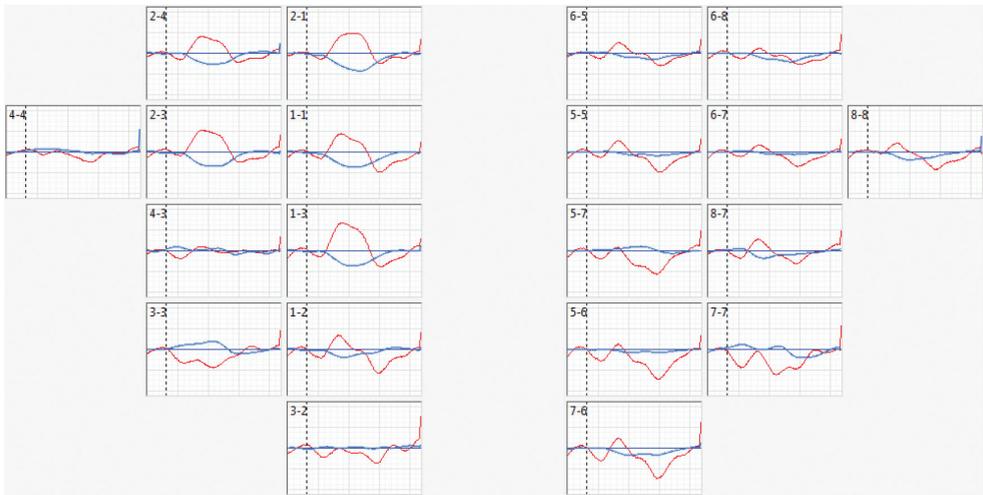
Figure 9. (Courtesy of NIRx Medical Technologies) shows different trigger signals that can be used to set the end and the beginning of psycho-physiological stimuli; the marker is set by clicking on the respective button (e.g., F1) or by pushing F1 key on the computer keyboard.

### 2.3. Topographic display

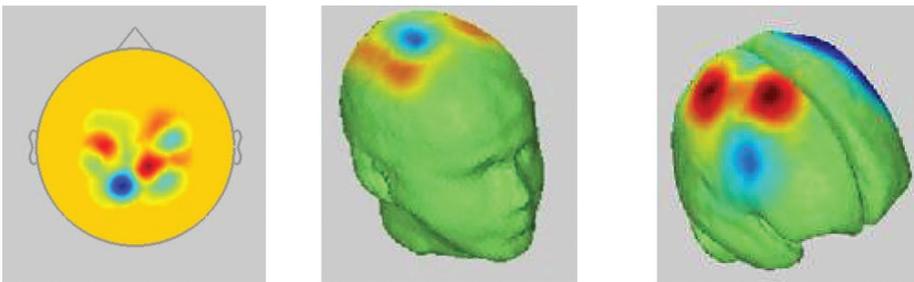
By using a NIRS technique, a rendering function is useful since it provides a hemoglobin topographic data into realistic 2D-3D coordinates. This function is given by another software that is in any case necessary in order to visualize hemoglobin fluctuations following psycho-physiological stimuli (**Figure 11**).

### 2.4. How to set and prepare the NIRS system properly: a recap

The NIRS hardware is attached to a pre-configured tablet or PC throughout a USB 2.0 cable. Every NIRS montage cap, on which sources and detectors are attached, follows the 128 standard EEG positions (known as the 10/20 international system).



**Figure 10.** (Courtesy of NIRx Medical Technologies) shows an example of block averaging display that has to be set before starting the recording session. Number of conditions need to be arranged in order to identify them graphically. The oxy (red) and deoxyhemoglobin (blue) traces displayed are a mean of the fluctuation during a fixed stimulus duration (3–10 s). Stimulus duration and number of conditions are required to be set before the recording session.



**Figure 11.** An example of the possible topographic view, in 2D or 3D mapping. (Courtesy of NIRx Medical Technologies).

Once the software is configured, the cap can be placed on the subject's head according to the pre-selected montage, in this case the prefrontal cortex montage.

Before starting to record, a calibration phase is necessary. The system will automatically determine the quality of emitted (sources) and detected (detectors) light signals by assigning a quality indicator for each defined channel. If optodes are placed correctly, signal quality is good or acceptable (see **Figure 3**) and the subject is in resting state, the calibration session can start.

Signal quality derives from multiple factors such as photodetectors' amplification level, estimated noise level (carefully inspect environmental light interferences), optode and skin contact, optimal distance between sources and detectors (30 mm). At the end of calibration, the channel quality signal allows to identify if the following steps have been considered:

1. Optode to skin optical contact.
2. Check sources and detectors position according to the defined montage.
3. Optimal distance between sources and detectors: 30 mm.
4. In case of complete loss of all channels, check the cable connection.
5. Avoid spreading of environmental light into the cap; do not place the subject under a bright light or put on the cap an additional black cap that avoids light to pass through.
6. Optode perpendicularity (both sources and detectors must stay in vertical position attached to the subject's skin).
7. Skin color, hair color or hair products such as hair gel can influence light reflection and absorption.

The criterion is to adjust signal quality each time in order to achieve a channel quality that is colored in green or yellow, not red or white that describes a critical loss of signal and a consequent exclusion of that channel during the subsequent data analysis.

If everything is fine, each channel is in its optimal condition and the recording phase can take place.

### **3. fNIRS: Beware of methodology!**

The main challenge for researchers is to apply NIRS technology to emotional research as standardized NIRS and fNIRS methods are not yet available.

The first problem is represented by noise, caused by heart-rate variation and Peripheral responses following emotional stimulation. Physical changes often go along with induced state of arousal such as facial muscle contraction or, as said before, increase in heartbeat. The NIRS technique can mitigate this problem by downranging the heartbeat frequency rate (see Section 2.2) although, if not properly set, this can bring to error of data assessment.

Aerobic process and energy consumption associated to muscular contraction may induce significant changes in oxyhemoglobin. However, Schecklmann et al. [2] found no relationship between electromyographic signals and oxyhemoglobin variation during a fluency task. Nevertheless, the influence of peripheral responses was analyzed including limited condition.

Further signal falsification is given by neural activation to emotional stimulation since variation in Hb-HbO concentration in this case may be due to vasoconstriction. A solution to this is to elicit two different emotional responses and statistically analyze the differences in Hb-HbO concentration between the two responses.

Another problem appears to be the time range (TR) selection that is the time needed for cortical activation to be visually inspected; many studies suggest that oxyhemoglobin drop values indicate cortical activation [3]. Suh et al. [4] claim that cortical direct stimulation induces a rapid increase in deoxyhemoglobin (1–2 s after stimulation) while the total hemoglobin value remains constant. This problem is avoidable by using high temporal resolution in order to evaluate statistically significant changes in Hb-HbO concentration variation.

### **3.1. Potential fNIRS application**

Theories on PFC's role in emotion processing [5–7] agree on PFC being the key area in which emotional reactions, motivation, attentional processes and behaviors take place.

As PFC is important in emotional processing, the evaluation of emotional intensity with NIRS becomes crucial.

Studies suggest that individual sensitivity to reward and stress may promote depression disorders [8, 9]; these results induce a deeper analysis of eventual biological predisposition that may lead to specific PFC responses to stimuli-induced emotions. Individual differences in terms of emotional responses can help in identifying eventual risk factors.

Using NIRS to analyze PFC activity when stimulated during rehabilitation and the evaluation of the rehabilitation program intensity, considering the abovementioned biological factors, may help to select the optimal rehabilitation method for each patient.

Primary function of emotion is to guide adaptive motor behavior [10]. Few studies focused on this important statement. It is well known that motor activity directly interacts with emotions and mood [11], and it has been shown that there is a bidirectional relationship that has been established between motor function and individual emotional experience [12].

## **4. From fNIRS to the definition of a rehabilitation model**

The ability of the brain to reorganize itself and change its activity associated to a given function in order to achieve a neurological control is well supported by studies in neural activation. This is a goal to be kept in mind while using a verified and controlled neuronavigation technique such as fNIRS. Nowadays, everyone is trying to find the best standardized

rehabilitation process while the entire scientific community agrees on the brain specific individuality that cannot be encoded. We can claim to know each functional brain area, but the information encoded inside is individual and only in a small part conventional. This is the main starting point in order to set individualized rehabilitation models through the use of neuronavigation techniques such as fNIRS.

In order to allow a cortical reorganization process, there is the need of a specific environmental stimulation, aimed at compensating the impairments. Regardless of which brain area is involved, the aim is to set up a model that can be verified each time with optical imaging techniques. According to this kind of rehabilitation model, the environmental stimulation needs to be grounded on the person's real life experiences so that the choice between different rehabilitation programs is based on the brain activity of a specific area involved during stimulation and verified thanks to NIRS. This choice has to be based not only on customary, logistic and organizational needs but also on cognitive, emotional and motivational patient's needs according to a functional brain activation point of view.

The main goal of the Cerebro rehabilitation model is to improve the functional outcome by supervising rehabilitation choices from time to time and to evaluate the emotional outcome by analyzing Hb-HbO variation in PFC since it is an area involved in emotional control [13].

#### **4.1. Cerebro model's application fields**

This neurofunctional rehabilitation model is applied to patients with behavioral cognitive impairment due to brain injury after a complete neuropsychological assessment.

Neurofunctional impairments are:

- Cognitive: like neglect, visuospatial disabilities, aphasia, agnosia, apraxia, amnesia, dyscalculia and attention deficit.
- Emotional-motivational: like apathy, emotional lability, irritability, depression and anxiety.
- Executive (behavioral): like disinhibition, control reduction, discriminatory ability, thought disorder, disorganization, reduced problem solving and lack in self-awareness.

Each of these impairments involves directly or indirectly the prefrontal cortex since it is charged with emotional control.

Others that can benefit from this rehabilitation processes are post-stroke patients, cerebrovascular diseases, traumatic brain injuries, multiple sclerosis, encephalitis and post-surgical cancer patients.

Neurodegenerative diseases are excluded from this rehabilitation procedure, apart from multiple sclerosis due to its remittent nature, since there is no evidence yet on how to treat them and due to lack of compliance. However, in case of a motor impairment together with cognitive impairment, that are usually not rehabilitated, our neurofunctional rehabilitation method may be applied in order to monitor brain areas and determine more appropriate choices that

would not be taken because of lack of compliance. The most important achievement in order to obtain autonomy in everyday life is being able to perform an adequate motor act and this can be done even if cognitively impaired.

#### *4.1.1. Definition and evaluation of neurofunctional impairments*

First, neuropsychological assessment needs to be integrated with neurofunctional measurement of the area involved using neuronavigation techniques such as NIRS and to be combined with the patient life experience and peculiarities such as everyday life, work, family, house, hobbies and emotions experienced.

Next step is to evaluate neuropsychological impairments from a behavioral and cognitive point of view.

- For cognitive impairments, preserved and altered networks reflecting impaired cognitive functions are evaluated with psychometric and standardized tests.
- For executive impairments and motivational disorders, direct evaluation of motivational levels is observed by analyzing patient's willingness and effort in taking part in the rehabilitation program together with suitability of social behavior, ability to control and inhibit thoughts and behaviors, static/fluid thinking and problem solving. These observations are measured with NIRS technique in order to set a starting value of Hb and HbO variation that will be taken as a baseline during each rehabilitation session in order to control metabolic brain fatigue.

Many questionnaires can be handed out and functionally measured with NIRS such as: Quick Exposure Check (QEC) [14], Cognitive Failures Questionnaire (CFQ) [15] and so on.

- Emotional functioning can also be observed with neuronavigation techniques; presence and entity of emotional disorders, such as emotional lability, irritability, depression and anxiety, changes in personality and caregiver relationship quality.

As before, analyzing brain activity while administering standardized questionnaires is very important in order to exclude misunderstanding of items and have a responsive measurement of brain activity while reading the questions. Standardized tests that can be administered are Neuropsychiatric Inventory Questionnaire (NPI-Q) [16], Beck Depression Inventory (BDI) [17], Geriatric Depression Scale (GDS) [18], Minnesota Multiphasic Personality Inventory (MMPI) [19], European Brain Injury Questionnaire (EBIQ) [20] and Big-Five Questionnaire (BFQ) [21].

- Emotional engagement and self-awareness deficits must be assessed through clinical observation and neurofunctional investigation with NIRS. Patient's compliance sometimes does not reflect the undergoing neurofunctional responses; patient may act as collaborative as usual despite his true engagement.

Collected data taken from the neuropsychological assessment allow a faster and more precise identification of neurofunctional impairments.

## 4.2. Rehabilitation goals

Defining the optimal rehabilitation program is the fundamental basis of the Cerebro model. Prefrontal cortex (PFC) activity is indeed one of the most significant areas involved in executive functions, therefore it is extremely interesting.

The main goal is achieved through a variety of subgoals directed to arouse natural daily-life responses.

Goals are structured according to three different rehabilitation phases:

- First phase must provide deficit awareness through rehabilitation processes based on life experience stimuli. Keep in mind that mirror neurons are everywhere not only in the motor cortex.
- Second phase must provide practical skills in order to compensate cognitive, emotional and behavioral impairments.
- Third phase is the conclusive one. It consists in strengthening acquired rehabilitation skills in order to match patient's life necessities.

### 4.2.1. Methods

Experiential living is what makes individuals unique; that is why the Cerebro rehabilitation program takes it into account.

The methodology used is based on cognitive and behavioral studies that can be outlined as follows:

- Specific stimulation of a cognitive impaired process. Check of excessive stimulation in the impaired area. The stimulation can facilitate information access that is relatively intact but no more accessible due to the impairments.
- Stimulation and functional reorganization of preserved cognitive processes.

Irrespective of the selected technique, cognitive and behavioral deficits must be assessed by Hb-HbO concentration analysis provided by neuronavigation (fNIRS).

Choosing strategies and rehabilitation goal depends on different factors:

- Deficit assessment of cognitive and behavioral impairment and related impact on everyday life.
- Proficiency level in coping strategies.
- Cognitive function analysis for goal-oriented activities.
- Individual features assessment like socio-cultural and educational context as well as experiential living.

- Etiology and localization of brain lesions.
- Emotional response following brain lesion.
- Motivation and compliance to treatment.
- Changing in personality.
- Disability and psycho-social consequences.
- Deficit awareness.
- Presence or absence of a good family support.

Time of monitoring with fNIRS is influenced by patient's hospitalization period. If the pre-fixed goal has not been achieved or if there are still dysfunctional areas that could be usefully considered for an optimal rehabilitation program, then a day-hospital formula is needed.

Changing in patient's behavior can be monitored throughout the rehabilitation period because the neuronavigation systems like fNIRS allow to change and adjust the rehabilitation program according to the patient's needs.

At the end of the rehabilitation program, a neuropsychological assessment is necessary to evaluate the improvement or stationarity of the early impairments via neuropsychologic standardized tests, questionnaires and so on. The results obtained are analyzed and serve to establish a long-term rehabilitation program applicable in everyday life.

Neurofunctional rehabilitation is planned by the psychologist in charge with the neuropsychologist experience in test administration according to the reported cognitive impairments. A speech therapist is needed to evaluate speech disorder in case of aphasia.

In addition, other health professionals are needed such as occupational therapists and physiotherapists for motor function disorders in order to improve everyday life autonomy in activities of daily living (ADL) or to discourage maladaptive behaviors.

Finally, care givers are important in order to set proper individual life-based stimuli, which is essential to this kind of rehabilitation model.

## 5. Conclusions

Near-infrared spectroscopy (NIRS) uses low-intensity optical radiations to measure changes in light absorption by the cortical vascular tissues in order to detect changes in local concentration of oxy- and deoxyhemoglobin as a correlate of functional brain activity. Several precautions are needed to obtain a clear and optimal signal that reflects the patient's brain activity. Due to its features, NIRS is the best and most practical way to depict emotional responses in prefrontal cortex (PFC).

Despite technical limitations, NIRS is a reliable method to quantify a stimulus reaction especially in PFC functioning in emotion processing. It allows to establish the optimal rehabilitation program according to a visual inspection of Hb-HbO concentration variation and by checking the functional area involved.

By measuring individual experience-based emotions encoded by PFC, it is possible to choose between different rehabilitation programs according to life experience but also to individual Hb-HbO variations.

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## Conflict of interest

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

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