

Review

A systematic review of the literature in relation to the theoretical knowledge base for the-Clinical-functional research by evaluation including the modern apparatus modality of functional exploration: near-infrared spectroscopy (Near - Infrared Spectroscopy - N.I.R.S. / Function Near-Infrared Spectroscopy - fN.I.R.S.) of blood oxygenation in the cerebral circulation at repose and during physical activity, respectively, in adolescents with hemiplegia in the context of Cerebral Palsy, compared to patients of the same age group with non-neurological disorders

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Abstract: fNIRS is also called Optical Topography (OT) or simply NIRS. Using - near-infrared spectroscopy - the amount of oxyhemoglobin and deoxyhemoglobin is measured to estimate cortical hemodynamic activity that occurs in response to neuronal activity. Next to EEG, NIRS/fNIRS is one of the newest non-invasive neurophysiologic techniques that can be used in portable settings. The device, OxyMon - with which we have the important opportunity to work is the first and so far the only one in Romania - uses as technology a continuous wave NIRS/fNIRS system with infrared light emitters that emit at least two wavelengths each (700-900nm). Specifically, a fiber end that connects to the OxyMon is called a connector: and a fiber end on the skin is called an optode (transmitter or receiver). Optodes are fixed in an optode holder. The distance between the optodes is called the source-detector distance or interoptode distance. An emitter optode and a receiver optode together form an optode combination or channel. NIRS/fNIRS is a non-invasive brain imaging method and is a suitable technique for detecting brain activity during motor dynamics. After using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (acronym PRISMA) method to quest for afferent knowledge, it resulted a quite small number of 10 related articles, of which only 6 remained eligible for our theme (4 were excluded for objective reasons). fNIRS is a niche field in which there are possibilities of deepening and of personal contribution within the doctoral research topic that we have proposed, being the first and only fNIRS apparatus in Romania, so the clinical-applied apparatus research represents an element that we have not encountered in the Romanian literature. The application of NIRS/fNIRS in neuromotor rehabilitation is still new and immature in the world, but we can expect many unique and significant discoveries through the research of neuro-myo-arthro-kinetic "apparatus" in relation to cortical hemodynamic activity. It is also noteworthy that these studies may provide new insights into the potential clinical applications of NIR spectroscopy. In the conclusion fNIRS is a promising tool for optimizing the rehabilitation of patients with cerebral palsy, offering an objective method for evaluation and guidance of treatment.

Keywords: cerebral palsy, functional near-infrared spectroscopy, teenager, oxyhemoglobin, deoxyhemoglobin, cerebral blood flow, physical exercise, fNIRS.

1. Introduction

Cerebral palsy (CP) is a nonprogressive neurological disorder caused by brain damage during the developmental period. As a result, patients often experience sensory and perceptual impairments in addition to other neurological dysfunctions. Spasticity, characterized by increased muscle tone and muscle stiffness, is the most common motor impairment in individuals with CP¹⁵. Numerous studies have shown a close relationship between motor function and brain network characteristics. Consequently, studying the brain function characteristics of children with CP is necessary to fully determine the functional state of patients and to improve their functional recovery.

fNIRS is also called Optical Topography (OT) or simply NIRS. Using near-infrared spectroscopy, brain activity is measured to estimate cortical hemodynamic activity that occurs in response to neuronal activity. Near-infrared spectroscopy (NIRS) is a non-invasive, portable technology which monitors oxygenation in the brain, muscle, and other organs. It detects subtle changes in tissue oxygenation in real time by measuring the capillary-venous oxygen saturation in the tissue directly beneath the sensor¹⁶. The signal is often compared to the BOLD (Blood Oxygenation Level Dependent) signal measured by fMRI and is able to measure changes in both oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb) concentration⁵.

fNIRS monitors cerebral hemodynamic changes during physical activity (motomed pedanlig in our study) and at rest providing information about the neuroplasticity of the motor cortex. It allows for the early identification of abnormalities in cortical activity, contributing to a more accurate prognosis.

The fNIRS represents one of the hybrid C.C.I. (Cerebral-Computer Interface) systems and can achieve better accuracy rate and performance than other systems. The implementations of C.C.I. vary, so the neuronal signal can be decoded from outside the skull (non-invasive: electroencephalography [EEG], functional near-infrared spectroscopy [fNIRS]) or inside the skull (invasive: local field potentials by epidural or subdural electrocorticography, single neuron activity [spikes] by intracortical implants)¹⁴. Non-invasive C.C.I. is typically detect and utilize electromagnetic potentials directly related to neuronal ensemble firing or associated hemodynamic changes, including regional changes in relative oxyhemoglobin and deoxyhemoglobin concentrations as well as changes in arterial blood flow velocities due to neurovascular coupling².

The microvascular organization of the brain is based on proportional intracapillary oxygen convection and parenchymal diffusion times¹¹.

Maintenance of physiologic cerebral oxygenation is achieved through a dense and complicated vascular network and a combination of convective and diffusive transport. Convection manages oxygen delivery, while diffusion governs oxygen extraction. Convection is responsible for transporting oxygen, bound to hemoglobin in erythrocytes, through the blood stream. Free and facilitated diffusion transfers oxygen from within microvessels to the mitochondria of brain cells⁶. Oxygen exchange takes place at the arteriolar and capillary beds where the surface area is maximized and the diffusion distance is minimized.

Both the pulsatility index (PI) and the resistivity index (RI) indicate changes in vasoconstriction and vasodilation in cerebral blood vessels⁸.

It is important to remember that the pulsatility index (PI) is an anticipatory measurement and depends on many hemodynamic variables, including cerebral perfusion pressure (CPP), cerebrovascular resistance, arterial bed compliance and pulse rate⁹.

Cerebrovascular autoregulation functions under dynamic steady-state conditions as a homeostatic mechanism to adjust cerebrovascular resistance and, consequently,

cerebral blood flow (CBF) when cerebral perfusion pressure (CPP) changes in the range of 50-170 mm Hg. Cerebral perfusion pressure and CSF depend on the difference between blood pressure at the Willis vascular polygon and intracranial pressure as well as central venous pressure and cerebrospinal fluid pressure.

IP describes the degree of downstream vascular resistance. Vascular beds with low resistance have high diastolic flow with rounded waveforms and low PI. In contrast, higher resistance beds have high diastolic flow, a peaked waveform and large PIs. In cerebral palsy although brain damage cannot be cured, it will not worsen over time.

Fortunately, neuroplasticity exists and there are two main types of neuroplasticity:

- a) Functional plasticity is the brain's ability to move functions from one damaged area of the brain to other unaffected areas.
- b) Structural plasticity is the ability of the brain to actually change its physical structure as a result of learning.

As has been reported in several studies, the degree of tissue neuroplasticity depends on the age of the lesion and the size of the lesion¹³. In addition, the location of the lesion, related to different functional areas, as well as hemispheric lateralization may also affect brain reorganization⁶.

Regarding cerebral circulatory flow, previous studies investigating cerebral perfusion in children with hemiplegia, including fMRI and single photon emission computed tomography methods, have reported conflicting results, which may be due to variations in the etiologies of hemiplegia within and between studies³. However, an increase in gray matter (GM) volume through structural neuroplasticity can be hypothesized to cause an increase in cerebral blood flow⁷.

Material and methods:

The NIRS/fNIRS technique is based on the Lambert-Beer law (1851), which describes the relationship between the optical density of the medium, the incident radiation with the transmitted one, the concentration of the medium, the distance between the light input and the light output point and the wavelength used¹². Measuring the NIR light diffusely transmitted through tissue enables the mapping of hemoglobin changes associated with brain activities. The spectrum of near-infrared from 700 to 900 nm can penetrate skull and tissue to a depth of a few centimeters, which is relatively immune to absorption from water and culture medium, i.e. an "optical window" for biological tissue¹⁰. Thus NIRS of this range provides the noninvasive measurement of hemodynamic change of the brain. The LASER emit light in the near-infrared spectrum to measure concentrations of substances that absorb the emitted light. The LASER fire one by one, so that the system can distinguish between infrareds spectrums. This principle is called the time-sequenced principle. The light is transmitted from the LASER through the skin to the receiver by optical fibers containing glass fibers. Specifically a fiber ending connecting to the OxyMon, is called a connector, and a fiber ending on the skin is called an optode (transmitter or receiver). The optodes are fixated in an optode holder. The distance between the optodes is called the source-detector distance or the inter-optode distance. A transmitter and receiver optode together form an optode combination or channel¹.

In order to identify the current state of research and level of knowledge on the chosen topic, we conducted a systematic literature review. Exclusion criteria were studies with incomplete data, abstract articles, non-peer-reviewed papers.

We used the widely used and internationally accepted Preferred Reporting Items for Systematic Reviews and Meta-Analyses¹⁷ (PRISMA) method of selection and filtering of the literature

Keywords, keyword combinations/syntaxes used for contextual query of the medical databases listed below in Table 1.

International medical databases searched: Elsevier, PubMed, PMC, PeDro (to check if the selected articles are indexed in the ISI international medical database) – accessed¹⁹ Eligible articles were those in English, open access, ISI/Web of Science indexed journals²¹.

Using, contextually, the words, keyword combinations/syntaxes listed in Table 1 resulted in the first stage of the query of the 4 international medical databases mentioned, 19 articles in the PMC;

After eliminating duplicates (same articles found in different queried databases) 10 articles resulted.

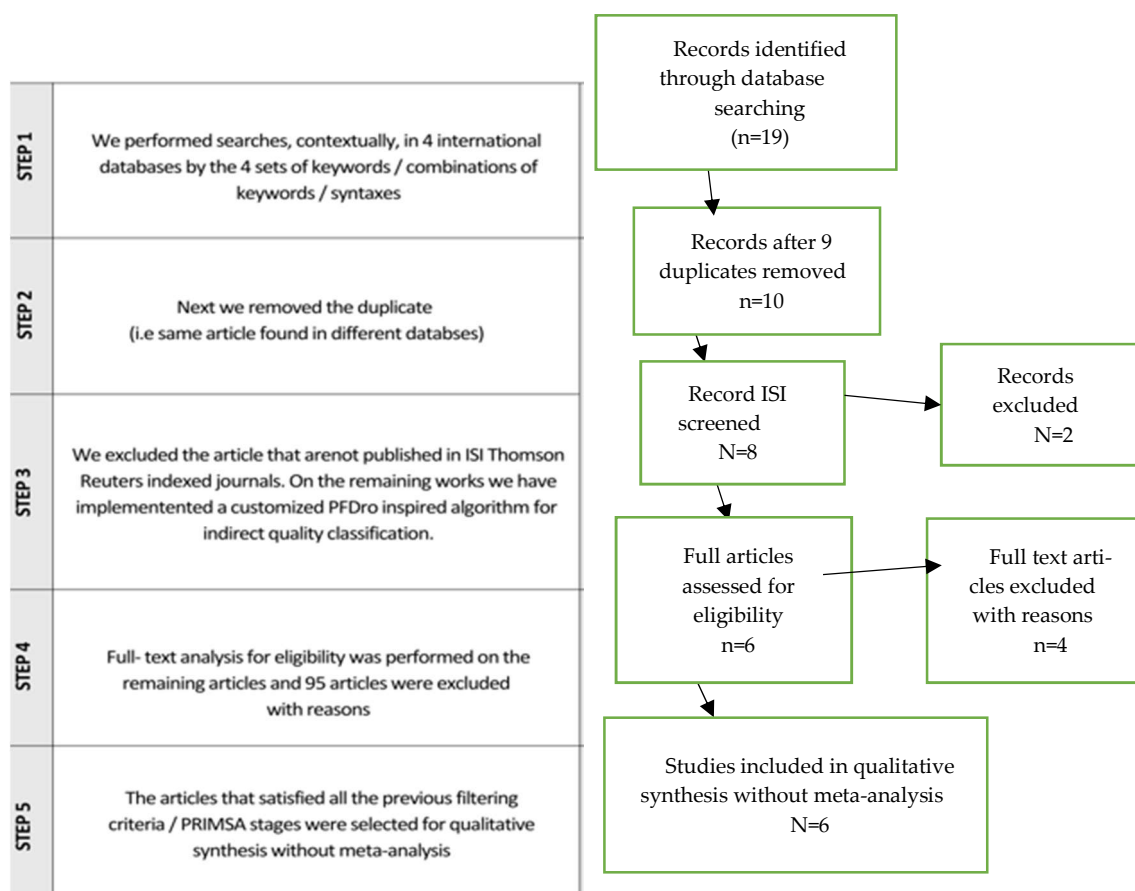
In the next step the indirect qualitative filtering process was performed by checking the publication of the selected articles in ISI indexed journals and then by applying an adapted version of the PEDro = Physiotherapy Evidence Database classification²⁰.

This meant that the basic criterion was a weighted calculation of the number of citations per year.

Table 1. Keywords, keyword combinations/syntaxes used for the initial search in databases and in a search engine respectively, national/international, total number of articles initially identified.

Keywords	Elsevier	PubMed	PMC	PEDro	Total
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "oxyhemoglobin"	0	0	0	0	0
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "deoxyhemoglobin"	0	0	0	0	0
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "fN.I.R.S"	0	0	0	0	0
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "fNIRS"	0	0	0	0	0
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "physical exercises"	0	0	0	0	0
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "physical exercise"	0	0	2	0	2
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "exercises"	0	0	6	0	6
"cerebral palsy" + "diplegia" + "cerebral blood flow" + "exercise"	0	0	5	0	5
"cerebral palsy" + "functional Near Infrared Spectroscopy" + "teenager"	0	0	3	0	3
"cerebral palsy" + "fN.I.R.S" + "teenager"	0	0	0	0	0
"cerebral palsy" + "fNIRS" + "teenager"	0	0	3	0	3
Total	0	0	19	0	19

Fig.1 The specific diagram of our PRISMA type of search and selection



Discussions and Results: Using Fnirs guides personalized therapies , indentifying active brain regions , and tailoring exercises to individual responses. He help us for creating specific protocols for different types of cerebral palsy .

For our patients (cerebral palsy type- hemiparesis), f NIRS can help idetify deviations in motor coordination such as difficulties in bilateral motor activity or asymmetries in brain activation between the affected and unaffected sides of the body .This can contribute to the development of therapeutic strategies aimed at improving coordination and functional mouvement.

This gave a customized weighting between number of citations and year of publication on a scale: 0-10 points (see Table 2 for each of the selected articles) => 6 articles remained to be checked full text for eligibility (belonging to the area of interest of our research; Figure 1).

Table 2. The articles resulting from our search

Nr.	Articol	Year	Cited count	Reference count	PEDro
1.	A Comprehensive Survey on the Detection, Classification, and Challenges of Neurological Disorders ;11(3):469. doi: 10.3390/biology11030469.	2022	71	307	10
2.	Heart Rate Variability in Children and Adolescents with Cerebral Palsy—A Systematic Literature Review; 9(4):1141. doi: 10.3390/jcm9041141.	2020	25	131	4
3.	Award ID: 16 Epilepsy Profile in Children with Cerebral Palsy 101:190-196. doi: 10.1016/j.seizure.2022.08.009.	2022	11	37	10
4.	Brain-Computer Interfaces for Children With Complex Communication Needs and Limited Mobility: A Systematic Review ; PMID: 34335203 ; PMCID: <u>PMC8319030</u> ; doi: <u>10.3389/fnhum.2021.643294</u>	2021	43	148	4
5.	Use of Invasive Brain-Computer Interfaces in Pediatric Neurosurgery: Technical and Ethical Considerations 38(3-4):223-238. doi: 10.1177/08830738231167736.	2023	29	119	9
6.	Characterizing a Common Class of Spontaneous Movements 15(3):4–17. doi: <u>10.3822/ijtmb.v15i3.719</u>	2022	6	24	8

This is a niche area in which there are possibilities of deepening and of personal contribution within the doctoral research topic that we have proposed, it is the first and only fNIRS device in Romania, so the clinical-applied device research represents an element that we have not encountered in the Romanian literature.

After the PRISMA selection, 6 articles were left, which shows that it is not a sufficiently studied topic at international level.

In Romania , research on fNIRS is still non-existent, although this technology could become an important tool in neuroimaging for study neuroplasticity in patients with hemiparetic cerebral palsy , providing a non-invasive , real-time approach for monitoring the rehabilitation process and brain reorganization.

Kinetherapy changes local cerebral perfusion in both study groups. fNIRS may in the future be added to the advanced imaging protocol to study neuroplasticity in these children.

We discuss how these methods could shape future medical recovery strategies based on the neurobiology of P.C.H and therapy-induced changes observed in oxygenation levels in the cerebral circulation.

Our main hypothesis is that microstructural brain lesions that develop early in life are associated with a disturbance of cerebral blood flow (CBF). Specifically, we hypothesize that patients with P.C.H will have in the area of brain injury (ROI): (i) a decreased amount of oxyhemoglobin both at rest and in movement (ii) a higher amount of deoxyhemoglobin released both at rest and in movement; compared to children with T.D.

fNIRS may in the future be added to the advanced imaging protocol to study neuroplasticity in the pediatric population.

We discuss how these methods could shape future neuromotor recovery strategies based on the neurobiology of P.C.H and therapy-induced changes observed in oxygenation levels in the cerebral circulation.

Conflict of interests: The authors declare no conflict of interest.

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5. Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury- David Edward Ross-2011
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7. Adaptive Neuroplasticity in Brain Injury Recovery: Strategies and Insights- Alexander Muacevic and John R Adler -2023
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