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REVIEW ARTICLE

Near-infrared spectroscopy as an auxiliary tool in the study of child development

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KEYWORDS

Child development;
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Abstract

Objective: To investigate the applicability of Near-Infrared Spectroscopy (NIRS) for cortical hemodynamic assessment tool as an aid in the study of child development.

Data source: Search was conducted in the PubMed and Lilacs databases using the following keywords: “psychomotor performance/child development/growth and development/neurodevelopment/spectroscopy/near-infrared” and their equivalents in Portuguese and Spanish. The review was performed according to criteria established by Cochrane and search was limited to 2003 to 2013. English, Portuguese and Spanish were included in the search.

Data synthesis: Of the 484 articles, 19 were selected: 17 cross-sectional and two longitudinal studies, published in non-Brazilian journals. The analyzed articles were grouped in functional and non-functional studies of child development. Functional studies addressed the object processing, social skills development, language and cognitive development. Non-functional studies discussed the relationship between cerebral oxygen saturation and neurological outcomes, and the comparison between the cortical hemodynamic response of preterm and term newborns.

Conclusions: NIRS has become an increasingly feasible alternative and a potentially useful technique for studying functional activity of the infant brain.

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PALAVRAS-CHAVE

Desenvolvimento infantil;
Espectroscopia de luz próxima ao infravermelho;
Processos hemodinâmicos

Espectroscopia de luz próxima ao infravermelho como ferramenta auxiliar no estudo do desenvolvimento infantil

Resumo

Objetivo: Investigar a aplicabilidade da espectroscopia de luz próxima ao infravermelho (NIRS) para avaliação da hemodinâmica cortical como ferramenta auxiliar no estudo do desenvolvimento infantil.

Fontes de dados: Revisão integrativa de literatura feita nas bases de dados PubMed e Lilacs, a partir da combinação das palavras-chave: “psychomotor performance/child development/growth and development/neurodevelopment/NIRS/spectroscopy/near-infrared” e seus correspondentes em português e espanhol. A pesquisa seguiu protocolo adaptado dos critérios estabelecidos pela Cochrane e teve como limite temporal de 2003 a 2013. Foram incluídas publicações nos idiomas inglês, português e espanhol.

Síntese dos dados: Foram localizados 484 artigos, dos quais 19 foram selecionados, 17 transversais e dois longitudinais, todos publicados em periódicos estrangeiros. A análise dos artigos permitiu agrupá-los, quanto à sua abordagem, em estudos funcionais e estudos não funcionais do desenvolvimento infantil. Os estudos funcionais abordaram o processamento de objetos eo desenvolvimento de habilidades sociais, da linguagem e cognitivo. Os estudos não funcionais discutiram a relação entre a saturação de oxigênio cerebral e o desfecho neurológico e a comparação entre a resposta hemodinâmica cortical de recém-nascidos prematuros e a termo.

Conclusões: A NIRS se torna, cada vez mais, uma opção viável e uma técnica potencialmente útil para estudos de atividade funcional do cérebro infantil.

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Introduction

Near Infrared Spectroscopy (NIRS) represents a breakthrough in techniques used for brain function assessment. This tool has been considered promising for the evaluation of children’s cerebral cortex function, contributing to the increase in knowledge related to neurodevelopment and cognition in children.¹⁻⁴

The action mechanism of spectroscopy is based on the fact that neural activity is accompanied by changes in blood oxygenation, cerebral blood flow and volume. Thus, different wavelengths within the near infrared spectrum (780-2,500 nm) are used, capturing different characteristics of light absorption and dispersion in biological tissue. The light originates from a source, migrates through the tissue and is captured by a detector. Considering that tissue dispersion is a constant, the attenuation of the amount of light captured by the detector can be calculated, providing an indirect measure of activity in this tissue. That is, variations in the concentration of oxyhemoglobin (HbO₂), deoxyhemoglobin (HHb) and total hemoglobin (HBT) are calculated, which allows a quantitative and qualitative assessment of hemodynamics and neuronal activation.^{5,6}

Compared with other neuroimaging techniques, NIRS has the advantage of being a noninvasive, portable, quiet, relatively low-cost and safer method, less sensitive to motion artifacts, as it does not require a tracer or carrier substance to be injected into the blood stream and does not

require irradiation.¹ Additionally, it allows children to move on their caregiver’s lap, where they remain more comfortable and, therefore, more likely to complete the examination (Fig. 1). Another advantage is that as newborns and infants tend to have fine hair and their skulls are thin and small, the ratio of loss of signal due to dispersion is less than that for participating adults.⁶

Although the assessment of cerebral hemodynamics seems to be advantageous, it is important to identify how the methodology has been used and in what kind of research in child-related areas. The aim of this study was to carry out an integrative review of the literature published in indexed journals in the period of 2003-2013, on the use of NIRS to assess cerebral hemodynamics as an auxiliary tool in the study of normal childhood development.

Method

An integrative review was carried out following an adaptation of the Cochrane criteria, which included: definition of the study databases, definition of target audience, time limit, definition of keywords, inclusion criteria for the selection of studies, study quality assessment, synthesis and interpretation of results.

The search was carried out in the PubMed and Lilacs databases, using a combination of the following keywords: “Psychomotor Performance”/“Child Development”/“Growth and Development”/Neurodevelopment, “NIRS”/“Spectroscopy,



Figure 1 Nine-month-old child undergoing near-infrared spectroscopy (NIRS) on the mother's lap.

Source: Personal archive, with the family's permission.

Near-Infrared" and their equivalents in Portuguese and Spanish.

The inclusion criteria for articles were: type of study (cohort, case-control, cross-sectional, randomized trials), target audience (children 0-7 years), language of publication (English, Portuguese and Spanish), available as full-text in digital media and temporal limits (June 2003 to June 2013).

The titles were selected by reading the abstracts in order to determine whether they addressed the subject of this research and if they met the inclusion criteria. The next step consisted in recovering the articles and read them in full. This step was performed in two stages: first, two researchers read and selected the articles independently and, second, the information was cross-checked and the articles were selected in agreement.

The next step was to identify the central ideas of each study, which were then grouped according to recurring themes, into thematic categories. These categories were analyzed, allowing the articulation among the assessed topics and the development of the knowledge synthesis.

Results

Based on the combination of the previously mentioned descriptors and databases, 484 articles were located. After applying the inclusion criteria, 19 articles were

selected, of which 17 were cross-sectional and two longitudinal studies.

The difference between the number of located publications and the number of selected publications is due to the fact that most of the identified studies consisted of review articles, with samples at age ranges above the one that was established for this study, studies carried out in animals, studies that were limited to exploring methodological aspects of the spectroscopy technique, studies published prior to the period established in the inclusion criteria, articles in other languages and not available in digital form.

All selected articles were published in 12 international journals, a heterogeneous distribution, highlighting the predominance of publications in the *NeuroImage* journal (26.3%). As for the distribution of articles by year of publication, there were four (21%) in 2012 and three (15.8%) each year in 2011, 2010, 2009 and 2007. The others were published in 2006 (5.3 %) and 2008 (10.5%).

Study analysis allowed us to group them concerning the use or not of stimulation paradigms to investigate cortical activation. Studies evaluating the neural activation during performance of stimulation paradigms were called functional studies. Functional studies addressed four topics related to child development, namely: object processing (Table 1), development of social skills and cognitive development (Table 2) and language development (Table 3). Non-functional studies were those that did not use specific stimulation paradigms, assessing only the spontaneous fluctuations of cortical hemodynamics (Table 4).

Regarding the methodology, all studies used multi-channel, continuous-wave NIR equipment with two wavelengths and most followed the standardization of the international 10-20 system of electroencephalography to locate optodes, with reported sample loss rate between 3% and 80%. The justifications for the losses, as specified by the authors, were: motion artifacts, obstruction by the hair, failure in the experimental protocol, crying and agitation, difficulty obtaining optical signal and intolerance to the equipment.

The studies on object processing were developed with children aged two to 12 months old and aimed to investigate cortical functional organization related to the visual perception of objects (color, shape and movement). The main results showed that, between two and three months old, it is already possible to identify functionally differentiated cortical regions for visual perception.⁷⁻¹⁰

About the development of social skills, the studies assessed functional activation in cortical pathways related to social skills of children between five and eight months of age, using images of the human face in different plans and different facial expressions. The results indicated that, at five months of age, there is already a specialized area of the temporal cortex activated by social stimuli.^{11,12} Furthermore, right hemisphere dominance was verified in the frontal plane perception and facial profile,¹² whereas cortical activation occurs bilaterally for the perception of dynamic social stimuli.¹¹

Studies on language development were carried out with children aged two months to four years, with the aim to analyze brain functional processing of language, mainly related to phonetic processing,¹³⁻¹⁵ prosody,^{16,17} the lateral-

Table 1 Characteristics of functional studies of cortical hemodynamics using NIRS to assess processing of objects.

Categorization	References	Objectives	Sample (n)	Main results
Objects processing	Watanabe et al. ⁷	To investigate the functional cortical development through hemodynamic responses measured by NIRS during the presentation of specific visual stimuli in children aged 2 months	40	Cortical functional regions appear at 2-3 months for visual perception
	Wilcox et al. ⁸	To investigate the applicability of NIRS in assessment of brain objects processing in children aged 6.5 months	35	NIRS is sensitive enough to assess the neural basis of object processing in infants
	Wilcox et al. ⁹	To evaluate the functional organization of visual areas of objects processing in children aged 3-5 months and 11-12 months	111	The child's cortex is functionally specialized for processing objects at the beginning of the first year, but the activation patterns change between 3 and 12 months, which may reflect a functional reorganization of the immature cortex or be related to differences in age-related cognitive processes
	Watanabe et al. ¹⁰	To study the visual perception and to understand the functional cortical organization in children aged 3 months	72	Sensory regions, association areas and the prefrontal region are functionally differentiated at 3 months of age and several regions of the cortex, including the prefrontal region, are activated during perception of visual events

ization of speech^{13,14,16,18} and the influence of the speaker's familiarity in speech perception.¹⁹ The results were consistent with those obtained through other neurophysiological methods, emphasizing that: responses to specific language phonemic contrasts are present at six months of age; however, these become consistent and lateralized only after 12 months.¹³ Differences in prosodic patterns were discriminated by infants between one and nine days of life¹⁷ and functional specialization of the right hemisphere for prosody processing is present, with a response pattern similar to that of the adult, at four years of age.¹⁶

The approach of cognitive development involved the study of cognitive flexibility in children aged three and four years, and memory in newborns. The main findings indicated that the development of cognitive flexibility skill is related to the development of the inferior prefrontal cortex and suggest that children develop prefrontal activations between the ages of three and four years.²⁰ About neonatal memory, a study investigated the capacity of newborns to memorize words, focusing on the causes of forget-

fulness in early childhood, testing the capacity of neonates to recognize words after a period of familiarization. It was observed that newborns are already capable of memorizing words hours after birth.²¹

The non-functional studies discussed the association between cerebral oxygen saturation and neurological outcome;²²⁻²⁴ and the comparison between the cortical hemodynamic response of preterm and full-term infants.²⁵ All used continuous wave equipment, ranging from two to 24 channels and only one used the international 10-20 system for positioning of the optodes with sample loss ranging from 14% to 56%. The reported causes for these losses were: neonatal death, diagnosed syndrome, follow-up losses and failure in the experimental protocol.

Children younger than 12 months were evaluated and the main results suggest that brain oxygen saturation values and oxygen extraction fraction may be related to neurological outcomes²²⁻²⁴ and that the oscillations in cerebral blood flow in the resting state differ between preterm and full-term infants.²⁵

Table 2 Characteristics of functional studies of cortical hemodynamics using NIRS to assess the development of social skills and cognitive development.

Categorization	References	Objectives	Sample (n)	Main results
Development of social skills	Lloyd-Fox et al. ¹¹	To investigate the functional activation in cortical pathways related to the social skills of children aged 5 months	36	Significant increase of oxyhemoglobin in two posterior temporal sites bilaterally, indicating that these areas are involved in the social brain network in young infants
	Nakato et al. ¹²	Investigate face processing in children aged 5 and 8 months	20	Brain activity for face perception is invariant in relation to the view (frontal or profile) at 8 months, but not at 5 months. The right hemisphere is dominant for the perception of the frontal and profile face
Cognitive development	Moriguchi; Hiraki ²⁰	Study the development of prefrontal function in children aged 3 and 4 years	13	Children showed better behavioral performance and significantly stronger lower prefrontal activation at age 4 than at 3 years. The children that performed better on tasks at 3 years showed significant activation of the right lower prefrontal region at that age and significant activation of bilateral lower prefrontal regions at four years. Children that had poorer performance at 3 years showed no significant lower prefrontal activation at that age, but significant activation in the left lower prefrontal cortex at four years. These results indicate that the development of cognitive skills can be supported by the development of the lower prefrontal cortex
	Benavides et al. ²¹	Investigate the capacity of newborns to memorize words	112	Retroactive interference is a major cause of forgetfulness in the early stages of language acquisition and the phenomenon of interference that causes forgetfulness is a selective one

Discussion

Before the advent of neuroimaging techniques, the association between brain regions and neurodevelopment was obtained primarily by clinical neuropsychological investigations of patients with brain injury and post-mortem examinations. With the advancement of this technology, it

became possible to investigate not only the brain areas involved in a particular skill, but also the neural circuits involved in a particular function.²⁶

Noninvasive methods have been explored to make inferences about neural correlates of processes linked to human development. Among these methods, some record magnetic (magnetoencephalography, MEG) or electrical fluctua-

Table 3 Characteristics of functional studies of cortical hemodynamics using NIRS to assess language development.

Categorization	References	Objectives	Sample (n)	Main results
Development of language	Minagawa-Kawai et al. ¹³	To investigate the development of the neural adjustment process to phonemic contrasts, specific of language in children aged 3-28 months	57	Phonemic-specific brain response was found from 6-7 months of age, but there was no lateralization. A consistent, phonemic-specific and lateralized response was only observed after 12 months
	Minagawa-Kawai et al. ¹⁴	To investigate the nature of the functional brain language processing at 4 months of age	12	At 4 months, the human brain is more responsive to the native language and speech processing is based on an interaction between generic audio systems and learning mechanisms
	Wartenburger et al. ¹⁶	Determine brain activations correlated with the perception and processing of prosody at 4 years	51	The results showed that the specific language processes in children depend on inter-hemispheric specialization, with left hemispheric dominance for the segmental information processing (phonological) and right hemispheric dominance for suprasegmental processing (prosodic). At the age of 4 years, the functional specialization of the right hemisphere for prosody processing is present, with a response pattern similar to the adult
	Bortfeld et al. ¹⁸	Evaluate the usefulness of NIRS as a technique to study infant speech processing in children aged 6 and 9 months	21	Results showed significant hemodynamic changes in the left temporal cortex in response to audiovisual stimulus when compared to visual stimulus alone, as well as relative changes in all stimulus conditions in homologous regions of the right cortex in the same children. The results are consistent with those obtained through other neurophysiological methods and highlight the usefulness of NIRS to establish neural correlates of language development in children aged 6 and 9 months

Table 3 (Continued).

Categorization	References	Objectives	Sample (n)	Main results
	Petitto et al. ¹⁵	To explore, with NIRS, early phonetic processing in monolingual and bilingual children aged 2 to 16 months	61	Monolingual and bilingual children showed activation in the same language areas classically observed in adults, including the left superior temporal gyrus and the left inferior frontal cortex, with an intriguing temporal difference of development: activation of the left superior temporal gyrus was observed earlier and remained with stable activity over time, while the left inferior frontal cortex showed greater increase in neural activation in older babies, corresponding to the precise age at which babies reach the first universal milestone of language acquisition. Bilingual babies maintained linguistic sensitivity open for a longer time
	Saito et al. ¹⁷	To assess, using NIRS, how the frontal lobe of newborns responds to changes in prosody	20	Newborns between 1 and 9 days can already discriminate differences in prosodic patterns
	Naoi et al. ¹⁹	To analyze the hemodynamic brain responses to speech directed to the child, using NIRS in children aged between 4 and 13 months	48	The answers vary depending on the child's age, the speaker's familiarity and also vary in relation to the speech directed to the child or the speech directed to the adult. These results suggest a differential function for the frontal and temporal areas in the processing of speech directed to the child by different speakers

Table 4 Characteristics of non-functional studies of cortical hemodynamics using NIRS.

Categorization	References	Objectives	Sample (n)	Main results
Association between perioperative brain oxygen saturation and neurological outcome	Toet et al. ²²	To analyze the association between the amount of oxygen saturation and brain fractional oxygen extraction, measured by NIRS and EEG in neonates with up to 48 hours of life and the development outcome	18	Values of oxygen saturation and fractional oxygen extraction are stable in children with normal development, but increase and decrease, respectively, in children with impaired development. The EEG showed a closer association with the development outcome
	Kussman et al. ²³	To evaluate the association between perioperative brain oxygen saturation measured by NIRS and neurodevelopmental outcome at 1 year of age	89	Perioperative periods of decreased brain oxygen saturation are associated with altered psychomotor development and brain abnormalities in infants undergoing reparative heart surgery
	Simons et al. ²⁴	To explore the association between perioperative brain oxygen saturation measured by NIRS and neurodevelopment at 2 years of age	27	Perioperative brain oxygen saturation measured by NIRS may be a useful predictor of language skills, but it does not seem to predict cognitive or motor sequelae at 2 years of age in children undergoing surgery for congenital heart disease
Cortical hemodynamics in preterm and term infants	Kato et al. ²⁵	To measure cerebral blood flow oscillations in preterm and term infants	19	The results suggest that the cerebral blood flow oscillations in the resting state differ between preterm and full-term infants and that the development of circulatory regulation and neural activity in preterm infants are influenced by extra-uterine environment

tions (electroencephalogram, EEG and amplitude-integrated electroencephalography, aEEG) that occur in neural activity; while others, such as functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIR spectroscopy or fNIRS), measure local changes in cerebral hemodynamic activity, which can be used to make inferences about the underlying neural activity.¹

Many of these techniques, which are well-established for use in adults, have restrictions for use in children. Among all brain imaging techniques, the fMRI is considered the

“gold standard” for noninvasive functional mapping of the human brain.²⁶ This technique stands out from the others due to its high spatial resolution and by displaying well-established routines of data acquisition and analysis, facilitating its use in research, among other reasons, because it is easier to make comparisons between results from different studies. However, as the MEG, the fMRI requires the participant to remain motionless, usually wrapped or restrained. There are a few published studies in children using these techniques; however, these works are generally

limited to the study of children while sleeping, sedated or very young ones.

For many years, the first choice for neuroimaging studies in children while awake was EEG, a technique with high temporal resolution, but relatively low spatial resolution.⁶ In this field, continuous brain monitoring through aEEG has been used in neonates to assess real-time brain function and for long periods, allowing a better classification of the encephalopathy severity, early detection of subclinical seizures and the monitoring of treatment response.²⁷ Abnormalities found in the aEEG early in life have strong predictive values of abnormal results at one year of age.²⁸

Compared with the aforementioned techniques, NIRS offers a new direction for the study of child development, as it has the following advantages over these methods: better temporal resolution, better safety level, it is silent and less sensitive to motion artifacts, requiring less rigid stabilization of the head and body without the need for a labeled or carrier substance to be injected into the bloodstream.²

The most commonly used and simpler NIRS method involves measuring the intensity of diffusely reflected light with sources that emit light continuously. Instruments that acquire such measurements are referred to as continuous-wave systems.²⁹ All studies discussed here resorted to this method, which, although it does not provide quantitative measurements of absolute concentrations of different types of hemoglobin, provides estimates of changes in their levels from a baseline value, thus reflecting variations in tissue oxygen use.⁵

The use of multiple channels with different combinations of sources and detectors has been described in the literature in recent years. Until the early 1990s, almost all NIRS systems employed one or two measurement channels, but over time, the number of channels in the available systems has increased, improving spatial resolution.²⁹ Of all the reviewed studies, most of them used multichannel acquisition systems, allowing greater coverage of the region of interest.

The advantages of increasing the number of channels are clear. However, this results in the inevitable increase in weight and size of the device that maintains the optodes positioning in the scalp. This may explain the greater proportion of optical data loss due to excessive movement artifacts. The losses reported in the literature vary from 12.5 to 70%,⁶ similar to the losses found in this review: 3-80% in functional studies and 14-56% in non-functional studies. A possible explanation for the greater loss in functional studies would be the use of more complex data collection protocols, employing a greater numbers of channels.

Although NIRS has been used for more than 35 years, it was not applied to children up until the mid-1990s. Investigations in this field have expanded rapidly, providing evidence that NIRS can be used to collect information about hemodynamics correlated to the neural activity in children from an early age, using tasks that assess cognitive skills, language acquisition, visual perception, social cognition and other functional aspects of the brain during childhood.³⁰ Moreover, non-functional NIRS studies have demonstrated its potential as a prognostic tool, based on the non-invasive monitoring of cerebral hemodynamics and oxygenation.^{22,31-33}

Based on the publications analyzed, it was possible to recognize advances in the use of NIR spectroscopy in the study of child development; however, some methodological obstacles inherent in the use of this technology must be considered. Consistent with the results of other studies reviewing NIRS, it was observed that there is great variability in the methods used for data acquisition and analysis. The use of different wavelength combinations and different separations between sources and detectors could affect the captured response. In the 19 studies included in the review, we identified seven different wavelength combinations used. The separation between optodes was more uniform, being two or three centimeters, which is adequate for the pediatric population.

Another question that should be addressed concerns the large differences in sample sizes of the studies (between 12 and 112 subjects) and significant losses due to the quality of the generated signal. While there is a good signal-to-noise ratio for optical imaging, the variation that is inherent in infant behavior requires that there be at least ten babies in each age group.³⁴ The reviewed studies analyzed samples with 12 or more children. However, one study that proposed to evaluate the association between the amount of oxygen saturation, the fractional cerebral tissue oxygen extraction and the result of development,²² with an initial sample of 18 children, lost nine of them due to death, ending up with a final sample of nine children and found developmental change in only one. Despite the importance of studies like this to extend the current body of knowledge that emphasize the validity of NIRS to study infant brain development, the interpretation of results obtained with small sample groups should be very cautious and their projection to other contexts or populations becomes impaired.

Moreover, the difficulty of determining the locations for positioning of optodes using external markers, especially in children, should be considered. A current trend in NIRS studies, and which was identified in 13 of the 19 articles included in this review, is the use of the international 10-20 system for electroencephalography for the positioning of optodes.

It is also necessary to define the number of experiments required to obtain a significant response. Finding the balance between the number of repetitions required to capture a reliable response without making the test long and stressful, seems to be a delicate aspect of research using NIRS in children. This is due to the fact that inadequate signals and motion artifacts often make it necessary to repeat the tests. The studies reviewed here showed not only a large variability in the number of experiments, as well as in the duration of tests, reinforcing the premise that there is yet no consensus in the literature about this aspect. Some authors emphasize that the use of long experiments could lead to a diminished response over time, as the body adapts to the stimulus that is repeated many times. Additionally, the study designs in blocks, with long periods of stimulation and rest, has potential risk for false positive/negative changes in the signal due to any low frequency fluctuation at baseline or motion artifacts.³⁵ On the other hand, some authors recommend that stimuli should be repeated at least 10 times, considering that sponta-

neous changes in cerebral blood volume are common, for instance, the so-called Mayer waves or slow vasomotion at 0.1 Hz. Such changes are about the same size as the functional activations and, therefore, may be misidentified. Repetition allows making averages of time series, reducing the influence of spontaneous changes, as they are not synchronized with the stimuli.³⁶

It is worth noting that this review aimed to emphasize NIRS as an auxiliary tool in the study of normal childhood development. For this reason, no studies that addressed developmental disorders were included, due to high specificity of each of them. However, it is necessary to stress that the current literature on NIRS has also emphasized the adequacy of this technology for the study of child development disorders and there is a growing number of publications in this area. In this context, studies on Autism Spectrum Disorder,^{37,38} Attention Deficit Hyperactivity Disorder³⁹ Cerebral Palsy⁴⁰⁻⁴² and Down Syndrome⁴³ have been highlighted.

In conclusion, NIRS is increasingly becoming a practical alternative and potentially useful technique for studies of functional activity of the infant brain. The development of equipment more adequate for use in children has increased, so that the results obtained when using NIRS technology are more reliable. It is worth mentioning that the spatial location of signals will never achieve the accuracy of fMRI, but in conjunction with other techniques, such as EEG, NIRS is emerging as an important non-invasive tool for the study of the developing brain.

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Conflicts of interest

The authors declare no conflicts of interest.

References

- Gervain J, Mehler J, Werker JF, Nelson CA, Csibra G, Lloyd-Fox S, et al. Near-infrared spectroscopy: a report from the McDonnell infant methodology consortium. *Dev Cogn Neurosci*. 2011;1:22-46.
- Nagamitsu S, Yamashita Y, Tanaka H, Matsuishi T. Functional near-infrared spectroscopy studies in children. *Biopsychosoc Med*. 2012;6:1-7.
- Kawakubo Y, Kono T, Takizawa R, Kuwabara H, Ishii-Takahashi A, Kasai K. Developmental changes of prefrontal activation in humans: a near-infrared spectroscopy study of preschool children and adults. *PLoS One*. 2011;6:e25944.
- Franceschini MA, Thaker S, Themelis G, Krishnamoorthy KK, Bortfeld H, Diamond SG, et al. Assessment of infant brain development with frequency-domain near-infrared spectroscopy. *Pediatr Res*. 2007;61:546-51.
- Lima A, Bakker J. Near-infrared spectroscopy for monitoring peripheral tissue perfusion in critically ill patients. *Rev Bras Ter Intensiva*. 2011;23:341-51.
- Lloyd-Fox S, Blasi A, Elwell CE. Illuminating the developing brain: the past, present and future of functional near infrared spectroscopy. *Neurosci Biobehav Rev*. 2010;34:269-84.
- Watanabe H, Homae F, Taga G. General to specific development of functional activation in the cerebral cortexes of 2- to 3-month-old infants. *Neuroimage*. 2010;50:1536-44.
- Wilcox T, Bortfeld H, Woods R, Wruck E, Boas DA. Hemodynamic response to featural changes in the occipital and inferior temporal cortex in infants: a preliminary methodological exploration. *Dev Sci*. 2008;11:361-70.
- Wilcox T, Stubbs S, Hirshkowitz A, Boas DA. Functional activation of the infant cortex during object processing. *Neuroimage*. 2012;62:1833-40.
- Watanabe H, Homae F, Nakano T, Taga G. Functional activation in diverse regions of the developing brain of human infants. *Neuroimage*. 2008;43:346-57.
- Lloyd-Fox S, Blasi A, Volein A, Everdell N, Elwell CE, Johnson MH. Social perception in infancy: a near infrared spectroscopy study. *Child Development*. 2009;80:986-99.
- Nakato E, Otsuka Y, Kanazawa S, Yamaguchi MK, Watanabe S, Kakigi R. When do infants differentiate profile face from frontal face? A near-infrared spectroscopic study. *Hum Brain Mapp*. 2009;30:462-72.
- Minagawa-Kawai Y, Mori K, Naoi N, Kojima S. Neural attunement processes in infants during the acquisition of a language-specific phonemic contrast. *J Neurosci*. 2007;27:315-21.
- Minagawa-Kawai Y, Van der Lely H, Ramus F, Sato Y, Mazuka R, Dupoux E. Optical brain imaging reveals general auditory and language-specific processing in early infant development. *Cereb Cortex*. 2011;21:254-61.
- Petitto LA, Berens MS, Kovelman I, Dubins MH, Jasinska K, The Shalinsky M. Perceptual Wedge hypothesis as the basis for bilingual babies' phonetic processing advantage: new insights from fNIRS brain imaging. *Brain Lang*. 2012;121:130-43.
- Wartenburger I, Steinbrink J, Telkemeyer S, Friedrich M, Friederici AD, Obrig H. The processing of prosody: evidence of interhemispheric specialization at the age of four. *Neuroimage*. 2007;34:416-25.
- Saito Y, Kondo T, Aoyama S, Fukumoto R, Konishi N, Nakamura K, et al. The function of the frontal lobe in neonates for response to a prosodic voice. *Early Hum Dev*. 2007;83:225-30.
- Bortfeld H, Fava E, Boas DA. Identifying cortical lateralization of speech processing in infants using near-infrared spectroscopy. *Dev Neuropsychol*. 2009;34:52-65.
- Naoi N, Minagawa-Kawai Y, Kobayashi A, Takeuchi K, Nakamura K, Yamamoto J, et al. Cerebral responses to infant-directed speech and the effect of talker familiarity. *Neuroimage*. 2012;59:1735-44.
- Moriguchi Y, Hirakic K. Longitudinal development of pre-frontal function during early childhood. *Dev Cogn Neurosci*. 2011;1:153-62.
- Benavides-Varela S, Gómez DM, Macagno F, Bion RA, Peretz I, et al. Memory in the Neonate brain. *PLoS ONE*. 2011;6:e27497.
- Toet MC, Lemmers PM, Van Schelvenb LJ, Van Bel F. Cerebral oxygenation and electrical activity after birth asphyxia: the irrelatoin to outcome. *Pediatrics*. 2006;117:333-9.
- Kussman BD, Wypij D, Laussen PC, Soul JS, Bellinger DC, DiNardo JA, et al. Relationship of intraoperative cerebral oxygen saturation to neurodevelopmental outcome and brain MRI at one year of age in infants undergoing biventricular repair. *Circulation*. 2010;122:245-54.
- Simons J, Sood ED, Derby CD, Pizarro C. Predictive value of near-infrared spectroscopy on neurodevelopmental outcome after surgery for congenital heart disease in infancy. *J Thorac Cardiovasc Surg*. 2012;143:118-25.

25. Kato I, Kusaka T, Nishida T, Koyano K, Nakamura S, Nakamura M, et al. Extruterine environment influences spontaneous low-frequency oscillations in the preterm brain. *Brain Dev.* 2013;35:17-25.
26. Cutini S, Moro SB, Bisconti S. Functional near infrared optical imaging in cognitive neuroscience: an introductory review. *J Near Infrared Spectrosc.* 2012;20:75-92.
27. Toso PA, González AJ, Pérez ME, Kattan J, Fabres JG, Tapia JL, et al. Clinical utility of early amplitude integrated EEG in monitoring term newborns at risk of neurological injury. *J Pediatr (Rio J).* 2014;90:143-8.
28. Laptook A. Amplitude integrated electroencephalogram (aEEG): has it found its niche in neonatal intensive care unit? *J Pediatr (Rio J).* 2014;90:102-4.
29. Minagawa-Kawai Y, Mori K, Hebden JC, Dupoux E. Optical imaging of infants' neurocognitive development: recent advances and perspectives. *Dev Neurobiol.* 2008;68:712-28.
30. Aslin RN, Mehler J. Near-infrared spectroscopy for functional studies of brain activity in human infants: promise, prospects, and challenges. *J Biomed Opt.* 2005;10:11009.
31. Nicklin SE, Hassan IA, Wickramasinghe YA, Spencer SA. The light still shines, but not that brightly? The current status of perinatal near infrared spectroscopy. *Arch Dis Child Fetal Neonatal Ed.* 2003;88:F263-8.
32. Meek JH, Elwell CE, McCormick DC, Edwards A, Townsend J, Stewart A, et al. Abnormal cerebral haemodynamics in perinatally asphyxiated neonates related to outcome. *Arch Dis Child Fetal Neonatal Ed.* 1999;81:F110-5.
33. Van Bel FV, Dorrepaal CA, Benders MJ, Zeeuwe PE, Van de Bor MV, Berger HM. Changes in cerebral hemodynamics and oxygenation in the first 24 hours after birth asphyxia. *Pediatrics.* 1993;92:365-72.
34. Hespos SJ, Ferry AL, Cannistraci CJ, Gore J, Park S. Using optical imaging to investigate functional cortical activity in human infants. In: Roe AW, editor. *Imaging the brain with optical methods.* New York: Springer; 2010. p. 159-76.
35. Taga G, Asakawa K, Maki A, Konishi Y, Koizumi H. Brain imaging in awake infants by near-infrared optical topography. *PNAS.* 2003;100:10722-7.
36. Wolf M, Greisen G. Advances in near-infrared spectroscopy to study the brain of the preterm and term neonate. *Clin Perinatol.* 2009;36:807-34.
37. Iwanaga R, Tanaka G, Nakane H, Honda S, Imamura A, Ozawa H. Usefulness of near-infrared spectroscopy to detect brain dysfunction in children with autism spectrum disorder when inferring the mental state of others. *Psychiatry Clin Neurosci.* 2013;67:203-9.
38. Kikuchi M, Yoshimura Y, Shitamichi K, Ueno S, Hiraishi H, Munesue T, et al. Anterior prefrontal hemodynamic connectivity in conscious 3- to 7-year-old children with typical development and autism spectrum disorder. *PLoS One.* 2013;8:e56087.
39. Tsujimoto S, Yasumura A, Yamashita Y, Torii M, Kaga M, Inagaki M. Increased prefrontal oxygenation related to distractor-resistant working memory in children with attention-deficit/hyperactivity disorder (ADHD). *Child Psychiatry Hum Dev.* 2013;44:678-88.
40. Chaudhary U, Hall M, Gonzalez J, Elbaum L, Bloyer M, Godavarty A. Motor response investigation in individuals with cerebral palsy using near infrared spectroscopy: pilot study. *Appl Opt.* 2014;53:503-10.
41. Kurz MJ, Wilson TW, Arpin DJ. An fNIRS exploratory investigation of the cortical activity during gait in children with spastic diplegic cerebral palsy. *Brain Dev.* 2014. Epub 2014 Feb 5.
42. Tian F, Delgado MR, Dhamne SC, Khan B, Alexandrakis G, Romero MI, et al. Quantification of functional near infrared spectroscopy to assess cortical reorganization in children with cerebral palsy. *Opt Express.* 2010;18:25973-86.
43. Imai M, Watanabe H, Yasui K, Kimura Y, Shitara Y, Tsuchida S, et al. Functional connectivity of the cortex of term and pre-term infants and infants with Down's syndrome. *Neuroimage.* 2014;85:272-8.