REVISTA CEFAC
SPEECH, LANGUAGE, HEARING SCIENCES AND EDUCATION JOURNAL
Rev. CEFAC. 2016 Jul-Ago; 18(4):965-973 doi: 10.1590/1982-0216201618422615

Revision articles

Near – infrared spectroscopy and auditory sensory processing in infants

Espectroscopia de luz próxima ao infravermelho e processamento sensorial auditivo em lactentes

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Source of support: Work carried out in the Post – Graduation course in Language and Hearing Sciences, Faculty of Medicine, Federal University of Minas Gerais – UFMG – Belo Horizonte (MG), Brazil, with a scholarship granted by the Coordination for the Improvement of Higher Education Personnel (CAPES).

Conflict of interest: non-existent

Received on: December 30, 2015
Accepted on: May 30, 2016

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ABSTRACT

Purpose: to systematically review, through the search in the Medline and Lilacs database, the use of near-infrared spectroscopy (NIRS) as a tool to evaluate the auditory function at the cortical level in infants.

Methods: integrative review based on the criteria established by the Cochrane Handbook including the definition of the guiding question (theme to be researched), definition of the database to locate the articles, and selection and critical analysis of the articles. The bibliographic search was performed from September to December 2014. The inclusion criteria were: articles published in English, Portuguese and Spanish related to the child population (infants aged from 0 to 24 months) and type of study (cohort, case-control, cross-sectional).

Results: 1674 articles were identified and 12 met the inclusion criteria of this study. In all articles, the auditory stimulation was used to measure brain hemodynamic changes, but in different areas of interest of the brain. They were grouped into three categories according to the type of stimulus: only vocal sounds, vocal sounds and other auditory stimuli and non-vocal sounds.

Conclusion: NIRS is an effective tool for the evaluation of the auditory function at the cortical level in the child population.

Keywords: Spectroscopy, Near-Infrared; Hemodynamics; Auditory Perception; Hearing; Central Nervous System

RESUMO

Objetivo: revisar sistematicamente, por meio de busca nas plataformas Medline e Lilacs o uso da espectroscopia de luz próxima ao infravermelho (NIRS) como instrumento para a avaliação da audição a nível cortical em lactentes.

Métodos: foi realizada uma revisão integrativa baseada nos critérios estabelecidos pela *Cochrane Handbook,* passando pelas etapas de definição da questão norteadora (o tema a ser pesquisado), definição das bases de dados para localização dos estudos, seleção e análise crítica dos artigos. A pesquisa bibliográfica foi realizada no período de setembro a dezembro de 2014. Os critérios de inclusão utilizados foram: artigos publicados nos idiomas inglês, português e espanhol, com a população infantil (bebês de 0 a 24 meses) e tipo de estudo (coorte, caso controle, transversal).

Resultados: foram identificados 1674 artigos e 12 atenderam os critérios de inclusão deste estudo. Todos os artigos utilizaram o estímulo auditivo para medir alterações na hemodinâmica cerebral, porém com áreas cerebrais de interesse diferentes. E foram agrupados em três categorias quanto ao tipo de estímulo: apenas sons vocais, sons vocais e outros estímulos auditivos e sons não vocais.

Conclusão: a NIRS é um instrumento eficaz para investigação da audição a nível cortical na população infantil.

Descritores: Espectroscopia de Luz Próxima ao Infravermelho; Hemodinâmica; Percepção Auditiva; Audição; Sistema Nervoso Central

INTRODUCTION

The development of the Auditory System begins in the intrauterine life and its maturation occurs during the childhood and adolescence. The integrity of the peripheral and central auditory system is a prerequisite for the acquisition and development of speech and language. It is important to make an investigation of the infant auditory sensitivity in the first months of life, both at the peripheral as the central level, in order to detect hearing disorders as early as possible to avoid consequences on the overall development of the child.

The hearing evaluation poses challenges. There are several non-invasive techniques that detect the cortical activity in response to sound stimuli, but they have limitations when applied to the child population. The Near-infrared spectroscopy (NIRS) is a promising tool, and has been used to assess the functional activation of the brain in children. This technology uses sources of visible light in the near-infrared electromagnetic spectrum range and evaluates photosensitive molecular components of the biological tissue[1,2].

Part of the near-infrared light is diverted and the other part is absorbed by the studied tissue. The change in the blood oxygenation in response to a stimulus indirectly reflects an index of neural activation, which is read through the path of the light beam. In the region where the cortical activation occurs, the blood flow and volume are changed, allowing to monitor, in a noninvasive way, the concentrations of oxyhemoglobin (HbO_2) and deoxyhemoglobin (HHb)[3-6].

The NIRS system comprises a laser source, detector, monitor screen and optical converter. The sources and detectors are positioned on the scalp, creating a light path between the source and the banana-shaped detector. The source-detector distance and the thickness of the tissues is important for the calculation of the depth of penetration of the light and spatial resolution[1,5].

This brain imaging technology is portable, silent, less sensitive to movement of the evaluated individual, allowing the evaluation of the child in the waking state and accommodated on the lap of the parents. It has a good spatial resolution and better temporal resolution compared with Functional Magnetic Resonance Imaging. It has been successfully employed in the presentation of auditory stimuli for investigation of the auditory skills in newborns and young infants[2,7-10].

Normally the coupling of the optodes in the head, reduction of artifacts in the signal and increase of penetration of light in the cortex is better in the child population than in the adult population[5] due to their thinner hair, skin and skull.

Although many studies have associate NIRS with auditory stimuli in the child population, in Brazil the use of this technology is still in the initial stage even in the evaluation of the infant population. The purpose of this study was to investigate, through an integrative literature review, the use of Near-infrared Spectroscopy (NIRS) as a tool for the evaluation of the auditory function at the cortical level in infants.

METHODS

An integrative review was carried out, which is a method that gather studies for a deep analysis of the analyzed theme, point out the gaps of the study for new researches, enable the synthesis of the investigated subject and evidences for the clinical practices[11-13].

This review was based on the criteria established by the Cochrane Handbook, including the following steps: definition of the guiding question (theme to be researched), definition of the database to locate the studies, and selection and critical analysis of the articles[12,14].

The guiding question of the study was: Can NIRS be used as an auxiliary tool in the investigation and evaluation of the auditory function at the cortical level in infants?

For the bibliographic search, the Virtual Health Library and PubMed were used for the search in the Lilacs and Medline databases. The languages used for the search of articles were Portuguese, English and Spanish. The last 07 years were considered for the research.

The following combination of descriptors and keywords found from the Descriptors in Health Sciences (DeCS) was used: "*Spectroscopy, Near-Infrared*", "*Electrophysiology*", "*Speech Perception*", "*Hearing*", "*Auditory cortex*", "*Auditory Diseases Central*" and respective correspondents in Portuguese and Spanish. They were combined with the Boolean markers "AND" and "OR".

This review included articles published in English, Portuguese and Spanish; type of study (cohort, case-control, cross-sectional); available in its entirety in digital media; articles related to children (infants from 0 to 24 months), and time limit (2009-2015).

It excluded review and meta-analysis articles, quotes repeated in the databases, articles that did not present aspects related to NIRS and/or to auditory stimulation defined in the purpose of this review, and

articles related to population aged above 24 months in average.

The evaluation of the articles to be included in the survey was carried out by the reading of the titles and abstracts, followed by the pre-selection and inclusion of articles considered relevant. After that, the pre-selected articles were read in full, and the articles that were in line with the theme of this study were included in this research (Figure 1).

RESULTS

By means of the search, 1674 articles were identified. Of these, 63 were selected for analysis of the titles and abstracts. From this pre-selection, 24 articles were selected for complete reading and detailed analysis. Two articles were identified by the references of the texts read in full and were included, totaling 26 full articles reviewed. Of them, 12 answered the guiding question of this study (Figure 1).

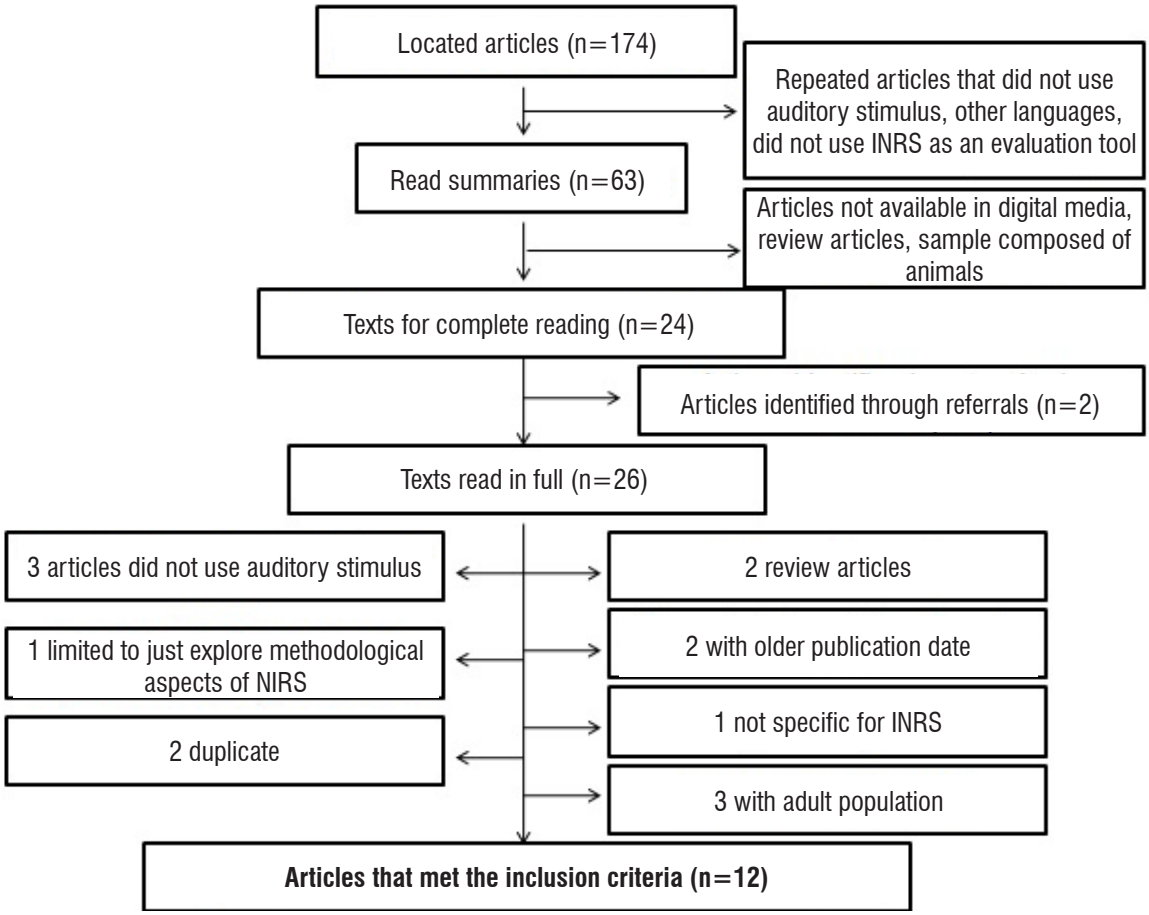

Figure 1. Flowchart of the literature review

Many of the publications found were excluded as they consisted of articles that did not use NIRS as an assessment tool, articles that did not use auditory stimuli to measure the brain hemodynamics, articles containing sample aged above 24 months in average, review articles, repeated articles, articles that were not available in digital media, articles that only describe the spectroscopy technique, other languages and animal studies.

It was found that the selected articles, which met the inclusion criteria of this study, are distributed in different years: two in 2009 (16.60%), one in 2010 (8.33%), five in 2011 (41.66), four in 2012 (33.30%) and none in 2013, 2014 and 2015. It should be highlighted that articles published in 2013 to 2015 were also found, but none of them used auditory stimuli and used sample aged up to 24 months in average. All articles were published in various international journals: *Frontiers Psychology,* with 02 articles*; Developmental Neuropsychology, The Journal of Neuroscience, Cerebral Cortex, Neuron, PLoS ONE, Philosophical Transactions of the Royal Society B, Journal of Cognitive Neuroscience, Neuro*

Image, Human Brain Mapping e Brain and Language, with 01 scientific article in each journal.

A wide variation of sample size (12 to 112 children), variation of age of inclusion (1.14 days to 16 months) and sample loss was observed in all articles. According to the report, the sample loss was caused by artifacts in the signal due to baby's cry and movements, hair obstruction, poor positioning of the probe, inability to get more than one block of trials and failure to obtain optical signals.

In relation to the methodology of the technique, all articles used the continuous wave NIRS device with multiple channels, from 6 to 94; with source-detector distance of 2-3 cm, and all of them used the international system 10-20 of electroencephalography for the positioning of the optodes. Different methodologies were observed regarding the application of the technique, collection and analysis of the results. However, 66% of the articles used ANOVA, analysis of variance.

In all articles, the auditory stimulation was used to measure brain hemodynamic changes through NIRS, but in different areas of interest of the brain. It was found that all articles included have investigated the temporal region and, in most of them, the combination with activation of other regions was observed: five were interested in the temporal and frontal region (41.66%); five in the temporal, frontal and parietal regions (41.66%); one in the temporal, frontal and occipital regions (8.34%) and one was only interested in the temporal region (8.34%).

Whereas in many of the articles the speech was used as auditory stimulus, it was decided to group them into three variable categories regarding the type of stimulus: only vocal sounds (25%), vocal sounds and other auditory stimuli (animal sounds, environmental sounds, music and pure tones; 41.66%) and non-vocal sounds (pure tones – 33.33%). (Figure 2)

It was possible to observe a similarity in the studies that used speech as auditory stimulus as they associated speech sounds to other sound stimuli, including audio-visual stimuli, monkey sounds, environmental sounds, musical sounds and speech with phonemic and prosodic differences, indicating the interest of the study to several brain areas.

The time of the stimuli ranged from 5 to 60 seconds, and the intensity from 45 to 75 dBNPS, which reveals that there is no standardization in the application of NIRS regarding time and intensity of stimulation necessary for changes of oxygenation in the brain region of interest.

In studies where only vocal sounds were used as stimulus, it can be observed that all the articles investigated the hemodynamic of the frontal and temporal regions, except 01 study[15] that investigated the parietal region in addition to these two areas. The brain hemodynamic responses were analyzed regarding the speech discrimination[16], perception of phonological[16] and prosodic[15] contrasts, development of the hemispheric laterality for speech[15] and influence of the mother's voice in the speech recognition[17]. The main results showed that phonemic changes activate the inferior frontal and inferior parietal regions and right temporal region; and the activation mainly occurs in the right temporal region for prosodic contrasts[15]. All of them can be observed by the variation of oxygenation detected by the NIRS. In newborns, it was observed that different syllabic structures caused activation in the frontal and temporal regions[16]. These same regions are activated in response to the familiarity, in the recognition of the mother's voice[17].

The studies that used vocal sounds and other stimuli have investigated brain hemodynamic responses to evaluate the perceptual processing during the exposure to audiovisual stimuli[18]; brain lateralization for speech sounds and non-vocal sounds (native and non-native speech, human onomatopoeia and monkey sounds)[10]; processing of vocal and prosodic specificity[19]; ability of the newborn to memorize words[6]; processing for linguistic and non-linguistic sounds in bilingual and monolingual children[20].

These studies showed important results, including the usefulness of the NIRS technology as a tool to monitor the hemodynamic activity in children, an activity that was found in greater proportion in the left temporal region in response to audiovisual stimuli compared only with visual stimulus[18]; greater lateralization in the left temporal region for the speech processing in comparison to non-vocal sounds[10]. They also show increased hemodynamic responses to human voice in the right and left temporal cortex when compared to non-vocal sounds in infants aged 07 months, and greater activation in the right temporal region in response to vocal stimuli modulated by emotion[19]. In a study it was noted that humans are able to memorize words hours after birth[6].

Finally, the articles that described the use of non-vocal stimuli addressed the sensitivity and activation of the auditory cortex for acoustic stimuli

Categorization	First author	Year	Specification of the stimulus	Main purpose	Sample (n)	Main results
Vocal sounds	Arimitsu	2011	Speech with phonemic and prosodic difference	To determine the degree of hemispheric specialization of (phonemic and prosodic) linguistic features in the early childhood.	17	Functional lateralization to the right temporal region for the processing of prosody and bilateral engagement of the auditory areas for phonemic contrasts.
	Gervain	2012	Speech	To explore whether neonates can discriminate different grammatical stimuli based on repetition.	22	Newborns present perception skills and combination necessary for language acquisition.
	Naoi	2012	Speech with phonemic and prosodic difference	To examine the effects of speech directed to the child (influence of familiarity) through the brain hemodynamic responses.	26	Speech directed to children increase the hemodynamic activity in the temporal region compared with speech directed to adults. The mother's speech directed to the child generates hemodynamic activity in the frontal areas.
Vocal sounds and other stimuli	Bortfeld	2009	Speech and Audiovisual	To evaluate the NIRS as evaluation method of the processing in specific cortical regions in older babies, in response to linguistic stimuli.	21	The NIRS is sensitive enough to evaluate the neural basis of perceptual processing in infants.
	Minagawa-Kawai	2011	Speech (Native and non-native language) and monkey sounds	Use the NIRS to review the issue of brain lateralization for speech and non-speech sounds in infants aged 4 months.	12	Through the analysis of the hemodynamic responses in infants aged 4 months, compared to stimuli that did not contain speech, the study clearly showed increased activation in the left hemisphere in response to the speech processing.
	Grossmann	2010	Words, musical and environmental sounds	In Experiment 1: To analyze the hemodynamic responses in temporal cortical regions due to vocal and non-vocal sounds in children aged from 04 to 07 months. Experiment 2: To measure the cortical response derived from vocal stimuli modulated by emotional prosody in infants aged 07 months.	16	In Experiment 1, it was found that 07 month-old infants had a significant increase in hemodynamic responses, in the upper right and left temporal cortex, to human voice compared to non-vocal sounds. In infants aged 4 months, an increase in the hemodynamic response was identified in response to non-vocal stimulus in the right temporal cortex. In experiment 2, an increase in the hemodynamic response was found in the right temporal region in response to vocal stimuli modulated by emotion in infants aged 07 months.
	Benavides-Varela	2011	Speech and musical sounds	To investigate the ability of newborns to remember words	112	Hemodynamic responses correlated with word recognition in the newborn brain were identified. The human being is able to memorize words hours after the birth. The memory of the newborn for words is affected when it is followed by similar acoustic stimuli.
	Petitto	2012	Speech and pure tones	To investigate the phonetic processing in bilingual and monolingual babies	61	The phonetic processing in bilingual and monolingual babies is made with the same brain tissue specific for language observed in adults.

Categorization	First author	Year	Specification of the stimulus	Main purpose	Sample (n)	Main results
Non-vocal sounds	Telkemeyer	2009	Noises with different frequency and modulation patterns.	To investigate the sensitivity of the auditory cortex to acoustic stimuli with different temporal structures in infants aged 3 months.	31	The auditory cortex of infants aged 03 months shows differential sensitivity of acoustic signals with varied temporal structure. The newborns show an increase of hemodynamic response to rapid acoustic modulations, especially at the relevant time interval for the perception of phonemes. The brain of the newborn shows a functional asymmetry to process slow acoustic modulations such as prosodic information, predominantly in the right hemisphere. From the birth, the brain appears to exhibit structural and functional properties especially related to language in order to facilitate one of the main needs of humans, communication.
	Telkemeyer	2011	Tones *	To investigate relevant precursors of the auditory perception in the decoding of speech in infants.	45	In infants aged 06 months, it was found that the rapid acoustic modulations lead to increased hemodynamic responses in the left temporal and parietal region in relation to the right region. On the other side, the slow acoustic modulations lead to hemodynamic responses in the inferior frontal and right temporoparietal region. In infants aged 03 months, there was a greater increase of oxy-Hb rate in the upper front and left posterior temporal regions for both acoustic modulations.
	Taga	2011	Pure tones	To study the phases related to the hemodynamic signs between the cortical regions in babies during the sound stimulation.	18	An increase in oxy-hemoglobin and a decrease in the deoxy-Hb was observed, not only in bilateral temporal auditory regions, but also in the occipital and prefrontal regions.
	Homae	2012	Musical sounds	To examine the possibility of three different stimuli to cause, in terms of time, different cortical activation in infants aged 03 and 06 months.	43	Hemodynamic responses were found to the sequence of sounds in both hemispheres.

Figura 2. Principais características dos artigos selecionados para esta revisão.

with different temporal structures[21-23], and the relation of hemodynamic responses among the cortical regions[24]. The results of this group were consistent as they reported that the right and left auditory cortex are equally sensitive to rapid acoustic modulations, while the slow ones are preferably processed by the right auditory cortex[21,22]. It was observed an increase in the oxyhemoglobin rates and hemodynamic responses not only in bilateral temporal auditory regions, but also in the occipital and prefrontal regions due to stimulation with pure tones[24] in addition to the temporoparietal region due to different sequence of tones[23].

DISCUSSION

The study showed that from the birth and during the development of the first months of life, the infant brain already presents a different sensitivity for the processing of acoustic signals, whether vocal or not, with different acoustic properties. These differences in the sound stimuli cause a differential pattern of brain activation and hemispheric specialization in the early childhood[22]. This result corroborates another study that suggests that the child is already able to have sound awareness, discriminate between the presence and absence of sound, and give correct responses in the search of the sound between the birth and four months of age[25].

It was also observed that one of the acoustic properties that activates different brain regions is the variation of temporal structure. An increase in the hemodynamic activity resulting from rapid acoustic modulations, especially in the relevant interval for the perception of the phoneme was observed in newborns. It is demonstrated that these modulations are bilaterally processed in a symmetric way in the temporal regions of the brain. On the other side, slow acoustic modulations generate more lateralized cortical activation to the right hemisphere of the brain. Although the auditory cortex decodes fast acoustic modulations, relevant for the phonemic decoding within the speech flow in a bilateral way, the phonemic contrasts preferentially activate the left hemisphere of the temporal region in babies. The prosodic contrasts predominantly activated the right temporal region[10,15,21,22]. Reinforcing the role of this region for the sensory processing of emotional speech signals. This mechanism is also essential as the prosodic organization of speech facilitates the acquisition of language by children[10,15,19].

The analyzed data show that, from the birth, the infants are able to perform the discrimination of speech sounds and their phonetic contrasts, and also of different grammatical structures (identical syllables and different syllables). The perception and speech discrimination, as already mentioned, consistently activate temporal areas of the left hemisphere, showing an efficient lateralization to the left hemisphere, which has major language centers. This reinforcement of the left dominance can be considered a neural precursor for the acquisition of language[10,16].

The results of the articles reviewed here corroborate the findings of another study, which shows the existence of a dominance of the left hemisphere for the language processing and perception of speech stimuli, and a dominance of the right hemisphere for perception of musical stimuli[26].

Regarding the group of articles that used auditory stimuli with words, hemodynamic responses were found due to the recognition of words in the brain of newborns[6,15]. This population was able to remember the words that were presented followed by parts of instrumental music. This suggests that the words and music are processed in different ways in the brain of the newborn[6], and that they have an early capacity for short-term auditory memory[15].

Regarding the results mentioned above, other studies denote that, in the first months of life, the baby is already able to select speech sounds, i.e., to discriminate phonetic contrasts of the languages that are or are not used to hear. The auditory system can analyze speech sounds, identifying them acoustically and recognizing them as sounds of the language to which it is exposed[25,27,28].

It was also possible to demonstrate that simple auditory stimuli (pure tones) trigger hemodynamic responses with the increase of the oxyhemoglobin rate and reduction of deoxyhemoglobin, not only in bilateral temporal auditory regions, but also in the occipital, parietal and prefrontal regions. When periodically presented, the auditory stimulation generates, in the temporal regions, cortical activity that is spread to neighboring regions, generating spontaneous activity. These results demonstrate the existence of short distance cortical connectivity in these regions[24].

All articles mentioned here used the NIRS method to locate the hemodynamic activity in response to sensory stimulation, providing a spatial resolution sufficient to measure the responses evoked in several brain areas. This method has been employed to study the functional development of the cortex in children and adults. Therefore, NIRS is a useful technique in this regard, non-invasive, easy to apply, tolerant to slight movements, which may be a complement to other existing techniques such as electroencephalogram, magnetoencephalography, functional magnetic resonance imaging to study the brain development in children[2,3,15,16].

Long-term studies with children and adults are required in order to standardize the responses of the cerebral hemodynamics to auditory stimuli in different cortical areas, to guide other studies with the use of NIRS and assist in the early diagnosis of changes in the auditory system at the cortical level.

CONCLUSION

This review shows that NIRS allows the investigation and understanding of the auditory perception and some of its components, such as detection, sound sensation, discrimination, attention and memorization of sounds, i.e., of the auditory sensory processing in the child population. Therefore, it is concluded that NIRS is an effective tool for the hearing evaluation at cortical level in infants, and can be used in combination with other existing and standardized methods of hearing evaluation.

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