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# Applicability of Mismatch Negativity in the child population: systematic literature review

## Aplicabilidade do *Mismatch Negativity* na população infantil: revisão sistemática de literatura

Dulce Azevedo Ferreira<sup>1</sup>, Claudine Devicari Bueno<sup>1</sup>, Sady Selaimen da Costa<sup>2</sup>, Pricila Sleifer<sup>3</sup>

### ABSTRACT

**Introduction:** *Mismatch Negativity* (MMN) is an electrophysiological potential that evaluates the brain's capacity to discriminate sounds, regardless of attentional and behavioral capacity. Because it is an objective and user-friendly measure, it becomes promising in the study of auditory processing research in children. **Purpose:** To verify the applicability of Mismatch Negativity (MMN) in children. **Research strategy:** A search was conducted in August and September 2016 using the descriptors Evoked Potentials, Auditory AND Children, Event-related Potential AND Children and Electrophysiology AND Children in bibliographic collection of the electronic databases Portal BVS (Medline, IBECs and LILACS) and SciELO. **Selection criteria:** The selection of articles was carried out in Portuguese, English and Spanish published up to September 2016 without initial date limitation and whose approach to Mismatch Negativity was with the child population. **Results:** The search strategy resulted in the selection of 23 articles classified as original articles. The studies evidenced several applications of MMN in children, including autism spectrum disorder, auditory processing disorders, cleft lip and palate, prematurity, and language-specific disorder, being the majority of them in dyslexia. **Conclusion:** Despite the great variability involved in the measures of MMN, there is a wide clinical applicability of this electrophysiological potential in the infant population.

**Keywords:** Evoked potentials, Auditory; Electrophysiology; Hearing; Child; Review

### RESUMO

**Introdução:** *Mismatch Negativity* (MMN) é um potencial eletrofisiológico que mede a habilidade do cérebro em discriminar sons, independente da capacidade atencional e comportamental. Por ser uma medida objetiva e de fácil utilização, torna-se promissora no estudo da investigação do processamento auditivo em crianças. **Objetivo:** Verificar a aplicabilidade do *Mismatch Negativity* na população infantil. **Estratégia de pesquisa:** Conduziu-se uma busca nos meses de agosto e setembro de 2016, usando os descritores *Evoked Potentials*, *Auditory AND Children*, *Event-related Potential AND Children* e *Electrophysiology AND Children*, nas bases de dados Portal BVS (MEDLINE, IBECs e LILACS) e SciELO. **Crerios de seleço:** Foram selecionados artigos em português, inglês e espanhol, publicados até setembro de 2016, sem limitação de data inicial, cuja abordagem do *Mismatch Negativity* fosse com a população infantil. **Resultados:** A estratégia de busca resultou na seleção de 23 artigos, classificados como artigos originais. Os estudos evidenciaram diversas aplicabilidades do MMN em crianças, incluindo transtorno do espectro autista, transtornos do processamento auditivo, fissura labiopalatina, prematuridade e distúrbio específico de linguagem, sendo a maioria em dislexia. **Conclusão:** Apesar da grande variabilidade envolvida nas medidas de realização do MMN, existe uma ampla aplicabilidade clínica desse potencial eletrofisiológico na população infantil.

**Palavras-chave:** Potenciais evocados auditivos; Eletrofisiologia; Audição; Criança; Revisão

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**Conflict of interests:** No

**Authors' contribution:** DAF and CDB analysis of the results, writing and review of the article; PS design and study design, study orientation, analysis of the results and article review; SSC design and study design, study orientation and article review.

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## INTRODUCTION

The integrity of the auditory system is vital for the development of speech, language and learning. Changes in any portion of the auditory pathway prevent the development of these abilities from occurring fully<sup>(1)</sup>.

Therefore, it is recommended that, in order to obtain an audiological diagnosis with more accuracy, objective and subjective assessment methods should be associated<sup>(2)</sup>. It is also important that tests capable of investigating auditory processing be incorporated into clinical practice<sup>(1)</sup> and, according to the American Speech-Language-Hearing Association (ASHA), it is recommended to use the electrophysiological evaluation for the Study of auditory abilities<sup>(3)</sup>.

Mismatch Negativity (MMN) is a long-latency auditory evoked potential that objectively portrays an electrical brain response in processing skills, sound discrimination, auditory memory<sup>(4,5,6)</sup>, and involuntary attention<sup>(7)</sup>. This potential has as main generator the auditory cortex and receives contributions from the frontal cortex, thalamus and hippocampus<sup>(8)</sup>. It is a cerebral automatic response, promoted by any discriminable change in some repetitive aspect of auditory stimulation<sup>(6,9,10,11)</sup>, indicating a mismatch between the new sensory input, in relation to a stored standard stimulus. In the short-term auditory sensorial memory<sup>(1,6,12)</sup>.

MMN is obtained by subtracting the response evoked by the rare stimulus in relation to the standard stimulus presented<sup>(4,9,10)</sup>, and the result appears as a wave with negativity<sup>(6,9)</sup>. The most commonly performed analysis occurs through the observation of wave latency and amplitude. When latencies increase or decrease in amplitudes, clinical and subclinical changes are objectively evidenced<sup>(2)</sup>. Latency informs the course time of processing activity, while wave amplitude demonstrates the extent of neural allocation involved in the cognitive processes of potentials<sup>(10)</sup>. MMN is a procedure that has a good correlation with the results found in subjective evaluations that, similarly, analyzed the ability of auditory discrimination<sup>(6,13)</sup>. Its main advantage, compared to other exams, is that the wave appears independently of the attention of the individual to the presented sound stimuli<sup>(1,4,6,7,10,14)</sup>, that is, it can be registered without the influence of the attention of the subject and without requiring tasks, making it particularly suitable for clinical studies in evaluating the child population<sup>(4,11)</sup>. Studies have shown that MMN can be a very useful evaluative means for recognizing changes in language<sup>(4,9)</sup> in children due to the possibility of assessing auditory processing deficit at an early age<sup>(9,13,15)</sup>. Capable of analyzing neurophysiological plasticity<sup>(13)</sup>. However, nowadays, it is observed that other aspects can also be investigated through the realization of MMN in this population.

MMN is important because it contributes to the investigation of disorders, mainly regarding the ability of auditory

discrimination. Thus, it is fundamental to recognize its diverse applicability and uses in the child population by health professionals, especially in the areas of speech therapy, neurology and otorhinolaryngology.

## OBJECTIVE

The objective of this systematic review was to verify the applicability of Mismatch Negativity in the infantile population.

## RESEARCH STRATEGY

As a guiding question, the following question was asked: "What is there in the scientific literature on MMN in children?"

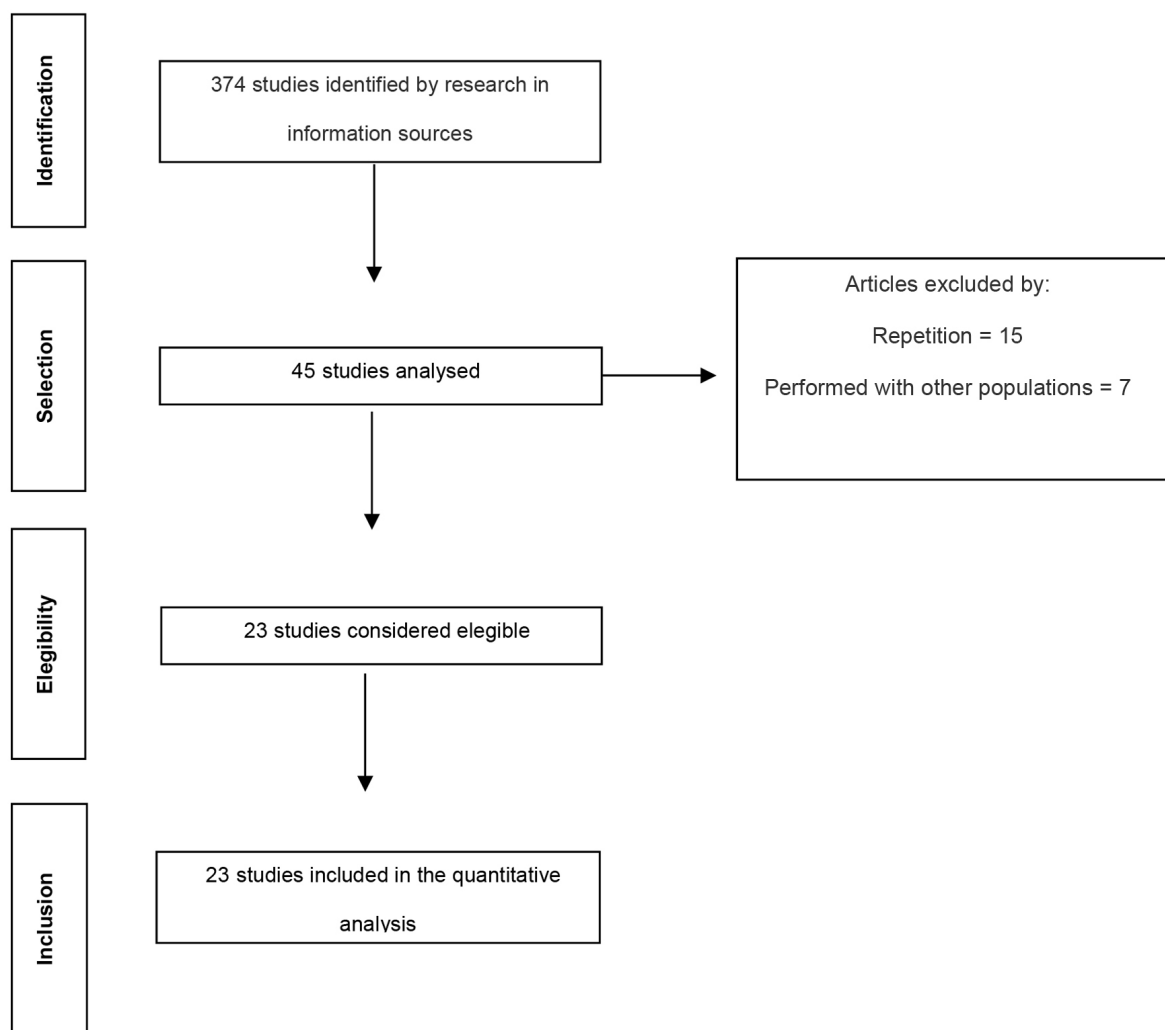
In order to obtain answers to this question, bibliographical researches were carried out between August and September of 2016, in the electronic databases VHL Portal (MEDLINE, IBECs and LILACS) and SciELO, aiming to carry out a systematic review of literature on a broad basis. The research included studies published until September of the year 2016, without limitation of starting date.

The selected descriptors were searched in the Medical Subject Headings (MeSH), so all terms were accessed in English only. No additional terms were used. A specific search strategy was developed, using the AND operator and the search refiner, with the limiting word Children, using the descriptors in pairs: Evoked Potentials, Auditory AND Children, Event-related Potential AND Children and Electrophysiology AND Children, aiming at identifying studies performed through the MMN in children. In this review, the words "Mismatch" and "Negativity" were not used because they are not considered descriptors in the English-language medical metadata system - MeSH.

## SELECTION CRITERIA

For the selection and evaluation of scientific studies, the following inclusion criteria were established: publications up to September 2016, original studies (case-control studies, cohort studies and controlled clinical trials) involving humans, with the objective of evaluating The Mismatch Negativity (MMN) in children, and studies published in English, Portuguese and Spanish. It was established, as a search limit, child, pre-school child and infant / newborn. Children were considered as children up to 12 years of age, according to the Statute of the Child and Adolescent (ECA)<sup>(16)</sup>. We excluded from the analysis studies in subjects older than 12 years, studies that did not use the MMN procedure, as well as publications that were about bibliographic review, letters to the editor, case studies and studies that were not directly linked to the topic.

The selection process of the studies included in this systematic review, analyzed by the Recommendation Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement<sup>(17)</sup>, is explained in Figure 1.



**Figure 1.** Synthesis of the process of obtaining the articles selected for the systematic literature review

## DATA ANALYSIS

After filtering by publication language, type of study and specific population, all the titles and abstracts of the articles were evaluated by two researchers. After the initial screening, the articles that fit the previously established selection criteria were read entirely.

For the analysis of the selected articles, the protocol based on the checklist of the international scale PEDro<sup>(18)</sup>, translated into Portuguese language, was applied to evaluate the methodological quality of the scientific studies. All selected articles presented information on study design, eligibility criteria, number of participants, descriptive data (sex, age), method of application of the procedure and presentation of results in MMN in the study population, through quantitative data and statistical analysis. The results of the analyzes were compared amongst three evaluators and the classification of the criteria was re-evaluated in a consensus meeting to verify the divergences. After that, it was performed the retrieval of the articles in full text.

## RESULTS

As an initial search result, 374 articles were identified, of which 45 were previously selected, according to the theme MMN in children. In the SciELO database, 3 articles were verified and, in the VHL database, 42. However, 15 articles were excluded because they were repeated and 7 because they were also evaluating adolescents. In total, 23 articles<sup>(4,12,19-39)</sup> were considered relevant and met the criteria proposed for the sample of this work.

From the analysis of the publications, it was verified that the studies had different objectives and methodologies. The main data of each article, such as authors, year of publication, place of publication, objective, population, sample, age and parameters of the MMN are described in detail in Chart 1.

The articles selected for this systematic review were mostly published between the years 2011 and 2015. The oldest publication was from 1997<sup>(39)</sup> and the most recent one from 2015<sup>(4)</sup>. Regarding the language of publication, it was verified that 3 articles were published in Portuguese. The other studies

**Chart 1.** Characteristics of included studies

Author (year)	Place of publication	Objective	Population	Sample	Age	Parameters of MMN
Romero et al. (2013) <sup>(19)</sup>	Brazil	To compare the findings of long-latency auditory evoked potential in children with and without ADHD.	Children with and without ADHD.	30 children 15 - TDAH 15 – without TDAH	8 to 12	Tone burst frequency and duration.
Soares et al. (2011) <sup>(12)</sup>	Brazil	To characterize the PAC and the PEALL in children with reading and writing disorders.	Children with reading and writing impairment.	12 children	8 to 12	Tone burst frequency.
Rocha-Muniz et al. (2015) <sup>(4)</sup>	Brazil	To investigate the discrimination of complex acoustic signals (speech) in the auditory system, through MMN, in children with specific language disorder (SLD), compared with auditory processing disorder (TPA) and typical developmental (TD).	Children with typical development, auditory processing disorders and specific language disorder.	75 children 25 - DEL 25 - TPA 25 - DT	6 and 12	Speech acoustic stimulus / ba / e / da /.
Zaric et al. (2014) <sup>(20)</sup>	Netherlands	To test the MMN relationship with individual differences in reading fluency in children with and without dyslexia.	Children with typical development and children with dyslexia.	61 children 41 - dyslexia 20 - DT	9	Speech acoustic stimulus of the vowels / a / and / or /.
Haapala et al. (2014) <sup>(21)</sup>	Finland	To evaluate the association between repetitive otitis media and atypical cortical neural coding, as well as pre-attentional attention in 2-year-old children.	Children with recurrent otitis media and typical development.	39 children 20 - with otitis média 19 – DT	22 to 26 months old	Speech acoustic stimulus / ke / e / pi /.
Koravand et al. (2013) <sup>(22)</sup>	Canada	To investigate the electrophysiological responses in children with hearing loss.	Children with normal hearing thresholds, children with hearing loss, and children with central auditory processing disorders.	40 children 16- norma hearing 12 - hearing loss 12 - PAC	9 to 12	Tone burst and speech / ba / e / acoustic stimulus.
Zuijen et al. (2013) <sup>(23)</sup>	Netherland	To investigate the auditory processing of syllables / bak / e / dak / in children at risk of dyslexia and typical development.	Children at risk of dyslexia and with typical development.	38 children 26 - dyslexia risc 12 - DT	2 months old	Speech acoustic stimulus / bak / e / dak /.
Zhang et al. (2012) <sup>(24)</sup>	China	To investigate the occurrence of categorical perception deficit in lexical mandarin tones in Chinese children with dyslexia.	Children with dyslexia and with typical development.	36 children 18 - dyslexia 18 - DT	average 10	Speech acoustic stimulus / pa / with frequency difference.
Noordenbos et al. (2012) <sup>(25)</sup>	Netherland	To verify the speech sound discrimination, through the MMN, in children at risk for dyslexia.	Children at risk for dyslexia and typical development.	61 children 31 – with risc 30 -DT	6	Speech acoustic stimulus / ba / e / da /.
Chobert et al. (2012) <sup>(26)</sup>	France	To examine the pre-attentional processing of syllables in children with and without dyslexia.	Children with and without dyslexia.	48 children 24 - dyslexia 24 – without dyslexia	9 to 11	Speech / ba / acoustic stimulus with varying duration.
Yang et al. (2011) <sup>(27)</sup>	China	To explore information about the central auditory system in infants with cleft lip and / or palate, through analysis of auditory evoked potentials.	Children with cleft lip and / or palate and normal children.	68 children 34 – with fissure 34 - children without fissure	6 to 24 months old	Tone burst with frequency variation.

**Chart 1.** Characteristics of included studies (cont.)

Author (year)	Place of publication	Objective	Population	Sample	Age	Parameters of MMN
Huottilainen et al. (2011) <sup>(28)</sup>	Finland	To verify the effectiveness of the Audilex dyslexia program in the cognition of underweight children.	Children of extreme low weight.	83 children	6	Tone burst with frequency variation.
Gomot et al. (2011) <sup>(29)</sup>	France	To examine hearing screening in children with autism spectrum disorders. To analyze the event-related potentials in early-grade children.	Children with autism and children with typical development.	54 children 27 - autism 27 - DT	5 to 11	Tone burst with frequency variation.
Ojima et al. (2011) <sup>(30)</sup>	France	To analyze auditory, non-linguistic processing in children with stuttering.	Two groups of normal children of different ages.	80 children 40 children in each group	6 to 11	Stimulating speech with words.
Kaganovich et al. (2010) <sup>(31)</sup>	USA	To verify association between absolute duration of similar vocal stimuli and processing difficulties in children with SLE.	Children with and without stuttering.	36 children 18 - stuttering 18 - without stuttering	4 e 5	Tone burst with frequency variation.
Datta et al. (2010) <sup>(32)</sup>	USA	To Investigate the relationship between MMN and behavioral tasks and investigate the influence of dyslexia training programs.	Children with a specific language disorder and with typical language development. Children with dyslexia and normal children.	18 children 9 - DEL 9 - DT	8 to 10	Speech acoustic stimulus / i / and / and /.
Paul et al. (2006) <sup>(33)</sup>	Germany	To evaluate the linguistic and social processing of pre-school children with autism spectrum disorder.	Children with autism and typical development.	79 children 58 - dyslexia 21 - normal	9	Acoustic stimulus / ba / e / da /. Acoustic stimulus / ba / e / wa /.
Kul et al. (2005) <sup>(34)</sup>	USA	To verify the influence of depression on auditory memory and attention, through the potentials related to events.	Children with depression who have memory deficit and concentration and control group.	58 children 29 - autism 29 - DT	1 to 5	Stimulation / ka / e / ta /.
Lepstö et al. (2004) <sup>(35)</sup>	Finland	To check the naming ability and auditory discrimination for speech sounds through the MMN.	Premature underweight children and control group children.	20 children 10 - depressive 10 - GC	10 to 12	Acoustic stimulus / taa / / ta / / kaa /.
Jansson-Verkasalo et al. (2003) <sup>(36)</sup>	Finland	To investigate the characteristics of the electrophysiological responses of MMN in socially isolated children and sociable children.	Socially isolated children and control group.	24 children 12 - premature 12 - GC	4	Tone burst frequency.
Bar-Haim et al. (2003) <sup>(37)</sup>	Israel	To study event-related potentials in children with cleft lip and palate.	Children with cleft lip and palate and healthy children.	45 children 23 - socially isolated 22 - GC	7 to 12	Tone burst frequency.
Ceponiene et al. (2002) <sup>(38)</sup>	Finland	To compare the results of MMN in children with aphasia and children with typical language development.	Children with aphasia and control group.	110 children 78 - fissure 32 - healthy	8	Tone burst frequency.
Holopainen et al. (1997) <sup>(39)</sup>	Finland	To compare the findings of long-latency auditory evoked potential in children with and without ADHD.	Children with and without ADHD.	24 children 10 - aphasia 14 - GC	3 to 7	Tone burst frequency and duration.

**Subtitle:** ADHD = Attention Deficit Hyperactivity Disorder; PAC = Central Auditory Processing; PEALL = Long Latency Auditory Evoked Potential; DEL = Specific Language Disturbance; TPA = Auditory Processing Disorder; DT = Typical Development; GC = Control Group; MMN = Mismatch Negativity



were written in the English language and no studies were written in Spanish. Regarding the place of publication, most articles, totaling 6<sup>(21,28,35,36,38,39)</sup>, were developed in Finland. Three articles were written in Brazil<sup>(4,12,19)</sup>, 3 in the Netherlands<sup>(20,23,25)</sup>, 3 in the United States<sup>(31,32,34)</sup> and 3 in France<sup>(26,29,30)</sup>. Studies have also been found in China<sup>(24,27)</sup>, Germany<sup>(33)</sup>, Canada<sup>(22)</sup> and Israel<sup>(37)</sup>.

There was great variation in the size of the sample, from surveys with only 12 subjects<sup>(12)</sup> to surveys that included 110 individuals<sup>(38)</sup>. The participants' ages ranged from 2 months<sup>(23)</sup> to 12 years of age<sup>(4,12,19,22,35,37)</sup>.

Regarding the parameters used to perform the MMN, most of the research used the speech stimulus<sup>(4,20-26,30,32-36)</sup> and other studies opted to perform the MMN with tone burst stimulus<sup>(12,19,22,27-29,31,37-39)</sup>. Regarding the tone burst stimulus, it was verified that some studies evaluated with frequency variation<sup>(12,27-29,31,37-39)</sup> and 1, by duration and frequency<sup>(19)</sup>.

Only one article<sup>(30)</sup> evaluated children without auditory complaints and without communication disorders, neurological or genetic alterations. The other articles included in this study investigated MMN responses in specific samples in the child population: children with reading and writing impairment<sup>(12)</sup>, attention deficit hyperactivity disorder (ADHD)<sup>(19)</sup>, language specific disorder (ADL)<sup>(4,32)</sup>, auditory processing disorders<sup>(4,22)</sup>, dyslexia, or presenting a risk factor for that<sup>(20,23-26,28,33)</sup>, repetitive otitis media<sup>(21)</sup>, autism<sup>(29,34)</sup>, stuttering<sup>(31)</sup>, depressed children<sup>(35)</sup>, premature and low weight children<sup>(28,36)</sup>, children with cleft lip and / or palate<sup>(27,38)</sup>, socially isolated children<sup>(37)</sup>, children with hearing loss<sup>(22)</sup>, children with aphasia<sup>(39)</sup>. Considering that a great part of the studies sought to perform evaluation in individuals with peculiar characteristics, 20 of

them<sup>(4,19-27,29,31-39)</sup> also included, in their methodology, control groups, to compare the results found in these individuals. The applicability of MMN in the child population can be seen in Chart 2.

To verify the scientific evidence of the 23 studies, the PEDro<sup>(18)</sup> scale was used. The goal of the scale is to help researchers identify whether the clinical outcomes of the therapies applied meet the criteria. There are 11 items in the checklist that investigate internal validity, external validity, and results that can be interpreted statistically. The methodological classification evaluated by the PEDro scale<sup>(18)</sup> and the scoring of articles, in each item of the scale, are available in Chart 3.

## DISCUSSION

It is understood that electrophysiological measures are more sensitive, objective and less variable in the evaluation of neural disorders than traditional behavioral measures<sup>(40)</sup>. The scientific literature emphasized the importance of verifying the use of MMN in the infant population and the need to know its applications in clinical practice<sup>(12)</sup>. Authors reported that MMN can be used to objectively evaluate patients with difficulty or impairment in communication, auditory discrimination, difficulty to respond consistently to stimulation, and in non-collaborative individuals, in order to evaluate the discrimination of different acoustic stimuli<sup>(1,41)</sup>. This review confirms that described in the literature, when it certifies that MMN applications are broad and include children with reading and writing difficulties, AD, dyslexia, stuttering, autism spectrum disorder, ADHD, auditory processing disorder, repetitive otitis

**Chart 2.** Applicability of MMN in the child population

Applicability	Nº of studies	Authors and year
Dyslexia	4	Zaric et al. (2014) <sup>(20)</sup> ; Zhang et al. (2012) <sup>(24)</sup> ; Chobert et al. (2012) <sup>(26)</sup> ; Paul et al. (2006) <sup>(33)</sup>
Children at risk for developing dyslexia	3	Zuijen et al. (2013) <sup>(23)</sup> ; Noordenbos et al. (2012) <sup>(25)</sup> ; Huotilainen et al. (2011) <sup>(28)</sup>
Specific language disorder (DEL)	2	Rocha-Muniz et al. (2015) <sup>(4)</sup> ; Datta et al. (2010) <sup>(32)</sup>
Auditory processing disorders	2	Rocha-Muniz et al. (2015) <sup>(4)</sup> ; Koravand et al. (2013) <sup>(22)</sup>
Cleft lip and palate	2	Yang et al. (2012) <sup>(27)</sup> ; Ceponiene et al. (2002) <sup>(38)</sup>
Low extreme weight and prematurity	2	Huotilainen et al. (2011) <sup>(28)</sup> ; Jansson-Verkasalo et al. (2003) <sup>(36)</sup>
Autism Spectrum Disorder	2	Gomot et al. (2011) <sup>(29)</sup> ; Kuhl et al. (2005) <sup>(34)</sup>
Attention deficit hyperactivity disorder (ADHD)	1	Romero et al. (2013) <sup>(19)</sup>
Reading and writing changes	1	Soares et al. (2011) <sup>(12)</sup>
Otitis media of repetition	1	Haapala et al. (2013) <sup>(21)</sup>
Sensorineural hearing loss	1	Koravand et al. (2013) <sup>(22)</sup>
Stuttering	1	Kaganovich et al. (2010) <sup>(31)</sup>
Depression	1	Lepstö et al. (2004) <sup>(35)</sup>
Social isolation	1	Bar-Haim et al. (2003) <sup>(37)</sup>
Aphasia	1	Holopainen et al. (1997) <sup>(39)</sup>
Children with typical normal development	1	Ojima et al. (2011) <sup>(30)</sup>

**Chart 3.** Methodological classification assessed by PEDro scale

	External validity (Max = 1)	Internal validity (Max = 8)	Interpretable results (Max = 2)	Total score (Max = 11)
Rocha-Muniz et al. (2015) <sup>(4)</sup>	1	2	2	5
Zaric et al. (2014) <sup>(20)</sup>	1	2	2	5
Haapala et al. (2014) <sup>(21)</sup>	1	2	2	5
Romero et al. (2013) <sup>(19)</sup>	1	2	2	5
Koravand et al. (2013) <sup>(22)</sup>	1	2	2	5
Zuijen et al. (2013) <sup>(23)</sup>	1	2	2	5
Zhang et al. (2012) <sup>(24)</sup>	1	2	2	5
Noordenbos et al. (2012) <sup>(25)</sup>	1	2	2	5
Chobert et al. (2012) <sup>(26)</sup>	1	3	2	6
Soares et al. (2011) <sup>(12)</sup>	1	1	1	3
Yang et al. (2011) <sup>(27)</sup>	1	2	2	5
Huotilainen et al. (2011) <sup>(28)</sup>	1	2	2	5
Gomot et al. (2011) <sup>(29)</sup>	1	2	2	5
Ojima et al. (2011) <sup>(30)</sup>	1	2	2	5
Kaganovich et al. (2010) <sup>(31)</sup>	1	2	2	5
Datta et al. (2010) <sup>(32)</sup>	1	2	2	5
Paul et al. (2006) <sup>(33)</sup>	1	2	2	5
Kuhl et al. (2005) <sup>(34)</sup>	1	3	2	6
Lepstö et al. (2004) <sup>(35)</sup>	1	2	2	5
Jansson-Verkasalo et al. (2003) <sup>(36)</sup>	1	2	2	5
Bar-Haim et al. (2003) <sup>(37)</sup>	1	2	2	5
Ceponiene et al. (2002) <sup>(38)</sup>	1	2	2	5
Holopainen et al. (1997) <sup>(39)</sup>	1	2	2	5

media, depression, among others. Some limitations of this work can be pointed out, such as the methodological diversity of the articles, regarding the parameters used to perform the MMN and presentation of the results found, regarding the values of latency and amplitude, and there is no standardization for population. There is no consensus to date on the best protocol to be used and normality patterns in the child population still need to be specified<sup>(6,13)</sup>, due to the fact that there are several parameters used to investigate and evaluate the Potential MMN, depending on the characteristics of the study population and estimated objectives.

The literature has pointed out that, in recent years, national and international scientific production regarding auditory evoked potentials has evolved greatly and great effort has been dispensed among researchers in the field. However, its indication and application still requires a greater effort in the search of investigations adapted to our reality, for the indication and safe use of the electrophysiological methods in populations of the speech-language clinic<sup>(42)</sup>. It is worth noting that, although there are researches that deal with the evaluation of MMN in the child population, there are still few studies in Brazil, only three studies<sup>(4,12,19)</sup> were found in the databases consulted for this review. It is believed that more studies in Brazilian children

should be performed, since MMN may be an evaluation tool of great utility in the identification of language disorders<sup>(4,9)</sup>. Neurophysiological plasticity, in the same way, can be evaluated through this potential<sup>(13)</sup>. Auditory processing is sensitive to the negative influence of several factors, such as environmental conditions, socioeconomic conditions, language disorders (phonology, writing, stuttering), peripheral auditory (otitis media), chemical (metal mercury) and neurological disorders (dyslexia, ADHD)<sup>(43)</sup>. It was observed that most of the studies included in this review<sup>(20,24,26,33)</sup> sought to evaluate the responses of the MMN potential in children with dyslexia. Dyslexia is characterized by difficulty with correct reading fluency and the ability to decode and spell, which may result from a deficit in the phonological component of language<sup>(44)</sup>. There is considerable evidence indicating a relationship of dyslexia and poor performance in several central auditory tests<sup>(45)</sup>.

Therefore, it is evident that more research is needed in order to solidify and insert the MMN in clinical practice, in order to complement other evaluation methods already consolidated and used for evaluation and monitoring of treatment in individuals with altered auditory processing. Extreme prematurity and low weight are associated with several developmental disorders of the neonate, such as auditory alterations related to the peripheral



auditory system and also changes in central auditory processing. In the consulted literature, it was found that preterm children had worse performance in the auditory processing behavioral evaluation when compared with infants born at term<sup>(46)</sup>. It was also observed that MMN also reported changes, showing decreased amplitude in preterm groups, in relation to the term groups<sup>(36)</sup>.

Numerous researches has suggested the association of LED to auditory processing deficit. In the present review, two studies<sup>(4,32)</sup> evaluated MMN in children with this disorder. The literature has provided evidence that discrimination of auditory stimuli would be compromised in children with SLI<sup>(47)</sup>. Therefore, poor performance in auditory processing may affect abilities to discriminate speech sounds, which could consequently affect perception and speech production<sup>(48)</sup>, a fundamental aspect for the development of children's language. Studies with the use of MMN in children with cleft lip and palate<sup>(27,38)</sup> and with recurrent otitis media<sup>(21)</sup> were found, showing the importance of such investigation with the use of an objective method, since otitis media and conductive hearing loss are pathologies that frequently occur in this population, leading to an indicator of risk for changes in auditory processing, language, speech and learning<sup>(49)</sup>.

Studies involving other characteristics such as autistic spectrum disorder<sup>(21,34)</sup>, ADHD<sup>(19)</sup>, depression<sup>(35)</sup>, social isolation<sup>(37)</sup>, aphasia<sup>(39)</sup> and stuttering<sup>(31)</sup> found in this review, evidenced the variety of applications with the use of MMN in children, not only in auditory issues and auditory processing, and this procedure is therefore capable of promoting greater knowledge and diagnostic accuracy in several areas of clinical practice. By evaluating the PEDro scale<sup>(18)</sup>, it was observed that few articles met the checklist criteria, mainly regarding items of internal validity. Thus, the overall score of the studies was quite low, because the research did not blindly evaluate, neither had secret allocation of subjects nor the random distribution of the groups. Despite the reported limitations, it was possible to reach the objective of this study, that is, to know the different applications of MMN in the child population.

## CONCLUSION

In spite of the great variability involved in the measurements of MMN and the limitations to the generalization of the data found, there is a wide possibility of clinical use of this auditory evoked potential in the children population, especially regarding aspects of oral and written language.

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