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Artículo Original

Avaliação eletrofisiológica da audição em crianças com perturbação do espetro do autismo

Auditory Brainstem Evoked Response in Children with Autism Spectrum Disorder

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Resumo

Objetivos: Descrever e caracterizar os achados das avaliações eletrofisiológicas da audição em crianças com perturbação do espetro do autismo, comparando-os com os de crianças com desenvolvimento adequado, dentro da mesma faixa etária.

Métodos: Analisaram-se os potenciais evocados auditivos do tronco cerebral(PEATC) (através do Vivosonic Integrity 5.2®) de 46 crianças (92 ouvidos) com limiares auditivos normais, divididas em dois grupos: um com 23 crianças com perturbação do espetro do autismo e um grupo controlo com 23 crianças com desenvolvimento adequado à idade. As latências absolutas das ondas I, III, V e as latências interpicos I-III, III-V e I-V foram analisadas nos dois grupos através dos testes estatísticos t-Student e Fisher.

Resultados: O grupo da perturbação do espetro do autismo (3 sexo feminino e 20 sexo masculino, com idade média de 3,7 anos) apresentou um aumento da latência estatisticamente significativo para o interpico I -III (2,27±0,14 mseg vs 2,13±0,12 mseg;p<0,001),III-V (2,00±0,12 mseg vs 1,95±0,10 mseg;p=0,047) e I-V (4,27±0,16 mseg vs 4,09 ± 0,13 mseg;p<0.001) comparativamente ao grupo controlo (9 sexo feminino e 14 sexo masculino, com idade média de 3,7 anos). Verificou-se que a latência da onda I do grupo da perturbação do espetro do au-

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tismo foi significativamente menor (1,52±0,11 mseg vs 1,61±0,20mseg;p=0,004) à do grupo controlo.
Conclusões: Neste estudo, as crianças com perturbação do espetro do autismo apresentaram alterações estatisticamente significativas nos PEATC, compatíveis com disfunção do sistema nervoso auditivo central. Estes resultados sugerem um comprometimento da via auditiva no tronco cerebral em crianças com perturbação do espetro do autismo.

Palavras chave: potenciais evocados auditivos do tronco cerebral, perturbação do espetro do autismo, crianças

Abstract

Objectives: This study aims to describe and characterize the findings of electrophysiological hearing assessment in children with autism spectrum disorder and compare them with children with proper development, within the same age group.
Methods: The auditory brainstem evoked response of 46 children (92 ears) with normal hearing, divided in two groups (one group with 23 children diagnosed with autism spectrum disorder and a control group of 23 children with age proper development), were analyzed through Vivosonic Integrity 5.2®. The absolute latencies of waves I, III, V and interpeak latencies I-III, III-V and I-V were compared in both groups by the Student's t-test and Fisher test.
Results: Children on the autism spectrum disorder group (3 female and 20 male, mean age 3,7 years) had statistically significant increased latency on Interpeak I-III (2,27±0,14 msec vs 2,13±0,12 msec ; p <0.001) , III-V (2,00±0,12 msec vs 1,95±0,10 msec; p=0.047) and I-V (4,27±0,16 msec vs 4,09 ± 0,13 msec; p<0.001) compared to children in the control group (9 females and 14 males with a mean age of 3.7 years). It was found that the wave I latency in the autism spectrum disorder group was significantly lower (1,52±0,11 msec vs 1,61±0,20msec; p=0.004) than the control group.
Conclusions: In this study, children with autism spectrum disorder showed statistically significant changes in auditory evoked potentials, consistent with a dysfunction of the central auditory nervous system. These results suggest an impairment of the auditory pathway of the brainstem in children with autism spectrum disorder.

Keywords: auditory brainstem evoked response; autism spectrum disorder; children

Introduction

The autism spectrum disorder is a disturbance on the brain development of early onset with a strong genetic basis and marked heterogeneity and may present from mild symptoms to severe changes. It is characterized by a lack of communication and social interaction and repetitive behaviors and restricted interests [1].

There has been having an increase in the disease prevalence and a predominance in males in a ratio of 4:1. Suggested explanations for the apparently growing prevalence include increased awareness, broadening of diagnostic criteria, changes in definitions, and improved screening and identification by providers[2].

No single aetiology has been identified for this heterogeneous disorder. Studies suggest that it is a genetic

disorder probably multigene, which leads to morphological, volumetric and functional changes in the central nervous system. Exposure to environmental modifiers contribute to the great variability in phenotypic expression [3].

The disturbance of language and the learning disabilities are disorders associated with autism that lead parents, pediatricians or general physicians to reference these children to an otolaryngology consultation[4].

Generally, the main complaint of the parents is the delay of spoken language. There is also an inconsistency of responses to sounds because of a change in sensory processing causing atypical responses to different stimuli - hyper or hyporesponsive[5].

Thus, the auditory brainstem evoked response is often the only test that gives us some indication of the hearing status of these children, since we are dealing with children who do not cooperate, possibly due to a deficit of attention and cognitive dysfunction. Auditory brainstem evoked response is an electrophysiological measure with electrical potentials originating from the auditory nerve and brainstem nuclei in response to a sound stimulus. They are recorded in form of waves and observed in the first 10 milliseconds. This exam provides an objective measure of the integrity of the auditory system from the auditory nerve to the brainstem. It is an objective examination without the active participation of the patient[6-7].

There are no universal agreements with regard to abnormalities of the brain structure, and no biomarkers have been detected for confirmation of clinical diagnosis.

Some articles have been published on the influence of autism spectrum disorder on the results of auditory evoked potentials of the brainstem, however this still remains controversial[1,2,4-8], respecting to the increasing, maintenance or decreasing of latencies times in comparison to control groups.

This study aims to describe and characterize the findings of electrophysiological hearing assessment in children with autism spectrum disorder and compare them with children with proper development, within the same age group.

Material and Methods

A retrospective study was conducted in a Portuguese hospital´s ENT service. This is a retrospective observational study where the anonymity and confidentiality of data is preserved. The authors of the study had no interference with the patients or the treatments applied. This study analyzed 46 children aged from 2 up to 16 years, with normal hearing, divided into two groups: one control group of 23 children with proper age development (9 females and 14 males with a mean age of 3,7 years) and a study group with 23 children diagnosed with autism spectrum disorder (3 female and 20 male, mean age 3,7 years). The children in the study group were selected from a list of children diagnosed with autism spectrum disorder that are followed in development unit of a district hospital. It was defined as inclusion criteria: diagnosis of autism spectrum disorder according to Diagnostic and Statistical Manual of Mental Disorders 5th edition criteria (DSM-V), age over two years, normal hearing thresholds determined by using evoked potentials system, type A tympanogram and no other neurologic diseases. It was defined as exclusion criteria children under the age of 2 years, altered auditory thresholds, type B or C tympanogram and children with metabolic dis-

orders, chromosomal or neurological diseases.

The auditory brainstem evoked response of these 46 children (92 ears) were analyzed through Vivosonic Integrity 5.2® equipment, without the use of sedation. The acoustic click stimulus with alternating polarity presented monaurally by insert earphones at 80 dB nHL at a presentation rate of 37,7 stimuli per second and with duration of 0.1 ms (total of 2000 stimuli) was used for the BAEP.

The absolute latencies of waves I, III, V and the inter-wave intervals of I-III, III-V and I-V were examined at 80db HL according to normal standard values proposed by *the evoked potential user manual* presented in Table 1 and compared in both groups. Statistical values were expressed as mean ± standard deviation (SD). These results were analyzed statistically in SPSS using the Student's t-test and Fisher's exact test. A *p* value less than 0,05 was considered significant.

The result of auditory evoked potentials was considered abnormal when at least one ear present alteration in latencies analysis. It was conducted qualitative analysis of data by comparing the normal and abnormal inter-group results. For this, the Fisher´s exact test was used.

A quantitative analysis of data was also performed through the mean and standard deviation of the results for each auditory evoked potential for each group. The latencies average of each wave and interpeak between the two groups where compared and verified their significance levels. A level of significance of 0.05 was adopted and Student's t-test was used.

Table 1: BAEP latency and interpeak normal standards for individuals above 24 months of age proposed by the evoked potential user manual.

	Wave I	Wave III	Wave V	Interpeak I-III	Interpeak III-V	Interpeak I-V
Mean (ms)	1,54	3,69	5,54	2,14	1,86	4,00
Standard Deviation (ms)	0,11	0,10	0,19	0,23	0,14	0,20

Results

The study sample is composed of 46 children distributed into the control and study groups. The two groups have equal dimension with a similar age distribution among them. There is a male predominance of children in both groups. (Table 2)

No statistically significant difference was observed in the comparison between the right and left ears of the absolute latencies of waves I, III and V and interpeak I-III, V, and IV in both groups. Therefore, the right and left ears were grouped, in each group, and the mean values of latencies and interpeaks were compared. Analyzing the latencies of auditory brainstem evoked response in the two groups, the results showed a statistically significant difference between the mean latency values of waves I, V and the inter-wave intervals of I-III, III-V and I-V.

Table 2: Demographic features of the subjects.

	Study Group - ASD* (N=23)	**Control Group (N=23)**
Gender		
Male	20	14
Female	3	9
Age (mean±SD) (years)		
Mean±SD	3,7±1,9	3,7±1,7
Min	2	2
Max	16	13

*ASD – Autism Spectrum Disorder

Children on the study group (autism spectrum disorder) had statistically significant longer latency on inter -wave I-III (2,27±0,14 msec vs 2,13±0,12 msec ; p <0.001) , III-V (2,00±0,12 msec vs 1,95±0,10 msec; p=0.047) and I-V (4,27±0,16 msec vs 4,09 ± 0,13 msec; p<0.001) in comparison with those of the control group. It was found that the mean latency value of wave I in the study group was significantly lower (1,52±0,11 msec vs 1,61±0,20msec; p=0.004) than the control group - quantitative data analysis (Table 3).

Table 3: Between-groups comparison of BAEP latencies of waves I, III and V and interpeaks I-III, III-V and I-V (80db)

	Wave I (msec)	**Wave III (msec)**	**Wave V (msec)**	**Interpeak I -III (msec)**	**Interpeak III-V (msec)**	**Interpeak I -V (msec)**
Control Group (N=23)	1,61±0,20	3,75±0,19	5,71±0,19	2,13±0,12	1,95±0,10	4,09±0,13
Study Group – ASD (N=23)	1,52±0,11	3,79±0,17	5,79±0,18	2,27±0,14	2,00±0,12	4,27±0,16
p-value (Student's t-	**0,004**	0,325	**0,037**	**<0,001**	**0,047**	**<0,001**

The study group showed 73,9% of altered results in auditory brainstem evoked response - qualitative data analysis (Table 4).

Table 4: Distribution of occurrence of normal and abnormal results on BAEP in the control and study groups

		Control Group		Study Group - ASD		p-value (Fisher's exact test)
		n	%	n	%	
BAEP	Normal	23	100%	6	26,1%	<0,001
	Abnormal	0	0%	17	73,9%	

Discussion

Given the results, in this study, the latency time of wave V, interwave intervals I-III, III-V and I-V is increased in children with autism spectrum disorder, with statistical significance. Thus, the electrophysiological evaluation provides evidence that there is a delay in auditory processing on the brainstem level in children with autism spectrum disorder in relation to children with typical development (control group). Results from the later studies have found significantly longer wave V and/or wave I–V interpeak latencies, in children with autism relative to typically developing controls[1,8-10]. Prolongation of interwave III–V[1,9,10] and interwave I–III[8,10,11] latencies have also been observed in children with autism. These findings corroborate the results of this study in which autistic children had a significantly longer transmission time on brainstem when compared to children with typical development. This delay in conducting the auditory stimuli through the brainstem can be explained by different mechanisms: hypoplasia of some nuclei of the brainstem, neuronal immaturity and brain overgrowth during the first years of life that consequently will affect the length of the cochlear nerve and auditory pathways in the brainstem which leads to increase in absolute and interpeaks latencies in auditory brainstem evoked response[1,2].

Thus children with autism exhibit a decrease in nerve conduction velocity.

However, the literature reports contradictory results on the auditory brain response of autistic children, involving prolongations, shortenings and absence of abnormalities in neurotransmission of auditory information[7]. The results reported by Russo et al.[12], Coutinho et al. [4] and Courchesne et al.[13] who also performed the auditory brainstem evoked response in two autistic children, and obtained normal absolute latencies of waves I, III and V and normal interwave intervals. Tharpe et al.[14] studied the auditory characteristics of autistic children, and observed no difference between them and the control group in auditory brainstem, which is not in accordance with the findings of this study. This can be explained by smaller sample sizes used in these studies and by the inclusion of a higher proportion of individuals with milder forms of autism.

Regarding the wave I, and as novelty per the current literature, children with autism in this study had lower latency times compared to the control group which may be explained by the hypothesis of neuronal complexity[5]. This theory holds that children with autism have better connectivity in short local neural connections which can be a cause of hypersensitivity to sound, feature of autism, and a shorter latency of wave I.

Table 4 shows that the study group had 73,9% of altered results in auditory brainstem evoked response agreeing to the study that indicated brainstem dysfunction in autistic children[15]. Similar results to the present study were found by another in which more than half (58,4%) of autistic individuals with normal hearing showed alterations in auditory evoked potentials of the brainstem, among them the delay wave V and the extension of Interpeak I-V[9]. This alleged dysfunction in the brainstem, affecting the processing of sensory afferents through the auditory pathways, can be part of a generalized neurological dysfunction process that explains a change in the social, cognitive and language, which are part of the autistic behavior.
The limitations of the present study are: a sample size that was not widespread and the study group was not divided by severity levels for the disorder autism spectrum.

Conclusion

These results are consistent to those described in the literature regarding the increase in wave V latency time, Interpeak I-III, III-V and I-V.
Children with autism spectrum disorder, experience changes in auditory evoked potentials brainstem suggesting auditory pathway impairment in the brainstem, alteration in synchronism generation of neuroelectrical impulses and / or structural and / or functional changes that interfere with the transmission of auditory stimuli along hearing pathway.
A novel finding, not yet described in the literature before, is the decrease in wave I latency in children with autism spectrum disorder.
New studies to examine the amplitude of wave I should be performed. The finding of an increase in the wave I amplitude, together with the decrease in wave I latency time could justify hypersensitivity to sound, characteristic of children with this pathology.

Conflict of interests: We have no conflicts of interest.

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