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Original Research Article

BRAINSTEM AUDITORY EVOKED POTENTIALS IN DOWN'S SYNDROME PATIENTS WITH AGE MATCHED NORMAL CHILDREN-COMPARATIVE STUDY

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Abstract

Background: Down's Syndrome (DS) presents a genetic disorder with diverse implications, including auditory abnormalities. This study investigates Brainstem Auditory Evoked Potentials (BAEPs) in DS children compared to age-matched controls, aiming to elucidate auditory processing anomalies associated with the condition. **Material & Methods:** Conducted in the electro physiology laboratory of JIPMER, 40 subjects (20 DS, 20 controls) aged 2-10 years were assessed. BAEPs were recorded using an EP-EMG machine. Parameters, including peak latencies and interpeak latencies, were measured. Statistical analysis employed unpaired t-tests with significance set at $p < 0.05$. **Results:** The results indicate distinct auditory processing patterns in Down's Syndrome (DS) children. On the right side, DS subjects exhibited a significant prolongation of Wave II latency ($p=0.002$) and a reduction in Wave IV latency ($p=0.045$). The delayed Wave II suggests potential disruptions in the cochlear nucleus, while the shortened Wave IV implies alterations in brainstem length or conduction velocity. Notably, the left side showed no significant changes, highlighting asymmetry. These findings underscore the intricate auditory complexities in DS, emphasizing the vulnerability of specific cerebral regions and warranting targeted interventions for hearing impairments **Conclusion:** The study unveils distinctive BAEP patterns in DS, shedding light on auditory processing intricacies. Findings highlight the interplay between genetic factors and neural responses, offering insights for targeted interventions addressing hearing impairments in DS.

INTRODUCTION

Down's syndrome (DS), characterized by a genetic abnormality involving chromosome 21, is a prevalent genetic disorder with distinct dysmorphic features typically identified soon after birth. The primary chromosomal abnormalities associated with DS include non-disjunction (94%), translocation (3.5%), and mosaicism (2.5%).[1] This disorder is recognized as the leading cause of genetically inherited malformations in human beings.

Individuals with DS often exhibit a spectrum of somatic abnormalities, affecting the head and face, leading to conditions such as brachycephaly, microcephaly, sloping forehead, and flat occiput.[2] Beyond the physical characteristics, DS is also linked to various health issues, with a notably higher incidence of hearing problems observed in DS patients. Hearing loss in DS can manifest as either conductive or sensorineural, with conductive loss often associated with middle ear issues such as otitis media or glue ear, while sensorineural loss results from damage to the cochlear nerve.[3]

Given the substantial impact of DS on cognitive functions, including IQ and learning processes, understanding and addressing hearing impairments become crucial. Education and making DS individuals self-sufficient in daily activities are hindered primarily by hearing impairments. Consequently, this study focuses on investigating Brainstem Auditory Evoked Potentials (BAEP) in DS cases, an essential neurological parameter associated with DS, and comparing these findings with those from a control group of normal children.[4]

Hearing, being a complex process, involves the transduction of acoustic stimuli, transmission of neural impulses through the auditory nerve, and subsequent conscious perception in the brain.

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Research has established the link between hearing and language abilities, emphasizing the importance of addressing hearing issues, especially in individuals with DS, who are prone to higher prevalence of hearing and otological disorders.[5]

Previous studies have demonstrated significant relationships between hearing impairment and cognitive functions in individuals with DS, indicating the necessity of exploring auditory potentials, such as BAEP, as potential indicators.[6-8]

The current study seeks to contribute to this body of knowledge by specifically examining the latency values of peak III and interpeak latencies (I-III) in older children with DS, comparing them with an age-matched control group.

Moreover, the study aims to shed light on the gender-related differences observed in BAEP, building upon the findings of previous research that identified statistically significant variations in interpeak intervals III-V.[9,10] Understanding the intricacies of BAEP, a process involving distinct waveforms (I-V), and their latencies, provides valuable insights into the central nervous system's anatomical and functional aspects related to hearing in DS patients.

MATERIALS AND METHODS

Study Setting: This study was conducted in the electrophysiology laboratory of the Department of Physiology at Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER). The study received approval from the JIPMER Research Council and Ethics Committee before commencement.

Study Design and Study Period: A cross-sectional study design was employed, and the study was conducted over a specific period. The exact study duration should be stated explicitly.

Study Participants: Participants were recruited from the Pediatric Outpatient Department and the Anatomy Department of JIPMER. The inclusion criteria encompassed children aged 2-10 years with Down's syndrome (DS), exhibiting characteristic features such as flat face, upward and slanted palpebral fissures, epicanthic folds, simian crease, short broad hands, and varying degrees of mental and growth retardation. A control group comprised of age-matched normal children without DS features.

Inclusion and Exclusion Criteria: Inclusion criteria encompassed children meeting the specified age range with characteristic DS features. Exclusion criteria involved individuals outside the age range or those not meeting the DS feature criteria.

Sample Size: A total of 40 subjects participated, with 20 in the study group (DS children) and 20 in the control group (age-matched normal children). The subjects were evenly distributed by gender (25 male and 15 female). Participants were selected through a combination of convenience sampling from the Pediatric Outpatient Department and referrals from the Anatomy Department for cases of DS requiring karyotyping.

Data Collection: All participants cooperated during the electrodiagnostic procedures, and no complaints or hesitations were reported. The study ensured a comfortable environment for the subjects. The BAEP recordings revealed specific observations, with no significant changes noted in the latency of waves and interpeak latencies on the left side in DS children compared to controls. On the right side, there was a significant prolongation of wave II and wave IV in DS children compared to controls, with no significant change in interpeak latencies.

The study recorded Brainstem Auditory Evoked Potentials (BAEPs) and ensured impedance levels below 5 ohms. Recordings were performed using an EP-EMG machine (NIHON KOHDEN-NEUROPACK M). Participants were instructed to come with oil-free hair after shampooing for better recording. Electrodes (Ag-AgCl) filled with conducting jelly were affixed to the recording area, and electrodiagnostic tests were performed following standard procedures. BAEPs were recorded using a brief click stimulus with specified parameters. External auditory canal examination was conducted, and if earwax was present, it was removed. Electrodes were placed according to the 10-20 system, and the equipment settings were standardized. Waveforms were averaged from 2048 trials, and latencies (peak latencies) of waves I-V and interpeak latencies of I-III, III-V, I-V were measured.

Ethical Issues: The study adhered to ethical standards, obtaining approval from the JIPMER Research Council and Ethics Committee. Informed consent was obtained from the parents or legal guardians of all participants.

Data Analysis: Data analysis was performed using unpaired Student's t-test with SPSS software (version 25). A p-value of <0.05 was considered significant.

RESULTS

Table 1 provides the mean ± SEM values for the latency measurements (L-I, L-II, L-III, L-IV, and L-V waves) of Brainstem Auditory Evoked Potential (BAEP) on the left side in normal healthy children (control group; n=20) and children with Down's syndrome (study group; n=20). The latency values represent various auditory processing stages, including the cochlear nerve, cochlear nucleus, superior olivary nucleus, lateral lemniscus, and inferior colliculus. [Table 1]

Table 2 presents the mean ± SEM values for interpeak latency measurements (IPL I-III, IPL III-V, IPL I-V) of BAEP on the left side in normal healthy children (control group; n=20) and children with Down's syndrome (study group; n=20). These interpeak latencies offer insights into the timing of

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neural processing along the auditory pathway. [Table 2]

Table 3 displays the mean ± SEM values for the latency measurements (L-I, L-II, L-III, L-IV, and L-V waves) of BAEP on the right side in normal healthy children (control group; n=20) and children with Down's syndrome (study group; n=20). Notably, significant prolongations are observed in L-II and L-IV waves on the right side in children with Down's syndrome. [Table 3]

Table 4 showcases the mean ± SEM values for interpeak latency measurements (IPL I-III, IPL III-V, IPL I-V) of BAEP on the right side in normal healthy children (control group; n=20) and children with Down's syndrome (study group; n=20). No significant differences are observed in interpeak latencies on the right side between the two groups, indicating preserved neural timing in certain aspects of auditory processing. [Table 4]

Table 1: Comparison of BAEP on left side among study participants

Group	L-I (ms) Mean ± SEM	L-II (ms) Mean ± SEM	L-III (ms) Mean ± SEM	-IV (ms) Mean ± SEM	L-V (ms) Mean ± SEM
Control	1.46 ± 0.043	2.49 ± 0.055	3.56 ± 0.036	4.6 ± 0.048	5.29 ± 0.044
Down's Syndrome	1.48 ± 0.063	2.54 ± 0.071	3.58 ± 0.077	4.65 ± 0.087	5.36 ± 0.090

Note: SEM: standard error of mean; LI, LII, LIII, LIV, and LV: Latency of waves recorded from cochlear nerve, cochlear nucleus, superior olivary nucleus, lateral lemniscus, and inferior colliculus respectively.

Table 2: Comparison of Interpeak latencies

Group	IPLI-III (ms) Mean ± SEM	IPLIII-V (ms) Mean ± SEM	IPLI-V (ms) Mean ± SEM
Control	2.05 ± 0.06	1.73 ± 0.033	3.82 ± 0.054
Down's Syndrome	2.04 ± 0.06	1.79 ± 0.051	3.83 ± 0.083

Note: SEM: standard error of mean.

Table 3: Comparison of BAEP on right side among study participants

Group	Mean ± SEM	L-II (ms) Mean ± SEM	L-III (ms) Mean ± SEM	L-IV (ms) Mean ± SEM	L-V (ms) Mean ± SEM
Control	1.42 ± 0.047	2.43 ± 0.042	3.49 ± 0.027	4.64 ± 0.057	5.29 ± 0.051
Down's Syndrome	1.53 ± 0.038	2.63 ± 0.044*	3.51 ± 0.060	4.46 ± 0.062*	5.29 ± 0.062

Note: *Significant P value; SEM: standard error of mean; LI, LII, LIII, LIV, and LV: Latency of waves recorded from cochlear nerve, cochlear nucleus, superior olivary nucleus, lateral lemniscus, inferior colliculus respectively.

Table 4: Comparison of Interpeak latencies on right side of the study participants

Group	IPL (I-III) (ms) Mean ± SEM	IPL(III-V) (ms) Mean ± SEM	IPL (I-V) (ms) Mean ± SEM
Control	2.04 ± 0.037	3.832 ± 0.047	1.79 ± 0.044
Down's Syndrome	1.92 ± 0.080	3.78 ± 0.064	1.81 ± 0.065

Note: SEM: standard error of mean.

DISCUSSION

Down's Syndrome (DS) is acknowledged as the most prevalent genetic pattern of malformation in humans, with a range of incidence mechanisms. Non-disjunction during meiotic division, Robertsonian translocation, and mosaicism contribute to 94%, 3.5%, and 2.5% of DS cases, respectively.[1] Ongoing research is unveiling the critical region on chromosome 21 (20-40 genes) responsible for DS, with genes like DSCR1 in region 21q22.1-q22.2 identified as potential contributors to the characteristic phenotype, including mental retardation (MR), facial features, hand anomalies, and congenital heart defects.[2]

Morphological alterations in individuals with DS encompass abnormalities in brain structure, including brachycephaly, abnormal convolutions and fissure patterns, reduced frontal lobe volume, and shortening of various brain regions, such as the superior temporal gyrus, hippocampus, cerebellum, and brainstem.[10] The identification of the DSCR1 gene expressed in the brain and heart further emphasizes the intricate interplay between genetic factors and morphological characteristics in DS.

Historically, DS has been associated with hearing loss, prompting investigations into auditory function. Prior studies on Brainstem Auditory Evoked Potentials (BAEP) in DS patients have reported notable findings. Shortened latencies of waves III, V, and interpeak intervals III-V, I-V were observed, potentially attributed to the smaller brain size and simpler afferent auditory pathways in DS subjects.[9] Kakigi et al,[11] highlighted shorter latencies in DS patients, attributing them to a smaller brainstem or faster conduction velocity.

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However, contradictory findings, such as prolonged interpeak latency IV-V and smaller wave V, suggest physiological dysfunctions in specific brainstem regions.

In the current study, BAEPs were assessed, focusing on latencies of waves I-V and interpeak latencies I-III, III-V, I-V. Significant prolongation of latency in Wave II and a reduction in latency for Wave IV on the right side were noted, while the left side exhibited no significant changes. The prolonged latency of Wave II, generated from the cochlear nucleus, might be linked to erosion of the bony modiolus due to secretory otitis media, leading to nerve fiber damage. Conversely, the reduced latency of Wave IV may be associated with a shorter brainstem length, resulting in faster conduction and shorter conduction duration. Notably, the significant changes observed on the right side may be indicative of altered cerebral dominance in individuals with DS.

The present findings contribute to the understanding of auditory processing in DS, shedding light on specific alterations in BAEPs. The intricate relationship between genetic factors, morphological characteristics, and auditory function underscores the multifaceted nature of DS. Further research exploring the genetic markers influencing auditory processing and the implications of brain morphological variations is warranted. Such investigations may pave the way for targeted interventions addressing hearing impairments and cognitive aspects in individuals with DS, potentially improving their overall quality of life.

While this study offers valuable insights into Brainstem Auditory Evoked Potentials (BAEPs) in Down's Syndrome (DS), several limitations should be acknowledged. The sample size is relatively small, limiting the generalizability of findings. Additionally, the study primarily focuses on auditory potentials, neglecting a comprehensive assessment of cognitive and neuroanatomical aspects. The heterogeneity within the DS population, encompassing varied genetic mechanisms, necessitates further research for a more nuanced understanding. Moreover, the cross-sectional design precludes establishing causal relationships. Future investigations with larger, diverse samples and comprehensive assessments are essential for a holistic exploration of DS characteristics.

CONCLUSION

This study delves into Brainstem Auditory Evoked Potentials (BAEPs) in Down's Syndrome (DS), unraveling distinctive patterns of auditory processing. The findings contribute to the intricate understanding of DS, emphasizing the interplay between genetic factors and neural responses. While limitations exist, the study provides a foundation for further research exploring targeted interventions addressing hearing impairments in DS. Comprehensive investigations integrating cognitive and neuroanatomical aspects are imperative for a holistic comprehension of DS characteristics and potential therapeutic interventions.

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