Original Article

Assessment of the Binaural Interaction Component of the Auditory Brain Stem Response in Children with Stuttering

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ABSTRACT

Introduction: This study aims to compare the binaural interaction component of auditory brainstem response (ABR-BIC) between children with stuttering and normal peers, and to correlate ABR-BIC parameters with stuttering severity instrument -3.

Patients and Methods: Twenty Stuttering children, diagnosed according to the criteria of stuttering severity instrument -3, and 20 normal age and gender matched peers were included. Click evoked ABRs were recorded through right monaural, left monaural and binaural stimulation at 80 dBnHL in both study groups. ABR-BIC was calculated as the difference between the binaurally evoked ABR response and the algebraic sum of the left and right monaural responses, and ABR-BIC parameters were measured.

Results: ABR-BIC latency and duration were significantly prolonged in the stuttering group compared to the control group, while ABR-BIC amplitude and area under the curve (AUC) were comparable. Also, ABR-BIC amplitude and AUC were significantly correlated with stuttering severity.

Conclusion: The results of this study point to impaired timing and reduced overall magnitude of binaural interaction at the brainstem level in stuttering children.

Key Words: Auditory brainstem response, binaural interaction component, stuttering.

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INTRODUCTION

Stuttering is developmental deficit which affects fluency of speech. It is characterized by interrupted flow of speech by prolongation of sounds; syllables; words or sentences, involuntary repetitions and involuntary silent blocks, during which one who stutters cannot produce sounds.[1] Functional stuttering develops in early childhood before puberty without any brain damage, any physical impairment or any other cause. It is first observed between ages 2 and 4 years following a period of fluent speech. Generally the incidence of stuttering is 1%, but it increases to about 4% in preschoolers and schoolers. In the sex difference, it is seems to be more common in male than females.[2]

Subjects with persistent developmental stuttering (PDS) have functional and structural abnormalities in the central nervous system, which include unusual brain activation in the auditory and motor regions, along with gyral and planum temporal anomalies.[3] Stuttering has also been associated with auditory cortical dysfunction in previous electrophysiological studies. Ismail *et al*.[4] observed that, when blocks and intraphonemic disruptions were the most prevalent core behaviours, obligatory potentials of children with stuttering severity Bloodstien IV revealed substantially delayed latencies and lower amplitudes. Furthermore, in stuttering children with associated behaviours (such as head nodding, eye blinking, feet tapping and flaring nostrils), P1 and N1 latencies were both prolonged. Jerônimo *et al*.[5] found that Mismatch Negativity and P300 had significantly longer latencies , besides higher amplitudes of the Mismatch Negativity, in stuttering children in both ears, and the stuttering group showed abnormal morphology of the waves.

Stuttering has also been described as a problem with timing.[6] and mistiming is not limited to the speech motor regions. Furthermore, findings from central auditory processing investigations in stuttering children[7] and adults[8] established that those who stutter are different from normal controls in some elements of auditory temporal information processing. Moreover, stuttering has been linked to defective auditory feedback[9, 10].

The auditory brainstem has been suggested as a possible source of central auditory deficiency in stutterers by several researchers using both electrophysiological

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and behavioural studies.[11-18] Electrophysiological tests like the auditory brainstem response (ABR) have been proven to be quite effective in detecting brainstem timing abnormalities.[19]

Binaural interaction is the mechanism by which signals detected amidst background noise are enhanced by the brainstem through detecting and calculating the little timing differences between binaural sounds.[20] This activity is recorded at three brainstem levels: the inferior colliculus, the nuclei of lateral leminiscus and the superior olivary complex.[21] Binaural interaction component (BIC) is a solid repeatable difference response which mirrors continuing binaural signal processing.[22] The BIC in ABR (ABR-BIC) represents the difference between the binaurally recorded ABRs and the algebraic sum of right and left monoaural responses, and it results from the amplitude difference at peaks IV and VI.[23] Typically, binaural interaction is assessed by means of behavioural tests, for instance: Masking Level Difference (MLD), auditory localization and lateralization, and binaural fusion tests. MLD has been previously assessed in stutterers, where some studies showed poorer MLDs in stuttering subjects[16,18], while others failed to show significant differences from norms.[24,25] Yet, behavioural tests are hard to carry out on young children with stuttering.[26] Consequently, using an objective measure, ABR-BIC, to evaluate binaural processing at brainstem level is advantageous.

PATIENTS AND METHODS:

1. Objectives:

To compare the ABR-BIC between children with stuttering and age matched normal peers, and to correlate the different parameters of BIC to the severity of stuttering.

Study design:

2. Subjects:

This study included 40 children, attending attending the Audio-vestibular medicine unit of Alexandria Main University Hospital. A written informed consent was obtained from the guardians of subjects who participated in the study.

They were divided into two groups:

1. Study group that consisted of 20 children diagnosed with stuttering disorder by speech therapists in in phoniatric department - Alexandria main university hospital.

2. Control group who consisted of 20 age and gender matched individuals.

The current study was done after approval of research ethics commission of of faculty of medicine of Alexandria University IRB NO: 00007555 –FWA NO: 00018699 which is guided by the statement of principles of the declaration of Helsinki and the Belmont Report. Informed consents were taken from all participants' guardians. All participants had normal middle ear function and normal peripheral hearing. Any child with deformities of the external ear or history of middle ear problems was excluded.

3. Methods:

3.1. History

Participants in the study gave a full history, including information on their medical history, prenatal; natal and postnatal history, family history, developmental milestones, history of middle ear abnormalities, and a review of any prior medical investigations. Assessment of the severity of children with stuttering was done using stuttering severity instrument score -3.[27]

3.2. Basic examination:

Otoscopy, tympanometry, and acoustic reflexes were performed on all individuals, as well as pure tone audiometry (PTA) (when applicable). The external auditory canal and tympanic membrane were examined using otoscopy. The 226 Hz tympanometer model was used to perform immitancemetry and ipsilateral acoustic reflex thresholds at 0.5, 1, 2, and 4 kHz. "Clarinet, Inventis, Padova - Italy". The audiometer (AD229E, Interacoustics, Assens, Denmark) was used to perform PTA in a double-walled sound-treated room. TDH39 headphones, calibrated according to ISO 389, were used to measure air-conduction thresholds. PTA was only done if the subject cooperated. In children who refused to cooperate with PTA, ABR thresholds were measured for each ear. Only children with hearing thresholds of 20 dBnHL or less in both ears were included study. The study only included children with normal PTA or ABR thresholds and normal middle ear functioning.

3.3. Click evoked ABR and ABR-BIC recording:

Interacoustics Eclipse EP 25 (Interacoustics, Assens, Denmark) was used to record ABR in a quiet dark room, while patients slept. Two channel recordings were acquired. Electrodes on each mastoid were used as inverting (Reference) electrodes, an electrode on the high forehead as the non-inverting (positive) electrode and another electrode on the low forehead as ground. The electrode sites were cleansed, and oil removed to ensure that the top layer of skin (epidermis) was clean to achieve low skin impedance. Disposable EEG electrodes were utilised. Impedances were tested after the electrodes were applied.

The individual electrode impedance was kept below 3 kΩ, and the inter-electrode impedance did not exceed 2 KΩ. The stimulus was a 100 µs broadband rarefaction click given at a presentation rate of 15.1/s with 1500 total sweeps and a 20-millisecond time window. Three M E-A-RTONE insert earphones were used to introduce the stimuli. A band-pass filter with a frequency range of 100–3000 Hz was applied to the recordings online. Traces more than 40 µV were rejected. ABR waves were obtained in all subjects by introducing clicks to the right ear, left ear, then binaurally at 80 dBnHL. For each of the three stimulation conditions, no less than three replicated ABR traces were averaged to provide individual grand average ABRs comprising a minimum of 4500 individual responses. The averaged data were filtered offline using a low pass filter with 2000 Hz cut-off frequency.

The individual waveform was extracted and changed to an XML-file using the Interacoustics Eclipse EP 25 clinical tool with research module license. The XML files were then uploaded to Microsoft Excel 2010 for further processing (Microsoft Corporation, Redmond, WA, USA). Microsoft Excel 2010 was then used to analyze the data.

The waveforms of the binaural interaction component (ABR-BIC) were obtained using this equation: [½(RR+LR-BR)+(LL+LR-BR)][28] where RR: Stimulation Right, recording Right and LR: Stimulation Left, recording Right and LL: Stimulation Left, recording Left and RL: Stimulation Right, recording Left and BR: Binaural Stimulation, recording Right and BL: Binaural Stimulation, recording Left.

Audiologists in the Audio Vestibular Medicine Unit of the Faculty of Medicine at the University of Alexandria performed all audiological assessments and data analysis. The binaural interaction component was calculated using Microsoft Excel 2010 addition and subtraction functions. The ABR-BIC peak was visually identified, and the amplitude was determined from the peak's highest positive point to the next trough. Duration was measured from the beginning of the wave (the point where the positive peak started from the baseline) to its end (the most negative part of the following trough) and the area under the curve (AUC) was measured by multiplying the amplitude of ABR-BIC by its duration.

STATISTICAL ANALYSIS:

The IBM SPSS software program version 20.0 was used to analyze the data. (IBM Corporation, Armonk, NY). The Kolmogorov-Smirnov test was employed to ensure that the sample distribution was normal. Chi-square test was used to compare gender between the control and study groups. Student T-test was used to compare age and latency of ABR peaks between both groups. Mann-Whitney test was used to compare the ABR-BIC parameters between the two groups. Spearman correlation was used to correlate the ABR-BIC parameters to the stuttering severity in the stuttering group. Significance of the obtained results was judged at the 5% level

RESULTS:

In terms of gender (χ^2 =1.129, *p=0.288*) and age (t=0.575, *p=0.569*), there was no statistically significant difference between stuttering children and controls. Boys represented 65% and girls represented 35% of the cases, while boys constituted 80% and girls constituted 20% in the control group. The age of the studied subjects ranged 3.10 – 10.60 years with a mean of 6.04 ± 2.50 years in the stuttering group and 3.0 – 11.50 years with a mean of 6.53 ± 2.94 years in the control group.

Between 0.25 and 8 kHz, pure tone thresholds were normal (15 dB HL or less), and equal in both ears (with in 5 dB), and tympanograms were normal in all subjects.

According to severity of stuttering, cases were divided into two groups (mild and moderate). Mild and moderate cases were equally represented where each category constituted 50% of the study population.

There was a significant delay of waves I, III and V latency (n = 20) in stuttering group when compared to the control group (Table 1)

ABR-BIC was recorded in all subjects in the control group and 17 out of 20 subjects (85%) in stutterers. ABR-BIC latency was significantly prolonged (U=27) and duration was significantly longer (U= 55). AUC was larger and ABR-BIC amplitude was smaller in stuttering children compared to the controls, but the differences were not significantly different. The ABR-BIC parameters of both groups are demonstrated in (Table 2). Figures 1, 2 and 3 show recordings of Binaural ABR, sum of monaural ABRs and ABR-BIC in one control and two cases. Case 1 (Figure 1) shows ABR-BIC of delayed latency and prolonged duration compared to the control (Figure 2). Case 2 shows no ABR-BIC (Figure 3).

Correlation of ABR-BIC parameters with stuttering severity instrument score -3 showed significant negative correlations with amplitude and AUC as shown in (Table 3).

Table 1: Comparison between the two studied groups according to Latency (ms) and interpeak latency (IPL) (ms)

	Cases (n = 20)	Control (n = 20)	t	*p*
Latency (ms)				
Wave I				
Min. – Max.	1.0 – 2.47	1.10 – 2.10	2.845*	0.008*
Mean ± SD.	1.79 ± 0.55	1.40 ± 0.26		
Wave III				
Min. – Max.	3.10 – 4.50	3.10 – 4.20	3.408*	0.002*
Mean ± SD.	3.99 ± 0.40	3.59 ± 0.34		
Wave V				
Min. – Max.	5.10 – 6.50	4.70 – 6.20	4.6347*	*<0.001**
Mean ± SD.	5.97 ± 0.32	5.40 ± 0.45		
IPL (ms)				
(I - III)				
Min. – Max.	1.60 – 3.20	1.80 – 2.80	0.619	0.541
Mean ± SD.	2.25 ± 0.54	2.16 ± 0.29		
(III -V)				
Min. – Max.	1.50 – 3.30	1.0 – 2.20	0.772	0.445
Mean ± SD.	1.90 ± 0.37	1.81 ± 0.33		
(I - V)				
Min. – Max.	3.40 – 5.20	3.50 – 4.80	1.598	0.120
Mean ± SD.	4.19 ± 0.57	3.95 ± 0.35		

t: Student t-test p: *p value* for comparing between the studied groups
*: Statistically significant at $p \leq 0.05$

Table 2: Comparison between the two studied groups according to ABR-BIC

ABR-BIC	Cases (n = 17)#	Control (n = 20)	U	*p*
Latency (ms)				
Min. – Max.	4.90 – 7.10	4.20 – 6.20	27.0*	*<0.001**
Median (IQR)	6.30 (6 – 6.4)	5.13 (5 – 5.3)		
Amplitude (μV)				
Min. – Max.	0.01 – 0.69	0.01 – 1.0	150.50	0.551
Median (IQR)	0.10 (0.05 – 0.29)	0.16 (0.08 – 0.27)		
Duration (ms)				
Min. – Max.	0.75 – 3.30	0.50 – 1.90	55.0*	*<0.001**
Median (IQR)	2.20 (1.40 – 2.62)	1 (0.67 – 1.25)		
AUC (ms.μV)				
Min – Max	0.03 – 2.13	0.01 – 1.80	144.50	0.437
Median (IQR)	0.29 (0.05 – 0.48)	0.13 (0.08 – 0.36)		

U: Mann Whitney test
p: p value for comparing between the studied groups
*: Statistically significant at $p \leq 0\ 05$
#:3 no waves cases

Table 3: Correlation between stuttering severity and ABR-BIC component for cases (n = 17)

ABR-BIC	Stuttering severity score	
	r_s	*p*
Latency (ms)	0.217	0.404
Amplitude (µV)	-0.597*	0.011*
Duration (ms)	-0.211	0.415
AUC (ms.µV)	-0.569*	0.017*

rs: Spearman coefficient
*: Statistically significant at $p \leq 0.05$

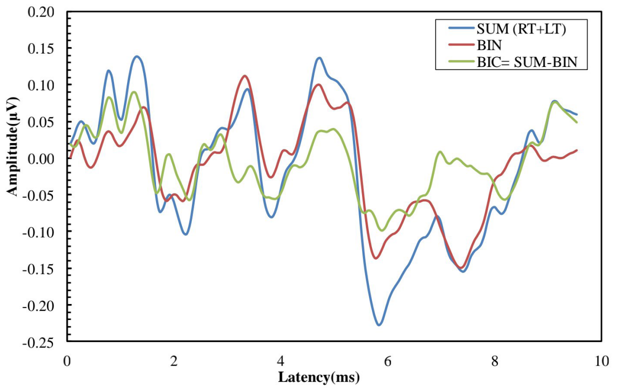

Fig. 1: Control: 7 years old male. ABR-BIC amplitude was 0.11 µV, latency was 5.05 ms, duration was 1.2 ms, AUC = 0.17 ms.µV). [Sum (RT+LT) = Sum of right and left monoaural responses, BIN=Binaural responses, ABR-BIC= Binaural Interaction Component]

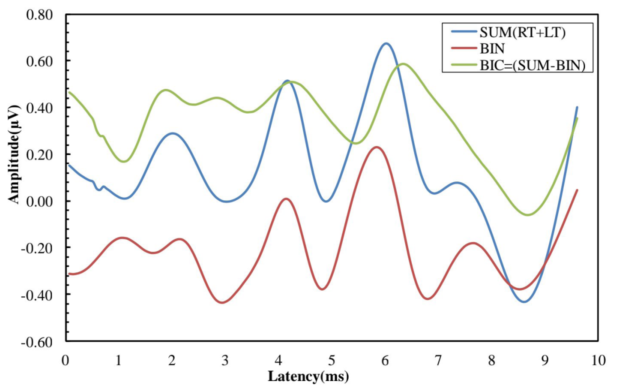

Fig. 2: Case 1: 4.4 year old male with mild stuttering severity (score: 20). ABR-BIC amplitude was 0.69 µV, latency was 6.4 ms, duration was 3.3 ms, AUC was 2.13 ms.µV). [Sum (RT+LT) = Sum of right and left monoaural responses, BIN=Binaural responses, ABR-BIC= Binaural Interaction Component]

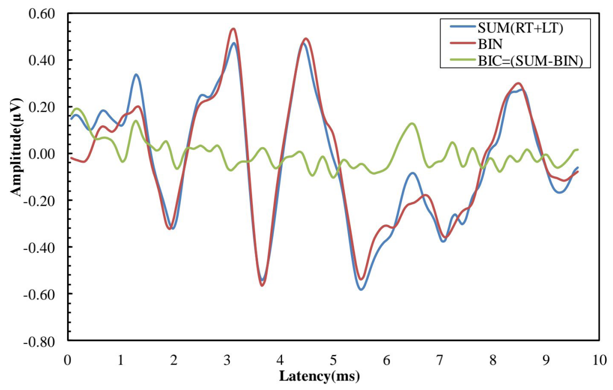

Fig. 3: Case 2: 4.5 years female with mild stuttering severity (score =20), she had no ABR-BIC at expected latency range. [Sum (RT+LT) = Sum of right and left monoaural responses, BIN=Binaural responses, ABR-BIC= Binaural Interaction Component]

DISCUSSION

The aim of this study was to compare the ABR-BIC between children with stuttering disorder and typically developing counterparts as an objective tool to evaluate the binaural processing at brainstem level.

Regarding gender and age, no significant difference was detected between children with stuttering and controls. Matching the age of the two study groups was crucial to avoid ABR age associated differences. In this study we avoided age as the confounding factor by precise matching of age between the two study groups. In stuttering children, boys represented 65 %, and girls represented 35 %. In normal children, boys constituted 80 % and girls constituted 20 %. In the current study, there was an almost two to one ratio of male subjects to females. The higher prevalence of the males among stutterers has been previously reported.[29]

In this study, there is a significant difference between cases and controls in absolute latencies of peaks I, III and V. The results of this study with ABR peak latencies are similar to the study of Goncalves *et al*.[30] who studied the ABR to clicks and recurring speech stimuli in normal children and those with phonological disorders. They reported that the absolute latencies of peaks I, III, and V were notably longer in the stutterers than in the controls. In opposition, other authors have reported normal latencies of click-evoked ABR in stuttering children.[31] The results of our study show that the brainstem auditory response to transient stimuli is less synchronous in stuttering subjects compared to norms. Some of the individual differences among studies may be attributed to different methodology and pathological diversity of stuttering.

Our results with ABR-BIC latency and duration show a considerably delayed latency and prolonged duration of the response in stutterers compared to normal children. The prolonged latency and duration of ABR-BIC may be due to impaired timing of transient stimuli as a part of prolonged monoaural ABR latencies (particularly wave V), a deficit in the binaural brainstem processing in stuttering children or both. Further studies are needed to elaborate this argument. Tahaei *et al*.[13] assessed speech evoked ABR in subjects with stuttering and found shallower V/A slopes, as well as delayed latencies of the onset and offset peaks, when compared with the control group. They postulated that this is linked to the temporal disorder in the auditory pathways, which leads to asynchronous propagation of auditory afferent information, thus, incompetent processing of transient speech stimuli such as stop consonants. In an investigation to uncover complexity differences between PDS and normal participants using the synthetic/da/stimulus, Mozaffarilegha *et al*.[12] applied the the Hurst exponent and fractal dimension to speech ABR signals. The linear time delay analysis revealed that, with the exception of wave V, the difference between normal and PDS participants was not significant. Additionally, Hurst exponent analysis revealed that the PDS and normal participants had a substantial group difference, and because the Hurst exponent is linked to the process's long-term memory, it is probable that memory changes in the speech ABR signal of stuttering subjects are lower than in normal population. In light of these findings, the authors suggested that stuttering is linked to a defect in speech encoding at the brainstem level, resulting in considerable deviations from norms. Another study by Mozaffarilegha *et al*.[11] observed that the visibility graph of speech ABR in PDS patients was more complex compared to normal subjects implying the existence of auditory cortical deficiency. Furthermore, the visibility graphs had a power-law topology and fractality, which is thought to be controlled by a mechanism linked to long-term memory of auditory system activity at the brainstem level.

Correlation between the stuttering severity, as measured by stuttering severity instrument score -3, showed a moderate negative correlation with ABR-BIC response amplitude and area under the curve, which suggests a link between reduced overall magnitude of the response in stutterers and the severity of their condition. Likewise, significant correlations were found between stuttering severity and the latencies of waves A and O of speech ABR.[13] Auditory temporal processing deficits have been strongly associated with the severity of stuttering.[7] Mismatch Negativity (MMN) amplitude, but not latency was strongly linked to the severity of stuttering.[32] Furthermore, binaural presentation of altered auditory feedback has been linked to diminished frequency of stuttering compared to monaural presentations to both right and left ears.[33] Conversely, two studies failed to find significant correlations of auditory processing[34], and latency and amplitude of auditory evoked magnetic fields with the severity of stuttering.[35]

Literature is contradictory whether the binaural interaction mechanism at the brainstem level is impaired in stutterers. MLD is well recognized as a behavioral test of brainstem binaural interaction. Kramer *et al.*[16] found that stutterers had significantly poorer MLDs in comparison to the non-stutterers. On the other hand, Liebetrau *et al*.[18] demonstrated that organic stutterers showed significantly poorer MLDs than norms, while functional stutterers performed comparable to controls. Also, Asal *et al*.[24] studied binaural central auditory processing in children who stutter using MLD, and found out they have intact brainstem binaural processing, and stutterers scored similar to the control group in their study. Rajab *et al*.[25] observed that the lower MLD scores in stutterers were not significantly different from controls. This controversy in the literature, and with the results of the current study, might be attributed to the following:

1. Different methodology: MLD is a behavioral test which uses a 500 Hz tone while ABR-BIC is an objective test which uses acoustic click: a broad-band stimulus.

2. Different age groups included in these studies, where some studies included adults , while other included school-aged children. In our study, a number of preschool children were also included. The underlying pathology of stuttering may differ as a function of age of the included subjects.

3. Stuttering itself is a symptom of a diverse spectrum of pathologies with similar clinical presentations, where different levels of the auditory pathway may be implicated

Our study has some limitations, which could be addressed in future research, which include investigating older age groups of study subjects such as school children and adults, covering a wider spectrum of stuttering severity, evaluating the influence of speech training on the ABR-BIC parameters. Moreover the sum of monoaural and binaural ABRs should be separately assessed to determine whether delayed ABR-BIC latency and prolonged duration are attributed to impaired timing of monoaural ABR responses, binaural processing deficits or both.

CONCLUSION

Stuttering children show considerably delayed latency and longer duration of ABR-BIC compared to fluent children. Moreover, there are significant negative associations between stuttering severity and the amplitude and AUC of ABR-BIC. This may point to impaired timing and reduced overall magnitude of binaural interaction at the brainstem level in this group.

CONFLICT OF INTEREST

There are no conflicts of interest.

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