




RESEARCH ARTICLE

Cortical auditory evoked potentials and hemispheric specialization of speech in individuals with learning disability and healthy controls: A preliminary study [version 1; peer review: 1 approved, 2 approved with reservations]

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Abstract

Background: Dichotic listening (DL) technique is a behavioral non-invasive tool which is used in studying hemispheric lateralization. Previous studies using behavioral DL have hypothesized that individuals with learning disabilities (LD) exhibit a lack of cortical specialization for processing speech stimulus. However, there is no event related potential (ERP) evidence, hence the main objective of the study is to explore hemispheric asymmetry using cortical auditory evoked potential (CAEPs) in normal hearing adults and also to compare the same in children with LD and healthy controls.

Methods: CAEPs were recorded in 16 normal hearing young adults, eight right-handed children with LD and their age matched controls. Two stop constants (/Pa/ – voiceless, bilabial, stop: /Ta/ - voiceless, alveolar, stop) were chosen for this experiment and presented in each ear and dichotically in two different orders (/pa-ta/, /ta-pa/). ERPs were processed using a standard pipeline, and electrodes readings over the left and right hemispheres were averaged to create left and right regions of interest (ROI). The CAEPs were analyzed for mean amplitude and peak latency of P1-N1-P2 components.




Results: The current study results suggest no statistically significant difference between the two stimulus in monaural condition and absence of order effect in dichotic condition. In healthy controls the CAEP latencies were shorter over the left hemisphere in both monaural and dichotic conditions in adults and control children. However, it was very evident that such a difference was lacking in children with LD.

Conclusions: Hemispheric asymmetry can be detected using CAEPs for speech stimulus. The measures are consistent and void of stimulus or order effect. Taken together, the findings of current study, both monaural and dichotic condition illustrates the hemispheric differences in processing speech stimuli in normal hearers. Absence of latency differences between hemispheres in children with LD indicate a lack of hemispheric asymmetry.

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Keywords

CAEPs, hemispheric asymmetry, dichotic listening, learning disability

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Introduction

The human brain is comprised of two hemispheres, and both hemispheres differ from each other in terms of anatomy as well as physiology. Among the two hemispheres, one is more active and demonstrates superior performance on specific tasks. This phenomenon is referred to as brain dominance or hemispheric asymmetry. This brain dominance seems to be related to the handedness of the person. In humans, brain dominance or asymmetry seems to be established early in fetal development. Dichotic listening (DL) is one of the conventional methods to study this cerebral dominance effect (Ahonniska *et al.*, 1993). In this test, two different auditory signals are presented to two ears independently, and the listeners are expected to recognize the signals presented to both ears. The DL test is sensitive to hemisphere differences to specific sounds (Brancucci *et al.*, 2008). The principle of this test is that speech is lateralized to the left hemisphere (Tervaniemi & Hugdahl, 2003), resulting in the individual preferring to repeat the stimulus presented to the right ear more often than the left ear. The vice versa is true when it comes to non-speech stimulus (Brancucci *et al.*, 2008). These effects are termed as right ear advantage (REA), and left ear advantage (LEA) respectively and highly correlates with the Wada-test (Hugdahl *et al.*, 1997). Since, it is a simple, effective and non-invasive equivalent of the Wada-test, it has been widely used in the assessment of various clinical populations. Therefore the DL technique has been used widely as a measure of cortical processing and auditory perception for several decades (Hugdahl *et al.*, 1997).

DL technique has been found to be useful in studying language lateralization in children with early focal brain damage (Brizzolara *et al.*, 2002; Carlsson *et al.*, 1992; Chilosi *et al.*, 2005; Isaacs *et al.*, 1996), aphasia (Bavosi & Rupp, 1984; Johnson *et al.*, 1977; Johnson *et al.*, 1978; Pettit & Noll, 1979; Selnes *et al.*, 1983), and stuttering (Brady & Berson, 1975; Blood & Blood, 1986; Curry & Gregory, 1969; Foundas *et al.*, 2004; Gruber & Powell, 1974; Robb *et al.*, 2013; Slorach & Noehr, 1973; Strub *et al.*, 1987). The DL test is particularly useful in the assessment of children with learning disability. The DL tests have been used to reveal cerebral dominance deficits (van den Noort *et al.*, 2008), subtypes of children with dyslexia (Cohen *et al.*, 1992), developmental changes in language lateralization (Porter & Berlin, 1975), and bilateral hemispheric processing deficits (Obrzut & Mahoney, 2011) in children with LD.

Traditionally, DL has been assessed using behavioral methods. However, electrophysiological methods, especially cortical auditory evoked potentials (CAEPs), would help in understanding the neurophysiology of dichotic listening. Since the left hemisphere is dominant for speech and language function, CAEPs in DL is evidenced by larger amplitudes and shorter latencies over the left hemisphere (Bayazit *et al.*, 2009; Eichele *et al.*, 2005; Friedrich *et al.*, 2017; Haaland, 1974; Morrell & Salamy, 1971). However, these studies have either focused on latency (Eichele *et al.*, 2005) or amplitude (Haaland, 1974; Morrell & Salamy, 1971), but not both. Hence, the complete cortical dynamics underlying processing is not yet known. Analyzing both these measures will provide information on the strength of cortical activation, as well as the efficiency of neural conduction.

Dichotic study involves the presentation of one stimulus to right ear and other stimulus to left ear. Previous studies have reported cortical changes using dichotic, but have not explored stimulus effect or order effect (Bayazit *et al.*, 2009; Eichele *et al.*, 2005; Friedrich *et al.*, 2017; Haaland, 1974; Morrell & Salamy, 1971). The physiological responses elicited using different stimulus may differentially influence evoked ERPs, since these are obligatory responses to external stimuli. It is important to rule out stimulus specific effects before commenting on cortical asymmetry using this paradigm. Hence, the current study aimed at studying the stimulus effect in monotic (/pa/ vs. /ta/) and order effect in dichotic condition (/pa-ta/ vs. /ta-pa/). The study also aimed at comparison of monaural vs. dichotic processing differences in the same individual. This will provide important insight on how cortical processing of dichotic listening differs from that of monaural listening.

Previous studies using behavioral DL have hypothesized that individuals with LD exhibit a lack of cortical specialization for processing speech stimulus. To date there is no literature evidence for this using ERPs. A handful of studies have utilized CAEPs to study DL in children with LD, and revealed a comparable amplitude between hemispheres indicating decreased cortical asymmetry for speech stimulus (Brunswick & Rippon, 1994). Hence studying cortical processing of dichotic listening using ERPs will further validate these findings. In this view, there is a definite need for a study to establish the monaural and dichotic auditory processing differences as reflected by CAEPs in healthy individuals and those with LD.

Methods

The study was carried out at the Department of Speech & Hearing, School of Allied Health Science, and Manipal. The study began on 1st August 2016 and continued till 20th August 2017. The study protocol was approved by Institutional Ethics Committee (IEC), Kasturba Hospital, Manipal (IEC 460/2016).

Participants

This study was a prospective observational study where 16 normal young adults (18–25 years), eight normal learning right-handed children (7–15 years) for the control group and eight right-handed individuals with LD (7–15 years) were recruited. Healthy volunteers were either students at the School of Allied Health Sciences, who were recruited through advertisement through notice board or members of the public who visited the department. They had the study explained to them and were recruited if interested in participating. All the Volunteers were provided with participant information sheet which had complete details of the study. Written informed consent was taken from all interested individuals prior to participation in the study.

All the participants were screened for the presence of hearing loss (Pure Tone Audiometry done using duly calibrated Mad-sen Astera (American National Standard Institute S3.43-1996) should be <15dBHL (decibels Hearing Level) for both air conduction and bone conduction tests, and middle ear dysfunction (Tymstar middle ear analyzer, Grason-Statler Inc., MN, USA). All the tests were carried out by investigators (audiologist) at Dept. of Speech and Hearing, School of Allied Health Sciences).

Individuals who were diagnosed with a learning disability at the Department of Psychology, SOAHS, Manipal University, Manipal and consented to participate in the study were included in the experimental group. Edinburgh's handedness inventory (Oldfield, 1971) was administered to the participants, and only right-handed individuals were selected for the study because handedness is considered as a major variable that affects cortical asymmetry. (Delorme & Makeig, 2004)

Stimulus preparation

Two speech sounds (/Pa/ – voiceless, bilabial, stop: /Ta/ - voiceless, alveolar, stop,), were selected as stimulus to elicit ERP. Syllables (/Pa/ and /Ta/) were used as a stimulus for both monaural and dichotic paradigms. Also, similar stimuli has been shown to be effective in eliciting LLR and used in studying cerebral asymmetry in the literature (Lawson & Gaillard, 1981). The above syllables were recorded using a standard microphone kept at a 6cm distance from the mouth (Extended data (Palaniswamy, 2018b)). A normal native Kannada speaker was asked to produce these two syllables with normal intensity and normal intonation. The dichotic stimulus was prepared using Adobe Audition version 1.0, where stimulus /pa/ was stored in the right channel and /ta/ was stored in the left channel to create a single /pa-ta/ dichotic stimuli, and vice-versa to create /ta-pa/ dichotic stimuli. Duration of the stimulus was trimmed so that both the stimulus had the same duration.

Stimulus presentation and LLR recording

All the measurements were carried out in an acoustically treated room. The 'SOUND' module of Stim system (Version 2) was used for stimulus presentation with inserts at an intensity of 70dB SPL. CEAPs were recorded using the 'Acquire' module of the SynAmps2 amplifier (Compumedics NeuroScan, Abbotsford, Australia). A 32 channel electrode cap used with combined mastoid as reference. Impedance at all electrode sites was maintained below 5k Ohms. Raw EEG recording were acquired with a bandpass filters set between 0 and 100Hz with a sampling rate of 1000/sec. The obtained EEGs were analyzed offline using a filter from 1 – 30 Hz, and artifact rejection was also be done offline (EEGLab version 13_6_5b (Delorme & Makeig, 2004)).

Conditions

The stimulus was presented in 3 conditions.

1. A monaural condition in which stimulus (/pa/ and /ta/) was presented to the right ear only
2. A monaural condition in which stimulus (/pa/ and /ta/) was presented to the left ear only.

In both, the monaural conditions patient will be asked to watch a silent movie and ignore the stimulus presented to the ear.

3. Dichotic passive attention condition in which the stimulus (/pa-ta/ and /ta-pa/) was presented to both ears simultaneously and the patient will be asked not to pay attention to the stimulus.

Stimulus effect and order effect

The current study used two stimuli (/pa/ and /ta/) to record CAEPs. In monaural condition, two stimuli were presented to each ear

one at a time to check whether the stimulus affects CAEPs. Similarly, in dichotic condition, /pa-/ta/ was presented to the right and left ear respectively, and the reverse of it, i.e., /ta-/pa/ was used to check if reversal of stimulus order had any effect on CAEPs. Thus a total of 6 conditions were obtained from a single participant.

Data analysis

Raw EEG data were imported to EEGLab version 13_6_5b (Delorme & Makeig, 2004), a free software commonly used for analyzing EEG/ERP signals offline, which runs on MATLAB (2010a). The following preprocessing steps were done serially on each data to obtain a final average waveform. After editing channel locations (BESA 4 shell dipfit spherical model) bad channels and bad blocks were visually inspected and interpolated using spherical interpolation method in the command line in MATLAB. The data was then subjected to high pass filtering with a cut-off frequency of 1kHz. Bin based epochs were extracted using ERPLAB version 6.14 (Luck, 2014) between -200 to 800ms time-locked to stimulus onset, and then were baseline corrected for the prestimulus duration (-200 to 0ms). Independent component analysis (ICA) was done to decompose multivariate ERP waveform into their subcomponent based on their source using the 'runica' command in EEGLAB, then analysed using MARA 1.1 (Multiple Artefact Rejection Algorithm) (Winkler *et al.*, 2011) which automatically removes the components with artifacts based on several parameters. Post artifact rejection, the waveforms were low pass filtered with a cutoff frequency of 30Hz and then rereferenced to common average. All the epochs were averaged in ERPLAB.

The region of interest (ROI)

A region of interest (ROI) is one of the prescribed methods of analyzing ERPs where few neighboring electrodes that represents a particular anatomical area for a specific purpose are selected for analysis rather than a single electrode. The basis of this type of analysis is mainly on certain assumptions. The first reason is to explore one's data. It is often useful to see the activity in areas of interest plotted for each condition or plotted against other variables. The second reason is to control Type I error by restricting the number of statistical tests to a few ROIs. The third reason is to limit testing to a specific brain region that is defined functionally by some information (Poldrack, 2007).

In the current study, two 2 ROIs with three electrodes in each hemisphere were selected, here in after synonymously referred to as right and left hemisphere electrodes. Left ROI was an average of 3 electrodes (C3, FC3, and CP3), and the right hemisphere ROI was an average of homologs of the these three electrodes (C4, FC4, CP4). For example, the latency of N1 component from C3, FC3, and CP3 are 108ms, 110ms, 112ms respectively; then the left hemispheric ROI is 110ms. The right and left hemispheric ROI were obtained for all the three conditions. Hence monaural right condition included monaural right ear right hemisphere electrodes (MonoR RH), and monaural right ear left hemisphere electrodes (MonoR LH). Monaural left conditions included monaural left ear right hemisphere (MonoL RH) electrodes, and monaural left ear left hemisphere electrodes (MonoL LH). Dichotic conditions included dichotic right hemisphere electrodes (DI RH) and dichotic left hemisphere electrodes (DI LH).

Grand mean average waveform across participants was used as a reference to decide the latency range of measurement. In the current study, for all the conditions across groups, P1 mean amplitude and peak latency was measured between 40 to 80 msec. Similarly, 90 to 140 msec, and 170 to 220 msec windows were used for N1 and P2 respectively. These mean amplitudes and peak latency measures for right and left ROIs were automatically measured using the measurement toolbox of ERPLAB for each participant and the output was written in .txt format then later exported to MS Excel 2016 and SPSS version 15 (SPSS Inc., Chicago)

Results

All the data were first tested for normality using Shapiro-Wilk's test, and the results showed that the latencies and amplitudes of all the components were normally distributed.

Since the use of two stimuli is inevitable in dichotic listening, it was a must to rule out any stimulus effect on CAEPs. In monaural condition, these two stimuli (/pa/ vs. /ta/) did not result in significant latency or amplitude difference in both right and left ear (Table 1). Similarly, in dichotic condition comparison of two stimuli in a different order (/pa-ta/ vs. /ta-pa/) also did not lead to any significant difference (Table 1) which ruled out order effect. Given this, data was combined across stimuli for rest of the analysis. ANOVA with repeated measures (3x2x3) was carried out to check for main effect and interaction effect.

P1 component

Results showed significant main effect between groups on P1 latency ($F(2, 29) = 23.50, p < 0.001, \eta^2 = 0.618$). Post hoc analysis revealed the shortest latency in adults with normal hearing compared to the other two children groups, which was statistically significant ($p < 0.001$). Though children with normal hearing had shorter latencies than children with LD, the latency difference did not reach significance ($p = 0.08$).

Further there was a significant main effect of hemisphere on P1 latency ($F(1, 29) = 31.8, p < 0.001, \eta^2 = 0.523$) and there was a significant interaction between hemisphere and group ($F(1, 29) = 3.2, p = 0.04, \eta^2 = 0.184$). These results were analyzed further by combining the condition and running a paired 't' test on the data for different groups. Results showed a significantly shorter latency over the left hemisphere when compared to the right hemisphere in adults with normal hearing ($p < 0.001$), and children with normal hearing ($p < 0.001$). However, such hemispheric difference was not significant in children with LD ($p = 0.08$) (Table 2). There was no significant main effect of conditions on P1 latency ($F(2, 58) = 1.609, p = 0.20, \eta^2 = 0.053$) (Figure 1 a, b and c).

Results also revealed that there is not any main effect of either groups ($F(1, 29) = 1.9, p = .08, \eta^2 = 0.12$), condition ($F(1.7, 51.5) = 3.1, p = .06, \eta^2 = 0.09$), or hemispheres ($F(1, 29) = 0.049, p = 0.82, \eta^2 = 0.002$) on P1 amplitude (Table 2) (Figure 2 a, b and c).

Table 1. Statistics of Stimulus effect for different components in all the three groups.

Component	Condition	Measures	Group		
			Normal Adults	Normal Children	LD Children
P1	Dichotic	Latency	t(15)=1.809, p=0.09	t(7)=-0.469, p=0.635	t(7)=0.649, p=0.537
		Amplitude	t(15)= 0.289, p=0.706	t(7)=0.998, p=0.315	t(7)=-0.087, p=0.931
	Monaural Left	Latency	t(15)=1.363, p=0.193	t(7)= -0.412, p=0.692	t(7)=-0.239, p=0.818
		Amplitude	t(15)=-0.044, p=0.965	t(7)= -0.447, p=0.668	t(7)= 0.470, p=0.652
	Monaural Right	Latency	t(15)=-0.083, p=0.935	t(7)= -0.057, p=0.961	t(7)= -0.168, p=0.872
		Amplitude	t(15)= 0.905, p=0.380	t(7)=0.030, p=0.977	t(7)= -0.302, p=0.772
N1	Dichotic	Latency	t(15)= 0.845, p=0.411	t(7)=0.201, p=0.866	t(7)= -0.138, p=0.898
		Amplitude	t(15)=1.835, p=0.086	t(7)=0.164, p=0.874	t(7)= -0.603, p=0.567
	Monaural Left	Latency	t(15)= 1.523, p=0.149	t(7)=-0.552, p=0.598	t(7)= 0.358, p=0.737
		Amplitude	t(15)=1.051, p=0.318	t(7)= -0.052, p=0.960	t(7)=0.763, p=0.218
	Monaural Right	Latency	t(15)= -1.048, p=0.179	t(7)=0.492, p=0.638	t(7)=-0.646, p=0.539
		Amplitude	t(15)= -1.364, p=0.193	t(7)=-0.889, p=0.404	t(7)=-0.068, p=0.984
P2	Dichotic	Latency	t(15)=-0.623, p=0.543	t(7)=0.567, p=0.588	t(7)=0.377, p=0.717
		Amplitude	t(15)=0.537, p=0.599	t(7)=0.399, p=0.702	t(7)=0.320, p=0.758
	Monaural Left	Latency	t(15)=0.469, p=0.646	t(7)=0.199, p=0.848	t(7)=-0.925, p=0.384
		Amplitude	t(15)= -0.296, p=0.771	t(7)=-0.306, p=0.768	t(7)=0.164, p=0.874
	Monaural Right	Latency	t(15)=0.658, p=0.521	t(7)=-0.208, p=0.841	t(7)=0.418, p=0.689
		Amplitude	t(15)=-1.067, p=0.303	t(7)= -0.297, p=0.796	t(7)= -0.078, p=0.940

Table 2. Mean and Standard Deviation of P1 Latency and Amplitude.

Group	Conditions	HEMISPHERE	Latency(in milliseconds)		Amplitude(in microvolt)	
			Mean	SD	Mean	SD
Normal Adults	Monaural right	LH	53.37	7.92	0.273250	0.2395121
		RH	64.7	10.5	0.118250	0.1459504
	Monaural left	LH	58.12	7.982	0.228625	0.2385755
		RH	64.75	10.580	0.114938	0.2454847
	Dichotic	LH	58	9.2	0.349875	0.1695063
		RH	63.63	5.1	0.295562	0.1470487
Normal Children	Monaural right	LH	64.00	4.781	0.223750	0.1059565
		RH	77.75	1.669	0.186250	0.2157338
	Monaural left	LH	58.12	7.982	0.141250	0.1523565
		RH	73.50	5.732	0.122500	0.1903193
	Dichotic	LH	63.63	10.889	0.301250	0.1854290
		RH	69.25	9.968	0.258750	0.2841246
LDs	Monaural right	LH	69.75	3.770	0.448750	0.8101012
		RH	72.25	6.628	0.345000	0.6979595
	Monaural left	LH	73.25	5.651	0.432875	0.6342833
		RH	76.50	7.387	0.591875	1.1768321
	Dichotic	LH	73.00	8.48	0.864375	0.8729218
		RH	74.75	9.91	1.078000	1.1805009

LH – Left Hemisphere, RH – Right Hemisphere

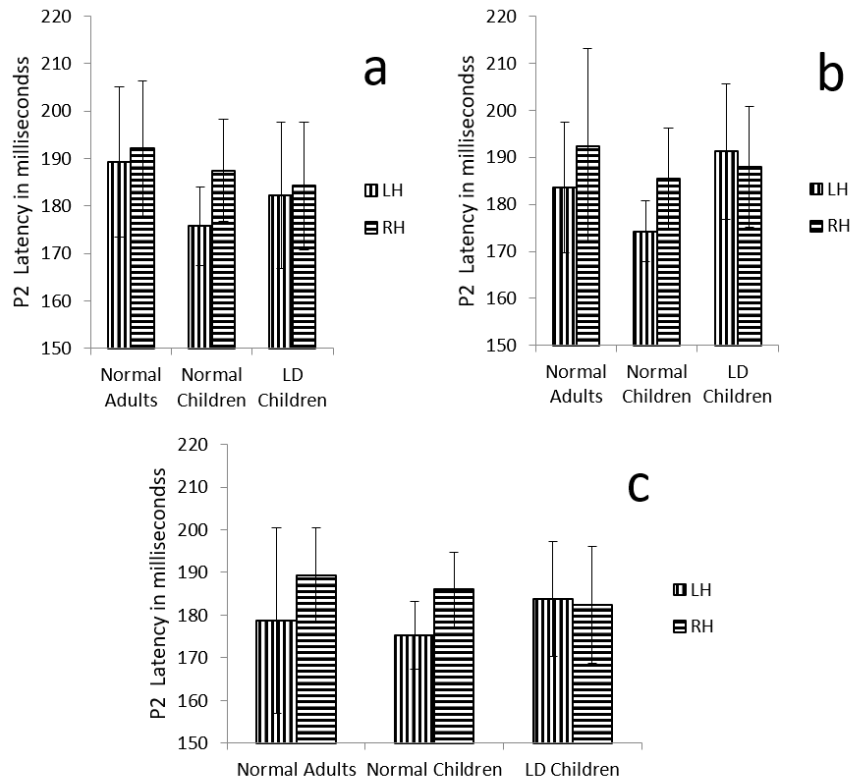


Figure 1. Graphical representation of P1 mean latency across (a) dichotic condition (b) Monaural Left conditions (c) Monaural Right condition in all three groups. The error bar represents +/- standard deviation. LH – Left Hemisphere, RH – Right Hemisphere.

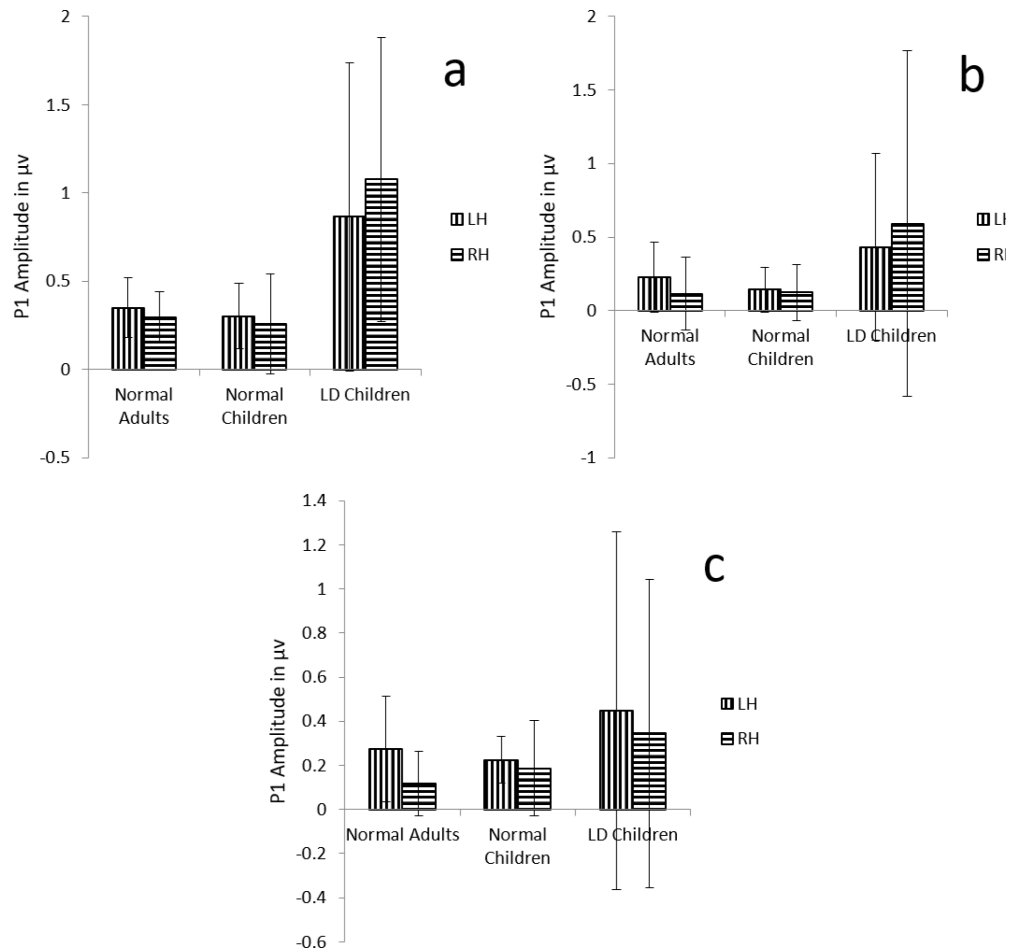


Figure 2. a) Graphical representation of P1 mean amplitude across (a) dichotic condition (b) Monaural Left conditions (c) Monaural Right condition in all three groups. The error bar represents \pm standard deviation. LH – Left Hemisphere, RH – Right Hemisphere.

N1 component

Results showed a significant main effect of group on N1 latency ($F(2, 29) = 4.1, p = 0.02, \eta^2 = 0.223$). Post hoc results showed no significant difference between any of the groups ($p = 0.066$), though similar a developmental pattern as P1 was seen in N1 latency also.

Further there was a significant main effect of hemisphere on N1 latency too ($F(1, 29) = 19.2, p < 0.001, \eta^2 = 0.399$), and also a significant interaction between hemisphere and group ($F(2, 29) = 5.4, p = 0.01, \eta^2 = 0.27$). These results were analyzed further by combining the condition and running a paired 't' test on the data for different groups. Similar to P1, N1 latency showed a significantly shorter latency over left hemisphere when compared to right hemisphere for adults with normal hearing ($p < 0.001$), and children with normal hearing ($p < 0.001$). However, such hemispheric difference was not significant in children with LD ($p = 0.716$) (Table 3).

There was also a significant main effect of condition on N1 Latency ($F(2, 58) = 5.9, p = 0.04, \eta^2 = 0.16$). Post hoc results

showed significant latency difference between dichotic and monaural left condition ($p = 0.04$) were N1 latency was shorter in dichotic condition compared to the monaural left condition. Such significance was not seen in any of other combinations (DI vs. MR and ML vs. MR) (Figure 3 a, b and c).

Results showed no significant main effect of either group ($F(1, 29) = 2.8, p = 0.07, \eta^2 = 0.162$) or condition ($F(1.5, 44.4) = 2.1, p = 0.132, \eta^2 = 0.06$) on N1 amplitude. But there was a significant main effect of hemisphere on N1 amplitude ($F(1, 29) = 11.2, p = 0.002, \eta^2 = 0.276$), and also there was significant interaction between condition and hemisphere ($F(1.9, 56.1) = 8.5, p = 0.001, \eta^2 = 0.227$). Further analysis revealed significantly larger amplitude over the left hemisphere in both the dichotic and monaural right condition ($p < 0.001$), and no such latency difference in the monaural left condition ($p = 0.893$) (Table 3) (Figure 4 a, b and c).

P2 component

Results showed no significant main effect of either group ($F(2, 29) = 3.2, p = 0.053, \eta^2 = 0.184$), or condition ($F(2, 58) = 0.79, p = 0.42, \eta^2 = 0.027$) on P2 latency.

Table 3. Mean and Standard Deviation of N1 Latency and Amplitude.

Group	Conditions	Hemisphere	Latency(in milliseconds)		Amplitude(in microvolt)	
			Mean	SD	Mean	SD
Normal Adults	Monaural right	LH	104.88	10.197	-0.766688	0.5287298
		RH	119.00	10.379	-.273875	.2474962
	Monaural left	LH	106.00	11.100	-.602312	.5355764
		RH	118.38	10.614	-.541500	.3053455
	Dichotic	LH	103.38	9.344	-.663438	.5343967
		RH	114.50	8.470	-.320625	.3266515
Normal Children	Monaural right	LH	111.25	10.740	-.433750	.3364919
		RH	122.75	8.345	-.240000	.3118608
	Monaural left	LH	115.75	9.647	-.585000	.3293283
		RH	124.25	11.081	-.633750	.3781510
	Dichotic	LH	105.75	10.714	-.435000	.4411997
		RH	119.25	8.681	-.113750	.4576941
LDs	Monaural right	LH	115.75	9.647	-1.22287	.6485111
		RH	115.25	10.634	-.463125	.6199522
	Monaural left	LH	120.50	6.568	-1.01687	.7616256
		RH	120.75	9.677	-1.03287	1.3203183
	Dichotic	LH	115.00	10.085	-.916875	.8203040
		RH	113.50	8.928	-.825375	1.5277259

LH – Left Hemisphere, RH – Right Hemisphere

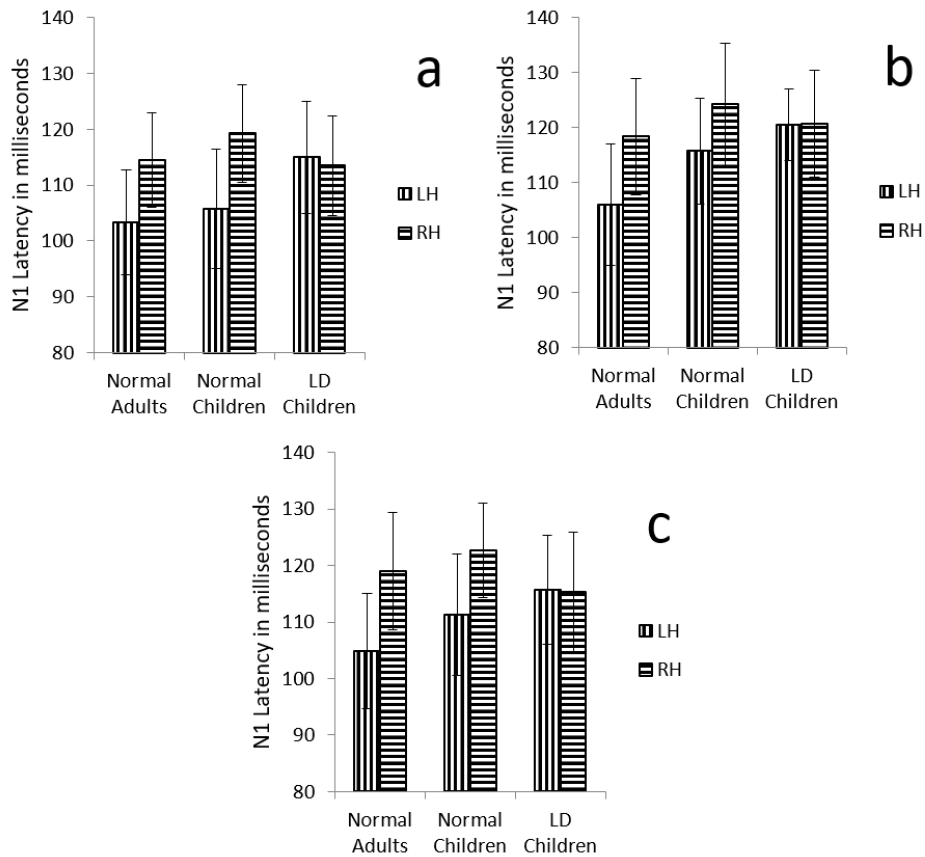


Figure 3. Graphical representation of N1 mean latency across (a) dichotic condition (b) Monaural Left conditions (c) Monaural Right condition in all three groups. The error bar represents +/- standard deviation. LH – Left Hemisphere, RH – Right Hemisphere.

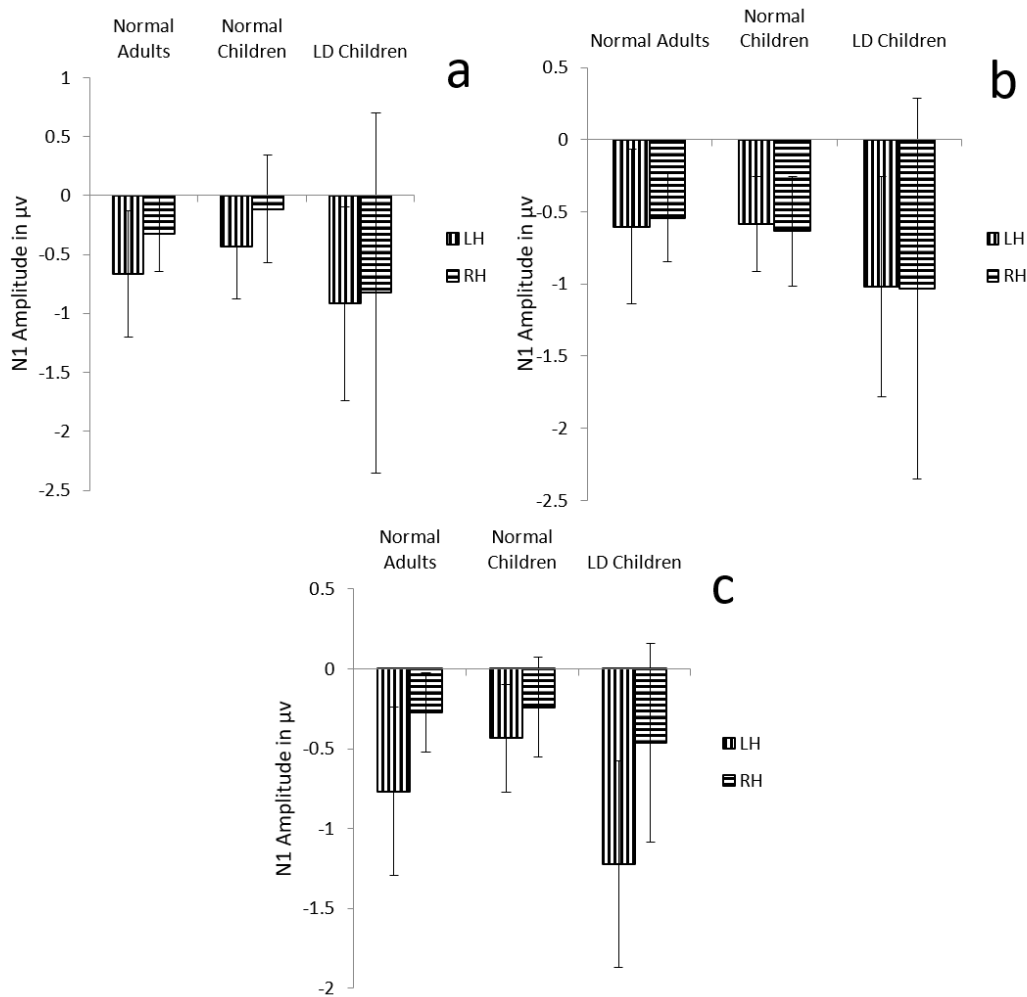


Figure 4. Graphical representation of N1 means amplitude across (a) dichotic condition (b) Monaural Left conditions (c) Monaural Right condition in all three groups. The error bar represents \pm standard deviation. LH – Left Hemisphere, RH – Right Hemisphere

Further, there was a significant main effect of hemispheres on P2 latency ($F(1, 29) = 4.2, p=0.04, \eta^2=0.28$), and there was no significant interaction between hemisphere and group ($F(1, 29) = 1.309, p=0.286, \eta^2=0.083$) (Table 4) (Figure 5 a, b and c).

ANOVA results showed no significant main effect of either group ($F(1, 29) = 2.2, p=0.17, \eta^2=0.133$), hemisphere ($F(1, 29) = 1.42, p=0.264, \eta^2=0.04$) or condition ($F(1.6, 46.4) = 0.73, p=0.486, \eta^2=0.02$) on P2 amplitude (Table 4) (Figure 6 a, b and c).

Discussion

This article explores the hemispheric asymmetry in three groups using CAEPs in a dichotic and monotic paradigms. While the preliminary aim of the study understands the neurophysiology of dichotic processing, the fact that monaural differences in CAEPs itself are not well understood. Hence it is worthwhile to discuss these findings in detail for the sake of better understanding of typical auditory processing.

In monaural stimulus condition, the results confirmed that the stimulus effect was negligible since the latencies evoked by stops in the current study ($[\text{pa}]$ and $[\text{ta}]$) were comparable. Further, it was observed that the latencies of P1, N1 and P2 components in the left hemisphere were shorter in latency compared to right irrespective of the ear stimulation (Figure 7, Figure 8, Figure 10 and Figure 11).

Similarly, dichotic condition resulted in insignificant order effect, and the CEAP components P1, N1, and P2 had significantly shorter latency over the left hemisphere compared to the right (Figure 9 and Figure 12), essentially the same results as in monaural stimulus condition. It is difficult to compare earlier studies using CAEPs in dichotic listening tasks since all the CAEP components were not studied. Nevertheless, N1 latency in the left temporal electrode was shown to have 5 ms shorter latency than that of the homologues of the right (Eichele *et al.*, 2005). Another recent study reported left central electrodes were 8 ms

Table 4. Mean and Standard Deviation of P2 Latency and Amplitude.

Group	Conditions	Hemisphere	Latency(in milliseconds)		Amplitude(in microvolt)	
			Mean	SD	Mean	SD
Normal Adults	Monaural right	LH	178.75	21.663	.354500	.2453096
		RH	189.38	11.189	.196875	.2130446
	Monaural left	LH	183.63	13.937	.287875	.1861655
		RH	192.38	20.659	.143875	.1596713
	Dichotic	LH	189.38	15.828	.482750	.3126850
		RH	192.12	14.338	.238937	.2055099
Normal Children	Monaural right	LH	175.25	7.996	.217500	.1900188
		RH	186.00	8.685	.140000	.4589429
	Monaural left	LH	174.25	6.541	.427500	.3143588
		RH	185.50	10.623	.252500	.3440826
	Dichotic	LH	175.75	8.242	.330000	.1808709
		RH	187.50	10.730	.148750	.1793988
LDs	Monaural right	LH	183.75	13.414	.581750	.8795953
		RH	182.50	13.680	.461625	.8612738
	Monaural left	LH	191.25	14.459	.410250	.8326422
		RH	188.00	12.829	.396625	.7828565
	Dichotic	LH	182.25	15.471	.647000	1.5321116
		RH	184.25	13.371	.758625	1.0994058

LH – Left Hemisphere, RH – Right Hemisphere

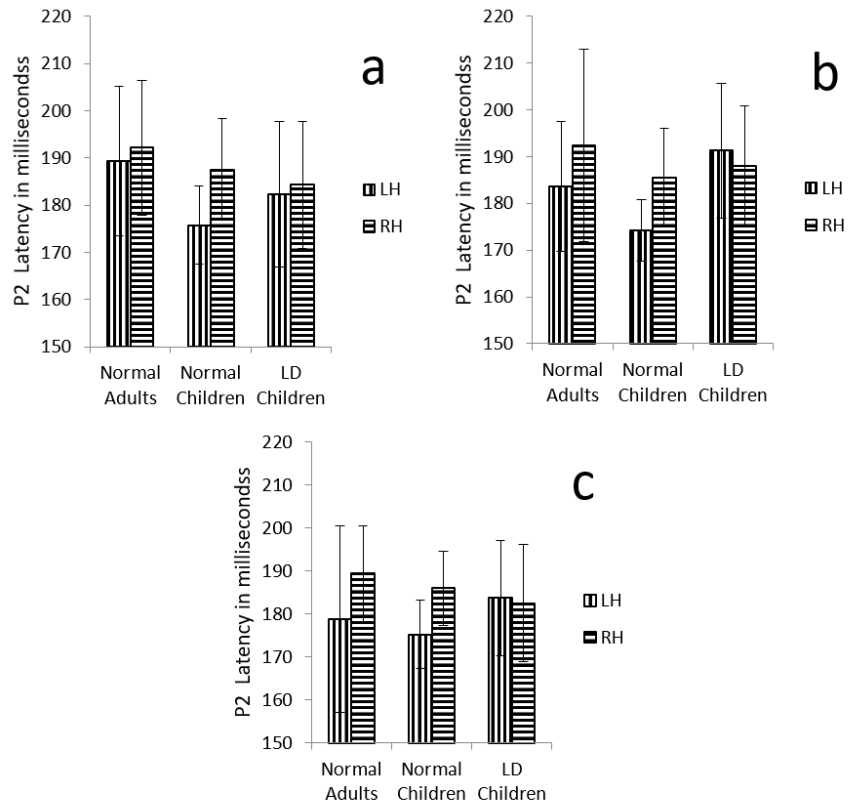


Figure 5. Graphical representation of P2 mean latency across (a) dichotic condition (b) Monaural Left conditions (c) Monaural Right condition in all three groups. The error bar represents +/- standard deviation. LH – Left Hemisphere, RH – Right Hemisphere.

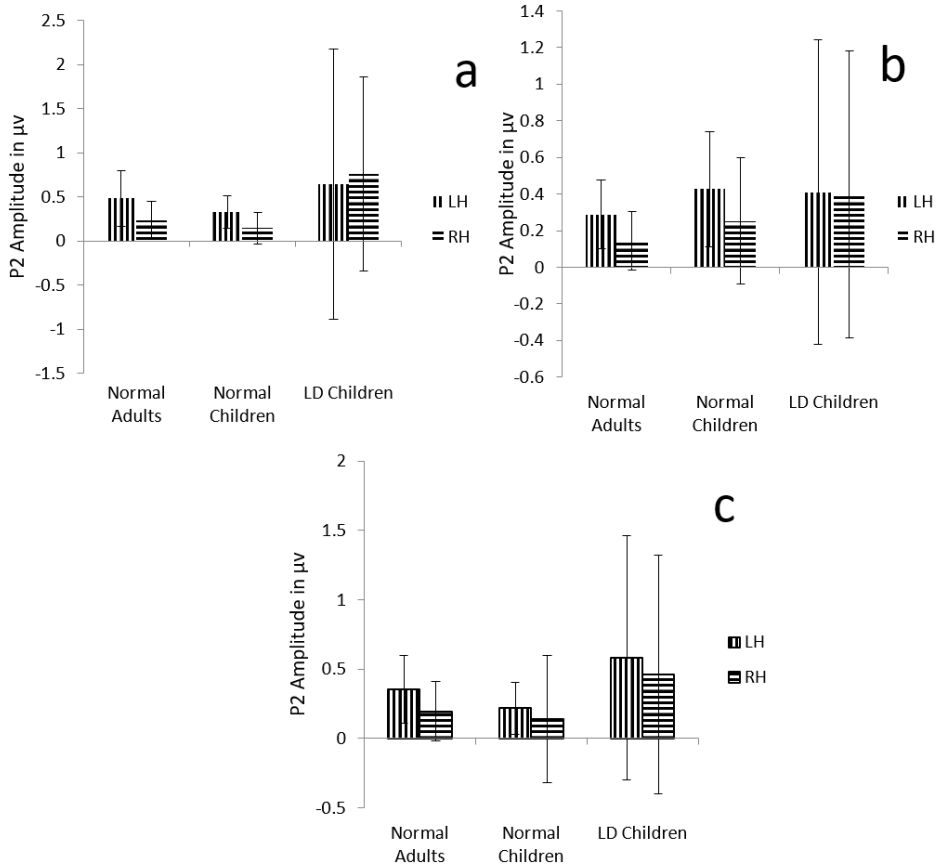


Figure 6. Graphical representation of P2 mean amplitude across (a) dichotic condition (b) Monaural Left conditions (c) Monaural Right condition in all three groups. The error bar represents \pm standard deviation. LH – Left Hemisphere, RH – Right Hemisphere.

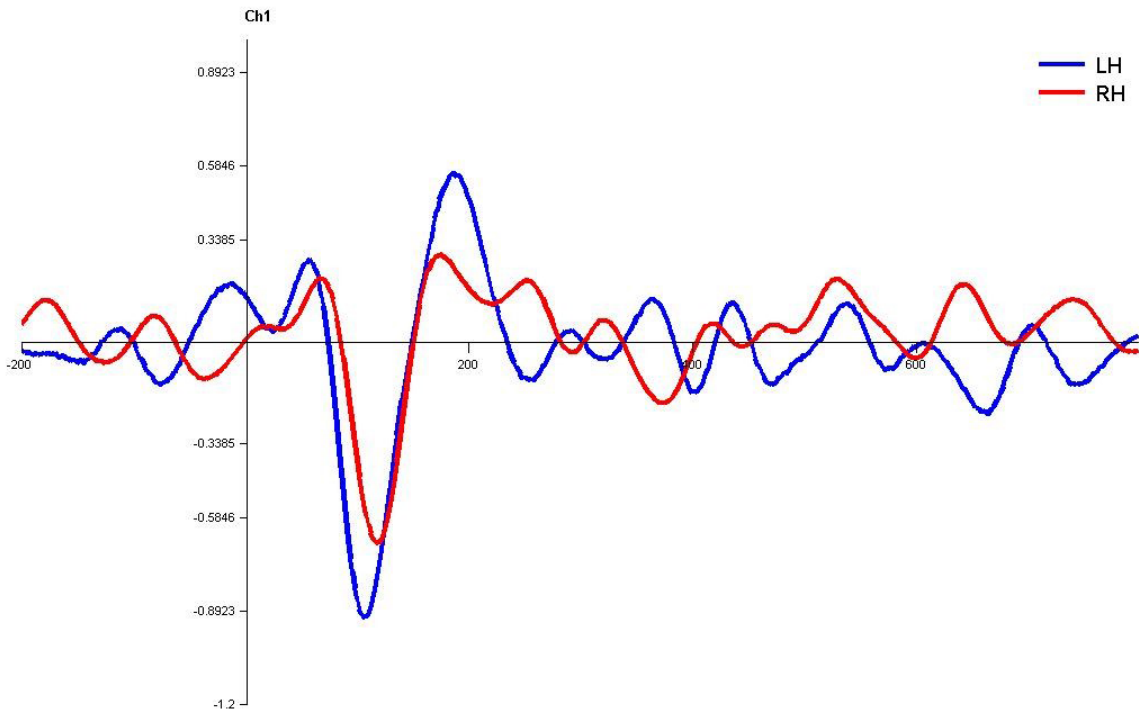


Figure 7. Grand average for normal adults in monaural left condition. Waveforms clearly depict shorter latency over left hemisphere than right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

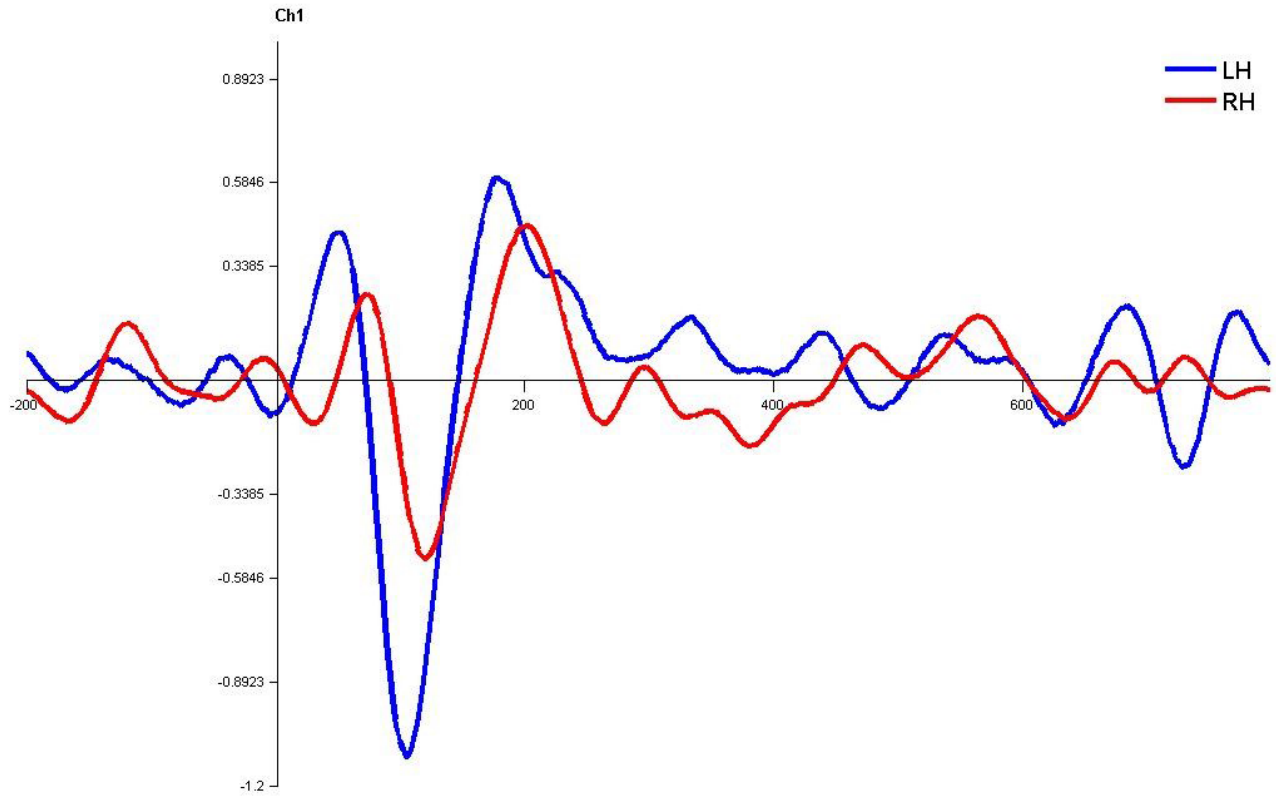


Figure 8. Grand average for normal adults in monaural right condition. Waveforms clearly depict shorter latency over left hemisphere than right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

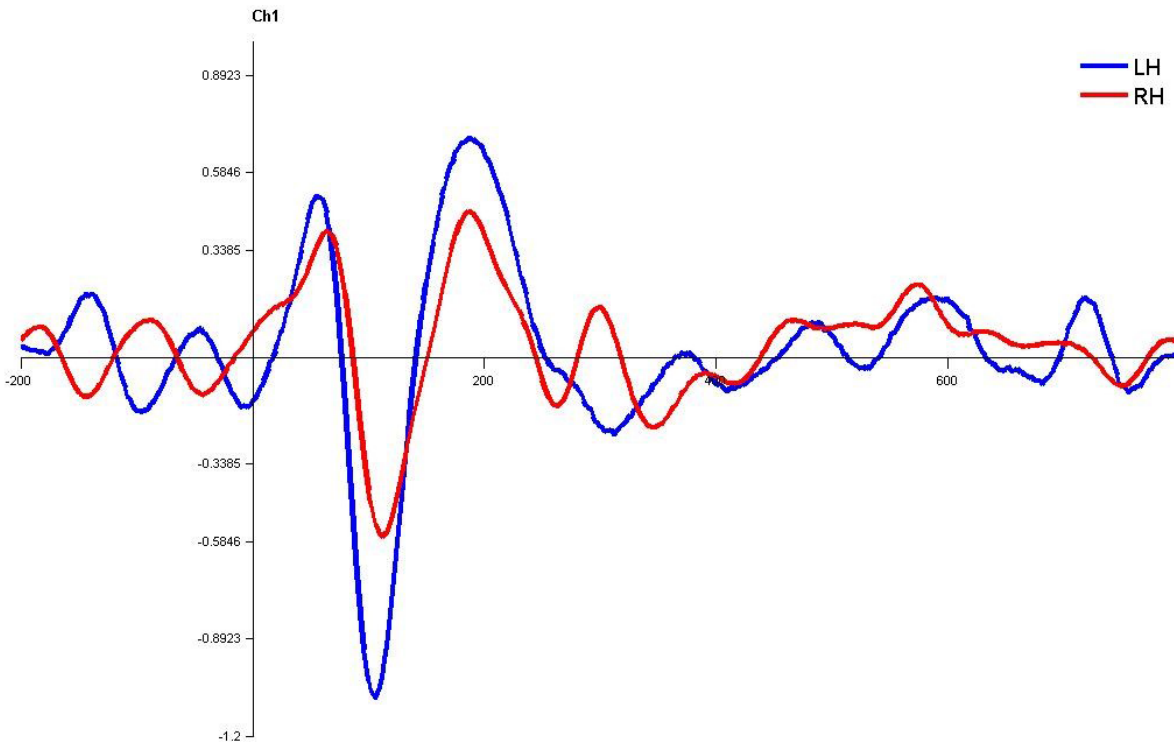


Figure 9. Grand average for normal adults in dichotic condition. Waveforms clearly depict shorter latency over left hemisphere than right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

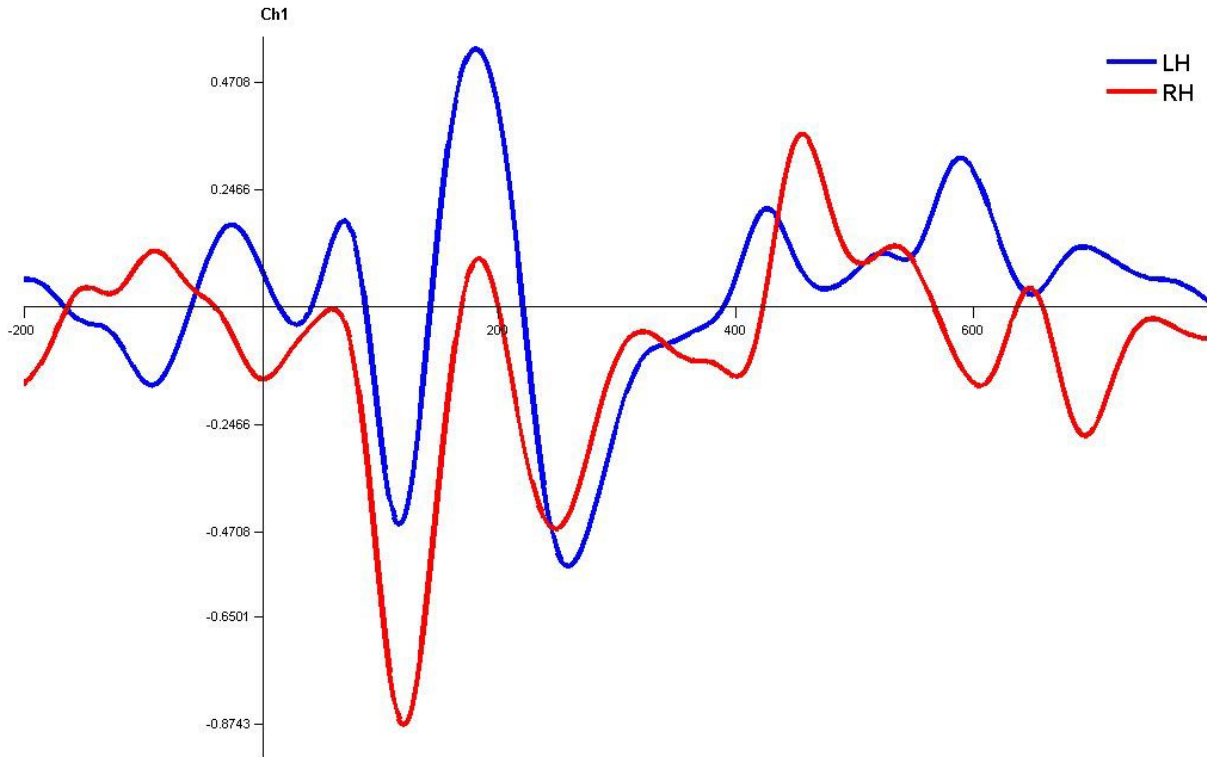


Figure 10. Grand average for normal children in monaural left condition. Waveforms clearly depict shorter latency over left hemisphere than right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

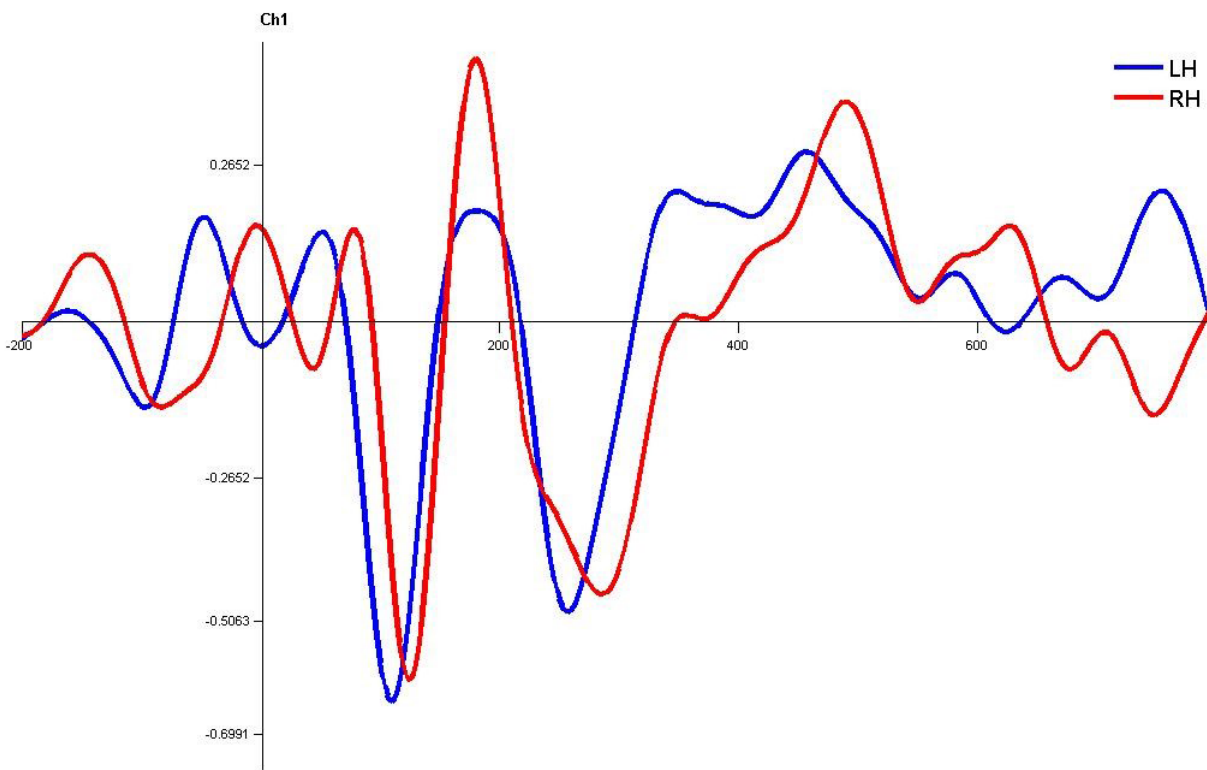


Figure 11. Grand average for normal children in monaural right condition. Waveforms clearly depict shorter latency over left hemisphere than right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

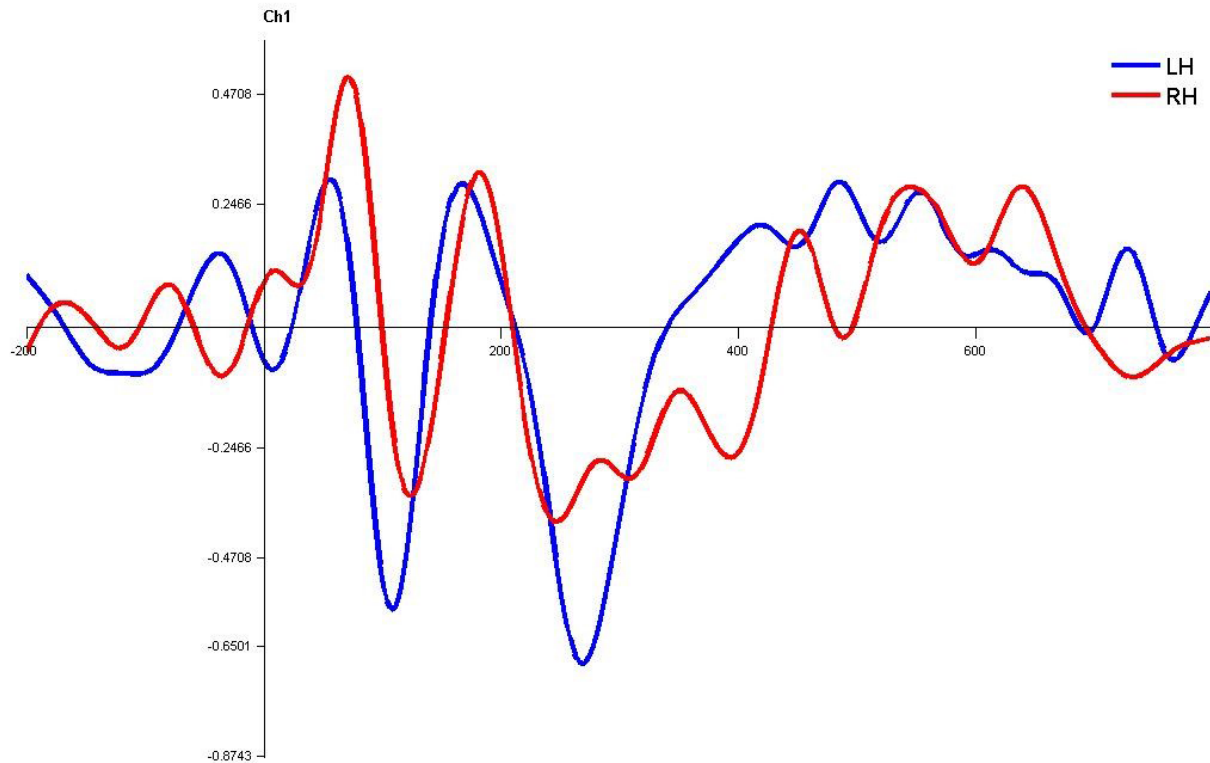


Figure 12. Grand average for normal children in dichotic condition. Waveforms clearly depict shorter latency over left hemisphere than right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

shorter than that of the homologues of the right region (Friedrich *et al.*, 2017). They hypothesized that, under high perceptual load, the N1 predicts perceptual preferences (Eichele *et al.*, 2005). However, in the current study a similar effect was seen even in monotic listening conditions. Hence, it can be said that there could be a common perceptual preference mechanism for both monaural and dichotic listening conditions and could be interpreted in the light of hemispheric specialization for speech processing.

Several behavioral and imaging studies in the literature have unanimously suggested that, the left hemisphere is specialized for processing speech and language related information (Ci *et al.*, 2016; Hinkley *et al.*, 2016; Ishikawa *et al.*, 2017; Morrell & Salamy, 1971; O’Grady *et al.*, 2016; Witelson & Pallie, 1973). Though the pathway and the neural substrates are fundamentally similar, due to unknown reasons, it is proven that the left auditory cortex is characterized to have a specialized function for speech stimuli (Corina *et al.*, 1992; Witelson & Pallie, 1973).

CAEP amplitude is a variable measure as a whole (van Hedel *et al.*, 2007). In the current study, P1 and P2 amplitude in monaural conditions were larger over the left hemisphere when compared to the right. Similar results were seen for N1 amplitude too, except in the monaural left condition. In the dichotic condition, all the CAEP components showed larger amplitude over the left hemisphere than right. Previous studies done using structured magnetic resonance imaging methods has shown similar results (Dos Santos Sequeira *et al.*, 2006). However,

In the current study, none of the amplitude measures reached significance, this may be due to the low sample size in the current study or due to the inherent variance of amplitude measures.

Children with LD

In children with LD, there was no significant latency difference between hemispheres in both monaural and dichotic stimulus conditions (Figure 4.7, 4.8 and 4.9 Figure 13, Figure 14 and Figure 15). This finding is very consistent between the P1, N1 and P2 components of CEAP. Similar findings were reported in earlier studies using neuroimaging studies on dichotic listening, where these individuals showed symmetrical activation of the bilateral auditory cortex (Illingworth & Bishop, 2009; Njemanze, 1991). Concerning amplitude, there was no significant trend.

In 1978, Galaburda, Geschwind, and colleagues hypothesized that patients with learning disabilities was associated with disruptions in brain asymmetry (Galaburda *et al.*, 1978). Few authors have argued that there could be atypical asymmetry in these individuals (Cohen *et al.*, 1992; Foster *et al.*, 2002; Hugdahl *et al.*, 1997), and others have stated that there is reduced normal asymmetry (Martínez & Sánchez, 1999; Koltuska & Grabowska, 1975). The current study findings are in line with the latter hypothesis rather than the former. Previous studies have reported reduced cortical asymmetries in brain regions including planamtemporale asymmetry (Foster *et al.*, 2002; Galaburda *et al.*, 1978; Galaburda *et al.*, 1985; Leonard & Eckert 2008), corpus callosum abnormalities that of the larger total callosal

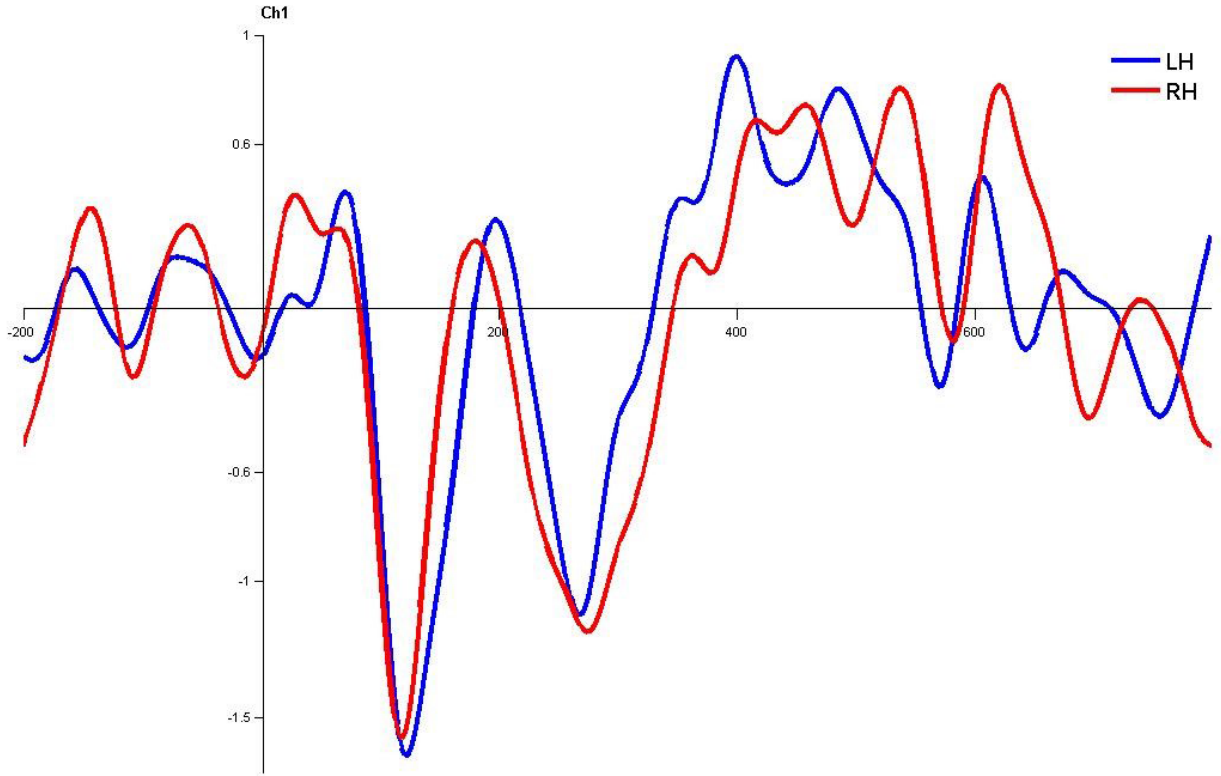


Figure 13. Grand average for LDs in monaural left condition. Waveforms clearly depict no significant latency difference over left hemisphere and right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

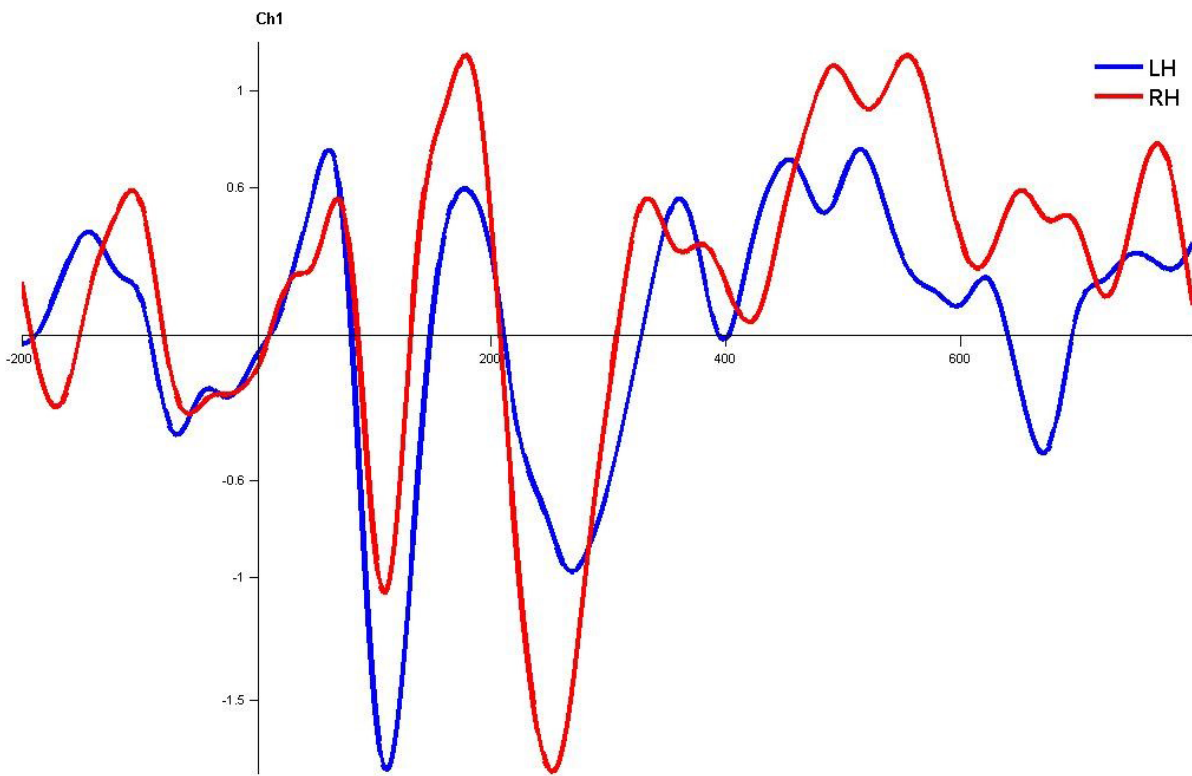


Figure 14. Grand average for LDs in monaural right condition. Waveforms clearly depict no significant latency difference over left hemisphere and right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

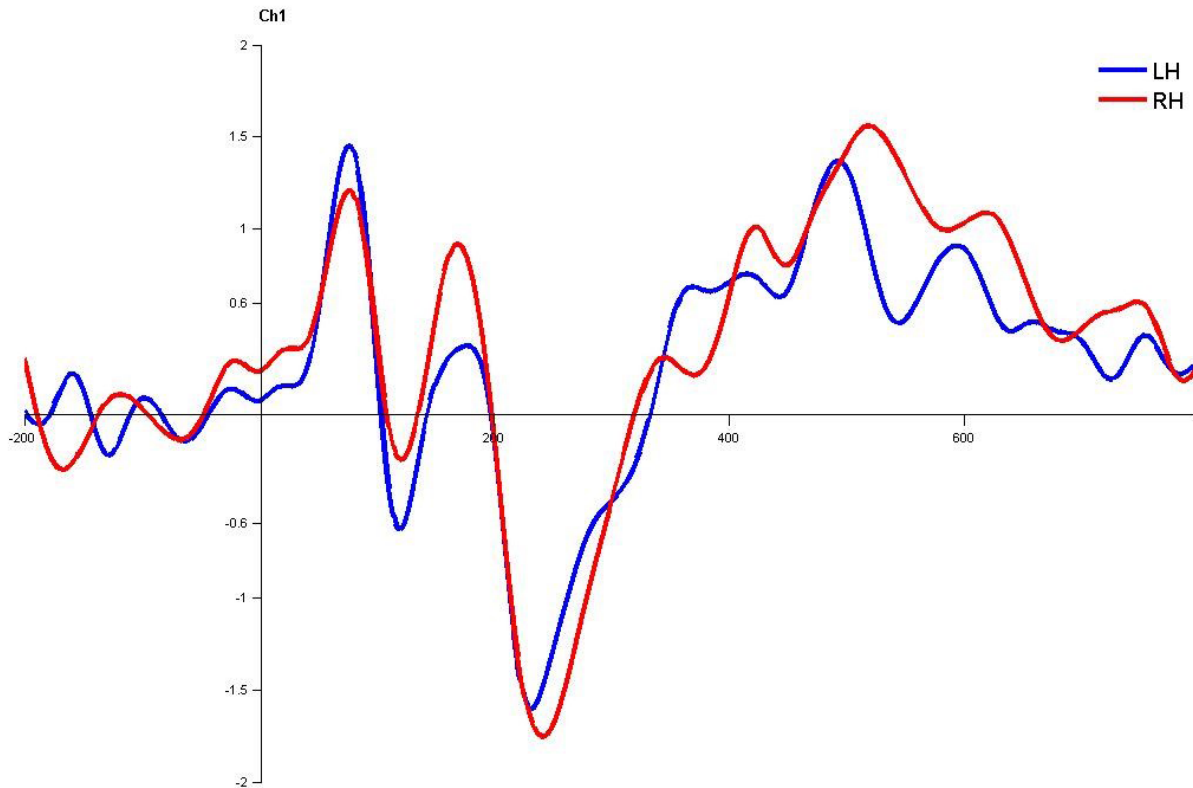


Figure 15. Grand average for LDs in dichotic condition. Waveforms clearly depict no significant latency difference over left hemisphere and right hemisphere. LH – Left Hemisphere, RH – Right Hemisphere.

areas and larger posterior (splenial) areas (Duara *et al.*, 1991), smaller anterior-most regions (genu) (Hynd *et al.*, 1995), larger posterior third of the callosum including the isthmus and splenium (Rumsey *et al.*, 1996). Apart from these, several other structures also have been reported to lack asymmetry including parietal areas (Habib & Robichon, 1996), the posterior region of the inferior frontal gyrus (Galaburda *et al.*, 1985; Hynd *et al.*, 1990), and Broca's area (Robichon *et al.*, 2000).

Though the current study findings could easily attribute to the established anatomical deficits that are associated in children with LD, the functional asymmetry/ deficits in decoding phonological information cannot be completely ruled out. Since speech processing is well differentiated from nonspeech stimulus right from the brainstem, as earlier evidence suggest (Abrams *et al.*, 2006; Ibañez *et al.*, 1989), the observed lack of asymmetry could be a combination of both functional phonological decoding deficits as well as the structural deficits. Further, a method that elucidates the speech-specific processing from non-speech processing is at this moment warranted.

Group effect

In the current study, there were significant differences between normal adults and individuals with LD in terms latency of CEAP components (P1 and N1), were the latencies were shortest in adults with normal hearing, shorter in children with normal hearing, and prolonged in children with LD. Previous ERP studies

on these individuals have shown mixed results. Though few authors have observed no latency difference in auditory late latency response (ALLR) using click stimulus except for P1 (Purdy *et al.*, 2002), other studies suggest that individuals with LDs often have prolonged latency when compared with controls in all ALLR components (Frizzo, 2015; Kumar & Gupta, 2014). The delay may be because of altered cortical functions (Pinkerton *et al.*, 1989), short attention span (Picton *et al.*, 1978), or deficits in auditory cortical information synchronization associated to auditory attention factors (Leppänen & Lyttinen, 1997).

Taken together, the findings of current study, both monaural and dichotic condition elucidates the hemispheric differences in processing speech stimuli in normal hearers. At the same time, these effects are either suppressed or absent in LDs. However, there is no previous evidence to support these findings. Hence the results have to be interpreted with caution and open for exploration.

Conclusion

The current study method is unique in comparison to previous CEAP studies, and is consistent in indicating cerebral asymmetry in normal hearers and LDs. The study failed to categorize learning disability subjects based on their specific learning disability. A lack of behavioral dichotic listening tests supplementing the electrophysiological findings can be considered as one

of the major drawbacks of the current study. Overall results indicate that shorter latency and larger amplitude in the left hemisphere irrespective of the ear of presentation may indicate left hemispheric preferences for speech stimulus in normal, but lack of this difference suggests void of hemispheric asymmetry in individuals LDs. However, there is no previous evidence to support these findings. Hence the results have to be interpreted with caution and are open for exploration. Hence, based on this preliminary evidence, it can be suggested that CEAPs can be used as one of the tools to study cerebral asymmetry. Latencies of CEAP components are more sensitive to hemisphere specific difference than amplitude.

Data availability

Underlying data is available from Figshare

Figshare: Dataset 1. P1, N1 and P2 Latency for all the group across all the condition

<https://doi.org/10.6084/m9.figshare.7358387.v1> (Palaniswamy, 2018a)

Figshare: Dataset 2. P1, N1 and P2 Amplitude for all the group across all the condition

<https://doi.org/10.6084/m9.figshare.7358396.v1> (Palaniswamy, 2018b)

Figshare: Dataset 3. Stimulus effect and order effect for Latency and Amplitude

<https://doi.org/10.6084/m9.figshare.7358417.v1> (Palaniswamy, 2018c)

All data is available under a [CC0 1.0 Universal](#) license

Extended data

Stimuli used to evoke Late Latency Response

Figshare: Extended data. Stimuli used for Evoking ALLR <https://doi.org/10.6084/m9.figshare.7358438.v1> (Palaniswamy, 2018d)

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Version 1

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Overview

In this article, Bhat and colleagues aim to characterize the cortical processing of dichotically-presented speech tokens, as reflected by cortical auditory evoked potentials (CAEPs). Several stimulus- and subject-related factors are considered as possible contributors to the observed CAEP morphology: stimulus type (/pa/ or /ta/), spatial order, hemisphere of measurement, and age. To explore these factors, three experimental conditions were administered to adult and pediatric participants, consisting of a monaural right presentation of each speech sound, a monaural left presentation of each sound, and two dichotic configurations of the unmixed speech sounds. Another objective is to examine the differences in CAEP morphology between healthy individuals and those with learning disabilities. This goal is motivated by previous findings that dichotic listening is a useful test to examine cerebral dominance deficits, developmental changes in language lateralization, and bilateral hemispheric processing deficits in children with learning disabilities.

Is the work clearly and accurately presented and does it cite the current literature?

There is a notable gap in the literature review for this paper regarding findings of the last ~ 15 years which have fundamentally changed scientific thinking around the cerebral lateralization of speech processing (e.g., Poeppel, 2003¹, Poeppel et al., 2012², Friederici & Alter, 2004³). The rationale for the study is generally clearly stated and the experimental conditions are logically designed to address the questions that the researchers have posed. However, the authors have failed to provide a convincing argument that the study has significant novelty or importance. Is the aim simply to fill a gap in the scientific reporting of CAEP amplitudes and latencies to dichotically-presented stimuli? Is there no greater motivation, perhaps pertaining to the clinical utility of these measures as either a diagnostic, or a method to study the neurophysiological underpinnings of learning disabilities?

There are several easily correctable errors in this paper which confuse the reader. First, the healthy adult and pediatric participants are repeatedly referred to as "normal hearing," but this is not a study of hearing impairment. According to the stated methodology, all participants, including those with learning disabilities, had to pass a screen for normal hearing, therefore all participants, including the disease group, must have normal hearing. Please refer to the control groups as "normal" or "controls", not "normal hearing." If the learning-disabled group does not have normal hearing, the methods should be updated.

Second, one of the figures is incorrect: below Table 1 of P1 latencies and amplitudes, Figure 1 should depict P1 latencies, but in fact shows P2 latencies. More minor issues include: the description of the amplitude measure as “mean amplitude” in the abstract when a peak amplitude was used, the description of participant demographics in the abstract suggests that only the pediatric participants were right-handed when all participants were right-handed, frequent misspelling of the acronym CAEP as CEAP, use of the acronym LLR before it is defined, and using the word “latency” rather than “amplitude” in the final sentence of the paragraph describing N1 amplitude results. Finally, as a general comment, the paper would benefit from editing for grammatical correctness.

The waveform figures in this paper would all benefit from considerable revision. First, none of the figures indicate which channels are represented. This can be inferred from the text but should be stated again in the figure or figure caption. The label “Ch1” above the vertical axis is particularly confusing. The units for voltage and time are also missing. Presenting each pair of waveforms in a separate, large figure makes it impossible to visually examine the effects of age, clinical group, or experimental condition. Please combine these waveforms in a way that facilitates the observation of these effects. The captions for the waveform figures are uninformative and sometimes incorrect. For example, Figure 10 states that “waveforms clearly depict shorter latency over left hemisphere than right hemisphere” when no latency differences are apparent. If anything, the latency of P1 appears to be slightly shorter in the right hemisphere. All figures, both bar graphs and waveforms, would benefit from the addition of symbols to highlight which experimental effects reached statistical significance.

Is the study design appropriate and is the work technically sound?

If the goal of this study is to support future clinical and experimental use of CAEPs to study cerebral lateralization in the processing of dichotic speech, there are two major flaws in the experimental design. First, there is no justification provided for treating the learning-disabled group as a homogeneous sample despite likely representation from a variety of subtypes (e.g., reading disabilities, attention deficit disorder, and arithmetic disabilities, among others). The importance of subtyping to improve the reproducibility of research using event-related potentials in learning-disabled children has long been acknowledged (e.g., Dool et al. 1993⁴).

Second, by failing to collect behavioral dichotic listening data from these participants, the authors provide no link between clinical and experimental research using behavioral and CAEP-based measurements. This is particularly important because behavioral dichotic listening paradigms do not simply reflect cerebral lateralization in speech processing, but also the influence of selective attention (Hugdahl, 2011⁵). The present study uses passive stimulation, except perhaps in the dichotic condition where it appears that attention deployment has not been controlled. Without knowing how the obtained CAEP measures relate to behavioral dichotic listening performance, it is impossible for clinicians or experimental scientists to weigh the relative merits of the two approaches. The purpose of highlighting these shortcomings is not to suggest that the paper is not worthy of publication, but rather to encourage the authors to appropriately address these issues in their introduction, discussion, and presumed future work that builds on these findings. Their brief mention in the paper’s conclusion does not constitute a sufficient acknowledgement of these important flaws.

A stated objective of this experiment is to compare monaural vs. dichotic processing in the same individuals. However, the methods section suggests that a silent movie was presented under the monaural conditions and not the dichotic condition. Is this indeed the case? Like the monaural conditions, the dichotic condition is passive, so a diversionary task is still desirable to help control the deployment of attention. If a silent movie was not used in the dichotic condition, what was the rationale for excluding it?

There may also be a problem with accurate measurement of CAEP peaks in this study. Automated or semi-automated methods to detect and measure CAEP peaks are commonly used and these algorithms must be supplied with search window bounds that are specified by the user. In this study, the search window bounds were selected based on visual evaluation of grand average waveforms across all participants. The selected windows for the P1, N1, and P2 components were 40 – 80, 90 – 140, and 170 – 220 ms, respectively. However, search windows that are selected based on the grand average waveform, particularly if computed across different experimental groups, may not perform well on all subjects. It is common for search window bounds to be subsequently modified to ensure that they truly encompass the peaks of interest at the individual subject level. While it is unknown whether the authors completed this type of inspection, the peak latencies that are reported in Tables 2 – 4 suggest that the selected window bounds for the P1 and P2 components may not have been adequate to detect these peaks at the individual level.

By converting the search window bounds to z-scores on the normal distribution defined by the mean and standard deviation of the observed peak latency, one can estimate the percent of participants whose peaks might lie outside the search window. Among healthy adult participants, the upper bound of the P1 search window may have failed to capture the true peak for 7.21% and 7.49% of participants (in both cases, 1 out of 16 participants) for the monaural right and monaural left conditions, respectively, in the right hemisphere. Among healthy pediatric participants, the upper bound may have failed to capture the true P1 peak for 12.92% and 13.57% of participants (both 1 of 8 participants) for the monaural left and dichotic conditions, again both for the right hemisphere. In the monaural right condition for this group, again for the right hemisphere, the observed mean latency (77.75 ms) lies nearly upon the upper bound of the search window (80 ms) and the standard deviation (1.669 ms) is the smallest observed in the study, suggesting a possible ceiling effect imposed by the search window. Thus, *the mean latency of the P1 may have been artificially lowered in healthy individuals, specifically for measurements taken over the right hemisphere.*

In children with learning disabilities, the upper bound of the P1 search window may have failed to capture 31.92% participants (2 of 8) in the monaural left condition, for measurements over the right hemisphere, as well as 20.33% and 29.81% of participants (1 and 2 of 8) for the left and right hemispheres, respectively, under dichotic conditions. Thus, *the mean latency for the P1 may have been underestimated across both hemispheres for participants with learning disabilities under conditions of dichotic stimulus presentation.*

While the search window selected for the P1 appears to have ended somewhat too early, the search window for the P2 may have started too late, particularly for measurements over the left hemisphere. In healthy adults, the lower bound of the search window may have failed to capture the true component peak for 34.46%, 16.35%, and 11.15% of participants (5, 2, and 2 of 16) in the monaural left, right, and dichotic conditions, all for measurements over the left hemisphere. The lower bound of the window may also have failed to capture 14.01% (1 of 16) participants in the monaural left condition for the right hemisphere. In healthy pediatric participants, the lower bound of the search window may have failed for all measurements over the left hemisphere, for 25.46%, 25.78%, and 24.2% of participants (in all cases, 2 of 8 participants) for the monaural left, right, and dichotic conditions, respectively. Thus, *the latency of the P2 in healthy individuals may have been artificially increased, particularly for measurements over the left hemisphere.*

For children with learning disabilities, the lower bound of the search window for P2 measurement may have failed to capture 15.15% (left hemisphere) and 18.14% (right hemisphere) of participants (in both cases, 1 of 8) in the monaural right condition. Measurement may also have been compromised over both

hemispheres in the dichotic condition, in which 21.48% (left hemisphere) and 14.25% (right hemisphere) of participants, both equaling roughly 1 of 8 participants, may have had peaks lying outside the search window. Thus, *the mean latency of P2 may have been artificially increased over both hemispheres in the right monaural and dichotic experimental conditions for children with learning disabilities.*

Overall, these statistical results suggest that the employed search window bounds may not have adequately captured the P1 and P2 components. However, there remains some question as to whether the reported search window bounds are in fact correct, due to the presence of latencies that lie outside these bounds in the datasets that are available via Figshare. Please specify whether visual inspection was performed to ensure that component peaks were accurately identified by the peak detection algorithm and ensure that the search window bounds that are reported in the methods section are correct. Finally, please indicate how many trials contributed to the averaged waveforms that were used for peak measurement, as the influence of noise on the observed peaks varies inversely with the number of trials used for averaging.

Are sufficient details of methods and analysis provided to allow replication by others?

One of the objectives of this study is to examine the utility of CAEPs to dichotic stimuli to identify altered speech processing in children with learning disabilities. What are the clinical demographics of the participants in this group? Please specify what learning disabilities the children were diagnosed with and, if possible, what clinical criteria were used to render the diagnosis. Please also specify which frequencies were tested to screen for normal hearing status.

It is helpful that the study stimuli are available via Figshare, but several important details of the speech stimuli are missing from the text. Please provide the durations of the speech tokens and specify how their intensities were matched to one another. It would be helpful to see the speech waveforms as a figure. Please specify the rate of stimulus presentation, how many stimulus trials were presented under each experimental condition, and how many of these trials survived data cleaning to contribute to the averaged waveforms.

Some details of EEG data processing are erroneously described. The “Data analysis” section states that “... bad channels and bad blocks were visually inspected and interpolated ...” but interpolation is a method that applies only to bad channels, not bad blocks of data. It also specifies that, “The data was then subjected to high pass filtering with a cutoff frequency of 1 kHz.” This is implausible because the data was originally acquired with a bandpass of 0 – 100 Hz. It would additionally be helpful to know how many ICA components were rejected per subject by the MARA algorithm.

If applicable, is the statistical analysis and its interpretation appropriate?

The first hypothesis tested is that component amplitudes and latencies do not differ between the two speech tokens (/pa/ and /ba/) or between the two spatial orders of these stimuli under dichotic listening conditions. To test this hypothesis, component amplitudes and latencies were compared via a series of *t*-tests that is summarized in Table 1. Problematically, it is not specified anywhere which electrode was used to obtain these measurements. Furthermore, the authors were concerned with hemispheric differences in speech stimulus processing, yet this analysis does not appear to take hemispheric asymmetry into consideration. What is the reasoning for this approach?

Following the statistical evaluation for stimulus effects, amplitudes and latencies were combined across stimuli. They were then tested by a 3 x 2 x 3 repeated measures ANOVA, but the factors for the ANOVA

are not stated when the statistical approach is introduced. The type of test to be used for pairwise post-hoc statistics should also be specified here.

The authors are to be commended for reporting means and standard deviations of component amplitudes and latencies, as well as effect sizes. These types of statistics are under-reported in the CAEP literature and doing so will benefit any research groups who wish to build on the results of this study. It is unknown to what extent the statistical results observed here might be impacted by amending the P1 and P2 search windows, if necessary.

The N1 statistical results require clarification. The N1 latency ANOVA found a significant main effect of group which was inspected via post-hoc tests, presumably paired *t*-tests. No significant differences were found between the groups, but only one *p*-value was reported ($p = 0.066$). Three pairwise contrasts should have been performed: healthy adults vs. healthy children, healthy adults vs. children with learning disabilities, and healthy children vs. those with learning disabilities. Was the same *p*-value obtained for all pairwise contrasts? If so, this should be clarified.

Unlike P1 and N1, there was no significant effect of group on P2 latency ($p = 0.053$). Significance might be reached if the P2 search window is amended. There is also a typographical error in the *p* value for the main effect of group on P2 amplitude.

Are all the source data underlying the results available to ensure full reproducibility?

Source data consisting of component latencies and amplitudes for all experimental groups across all experimental conditions are available via Figshare. However, these data tables are perplexing because many of the latencies lie beyond the reported bounds of the peak detection search windows. Were the search window bounds different than those reported?

Are the conclusions drawn adequately supported by the results?

As noted previously, the discussion section of the paper needs to address the shortcomings of this study's experimental design. The authors conclude that their results, demonstrating earlier component peak latencies over the left hemisphere than the right, are in line with known hemispheric specialization for language in healthy, normal individuals. This asymmetry was visible for both monaural and dichotic conditions of stimulus presentation and was generally observed in terms of larger component amplitudes over the left hemisphere as well. With respect to the children with learning disabilities, the authors state that their results are in line with the hypothesis that these children have reduced normal asymmetry. This conclusion does not appear to be supported by their results. No significant hemispheric latency effects were observed for the P1 or N1 in this group. Furthermore, inspection of Table 4 clearly indicates that, despite the lack of a significant interaction between hemisphere and group on P2 latency, earlier latencies in the left hemisphere were only observed in the learning disability group in the dichotic condition. Indeed, the authors later state that, "the observed lack of asymmetry could be a combination of both functional phonological decoding deficits as well as structural deficits." The discussion should be more consistent in describing the lack of hemispheric asymmetry in CAEP latencies in this group.

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Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Electrophysiology, neuroimaging, attention, cognition, hearing, hearing loss, brain injury, listening difficulties.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Referee Report 22 February 2019

<https://doi.org/10.5256/f1000research.18618.r43254>



Hemanth Narayan Shetty  ^{1,2}

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The authors have assessed hemispheric asymmetry using CAEPs. /pa/ and /ta/ stimuli in three conditions (mono R, L and dichotic (two orders)) which were used to record CAEPs on normal hearing adults, young adults children with age matched learning disabled children. All participants were right handed individuals. Results revealed a significant hemispheric asymmetry was observed in normal adults and adult children but not in LD children, irrespective of stimuli and conditions (MonL L hemisphere/ right hemisphere; monR R hemisphere/ left hemisphere and DI RH and DI LH).

Specific comments

Introduction

Recent studies were reviewed to strengthen their need. Research questions and hypothesis are missing. I felt purpose needs to still be strengthened on importance of CAEPs and hemispheric asymmetry. In addition, consider to mention the objectives of the study.

Method

Research design is missing.

Justification for stimuli specifically for hemispheric asymmetry is needed. Authors have told that in previous studies similar stimuli were used to assess hemispheric asymmetry thus we also used. This explanation is not correct. Consider to justify.

Is the stimuli is normalized? If yes, how have you normalized it? Since CAEP is exogenous potentials it is preferred to give acoustic characteristics of both stimuli (Spectrogram and spectra).

These stimuli were presented at 70 dB HL. How these stimuli are calibrated? Consider to write the procedure of calibration. Authors have used high intensity to deliver the stimuli, is there any specific reason?

ROI is well explained.

Ocular channel is activated? If yes, please specify. I know authors have removed bad channels and bad blocks were visually inspected. An eye blink induces artifacts and has an amplitude similar to that of a response.

Results

Authors have used appropriate statistical analyses to prove the aim of study. A repeated measure ANOVA with between subject factors as group was used to assess hemispheric asymmetry in each component of CAEP (peak latency and amplitude). I feel it is two way repeated measure (? condition* 2 stimuli) with between subject factor as groups. Thus, I suggest authors to mention the factors (3*2*3). In P1, N1 and P2 latencies what is the post hoc test used? Sometimes authors have used condition and hemispheric asymmetry interchangeably. Consider to maintain the same term through out the manuscript.

Stimuli* condition result is mentioned and what about the interaction effect of stimuli* condition* group. Though main effect of 'group' is not significant but interaction of stimuli and condition may have an effect on group. Consider to give the result of stimuli* condition* group. In condition there was a significant difference and authors have used paired sample t test. There are three groups (normal, young adult and LD). If these three groups are considered then authors should use alpha corrections. Anyway a significant difference has come but it is prepared to use alpha corrected.

In the same figures the waveforms of NH and LD for different condition is required rather than representing individually.

Discussion should have been in the heading of

a) hemispheric difference on each component of CAEPs

1. Latency
2. Amplitude

b) Between groups on on each component of CAEPs

1. Latency
2. Amplitude

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Hearing aids, electrophysiology, speech perception, tinnitus

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Referee Report 29 January 2019

<https://doi.org/10.5256/f1000research.18618.r42063>



Sandeep Maruthy 

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I am happy to have reviewed the article 'Cortical auditory evoked potentials and hemispheric specialization of speech in individuals with learning disability and healthy controls: A preliminary study'. The need for the study is well supported by the literature, authors have used cogent method and the results are reported well in light of hemispheric asymmetry in children with Learning disability. The study has the potential to make significant contributions to the understanding of hemispheric specialization in speech processing. However, I have few important concerns which I would like the authors to address, in order to bring more clarity and precision in the presentation of their findings.

Abstract

- It is not appropriate to state that there are no ERP studies. You may state that 'there is dearth of studies'.
- 'However, there is no event related potential (ERP) evidence, hence the main objective of the study is to explore hemispheric asymmetry using cortical auditory evoked potential (CAEPs) in normal hearing adults and also to compare the same in children with LD and healthy controls.' Split this into two sentences.
- 'main objective of the study is to explore hemispheric asymmetry using cortical auditory evoked potential (CAEPs) in normal hearing adults and also to compare the same in children with LD and healthy controls'. I am not convinced with this statement. I think the main objective of this study is

to assess hemispheric specialization in LD and the compare the same with a group of control subjects.

- The stimuli are syllables not consonants. The syllables should be uniformly reported in IPA.
- P1, N1 and P2 are independent components. Do not report as 'P1-N1-P2'.
- 'The current study results suggest no statistically significant difference between the two stimulus in monaural condition and absence of order effect in dichotic condition'. This is in which group?
- 'In healthy controls', who are the healthy controls?
- Overall, the abstract needs to be rewritten with the help of an English expert.
- In Dichotic tests, the two stimuli are presented simultaneously, not independently.
- 'CAEPs in DL is evidenced by larger amplitudes and shorter latencies over the left hemisphere'. Please specify the stimulus used in these studies (speech versus non-speech).
- Authors need to justify why the findings of independent studies on latency and amplitude cannot be taken together to understand the cortical dynamics. Why does a new study with both together need to be carried out?
- 'Stimulus-specific' instead of 'stimulus specific'.

Methods

- Avoid using the term 'healthy volunteers'.
- How did the authors ensure that the control participants did not have auditory processing deficits? In this study, it is not sufficient to ensure that they have normal hearing sensitivity.
- Syllables to be reported in IPA.
- How was LD diagnosed? Give more information about the degree of impairment.
- 6cm distance from whom?
- What does 'Extended data' refer to?
- What do authors mean by 'normal native speaker'?
- Write it as 'Speaker of Kannada' not 'Kannada speaker'.
- Define Kannada.
- I think the authors mean neutral tone and not 'normal intonation'.
- Why were participants not tested with behavioural DL? If tested, they could have been sure of normal binaural integration in their control participants. Further, relating the ERP findings with behavioural DL would have shed more light into the underlying mechanisms.
- What was the final duration of the stimuli?
- Was any kind of quality judgement done for the stimuli?
- Was normalization carried out for the two stimuli to keep the intensity equivalent?
- Consider providing waveforms of the stimuli, maybe with the time alignment as presented in the experiment.
- CEAPs to be changed to CAEPs.
- 'A 32 channel electrode cap used with combined mastoid as reference'. Add 'was' in between.
- The spacing between the digit and the corresponding unit (For example, 100 Hz) is not correct in most places.
- 'artifact rejection was also be done offline' - please rephrase.
- 'The stimulus was presented in 3 conditions'. Please rephrase this because you presented more than one stimulus in the third condition.
- 'In both, the monaural conditions patient will be asked to watch a silent movie and ignore the stimulus presented to the ear.' Needs to be changed to past-tense.
- Same comment for the next sentence.
- Why is it 'passive attention condition'? The authors, I believe, did not have an active attention condition.

- As I understand, the stimulus paradigm has not changed the order of the stimuli but only the ear to which they were delivered. In terms of time, in dichotic condition, /pa/ and /ta/ were presented simultaneously. In such a case, it should not be termed as '.
- The paragraphs on stimulus effect and the order effect needs to be rewritten to bring better clarity to the readers.
- I suggest that the section on 'stimulus' be shifted before the section on 'LLR recording'
- What was the total number of stimulus presentations?
- What was the task of the participants, particularly during dichotic listening? If they were passive, what were they doing during the recording?
- timelocked should read as 'time-locked'.
- Low pass should read as low-pass. Similarly for high pass.
- 'In the current study, two 2 ROIs with three electrodes in each hemisphere were selected, here in after synonymously referred to as right and left hemisphere electrodes'. Split this into two sentences.
- 'Here in after' should read as 'Hereafter'.
- 'the latency of N1 component from C3, FC3, and CP3 are 108ms, 110ms, 112ms respectively; then the left hemispheric ROI is 110ms'. Start the sentence with an 'if'.
- How was 'mean amplitude' measured?

Results

- I do understand that there was no significant difference between /pa/ and /ta/ in their latency or amplitude. That does not mean that there were no differences at all. Therefore, I am not convinced that the LLRs elicited for two different stimuli are clubbed together. This is likely to increase the variability in the data and mask subtle differences if any in the future analysis.
- I do see changes in the latency and amplitude LLR for different stimuli in the grand average waveform. Therefore, instead of comparing the mean amplitudes and mean latencies, a point-to-point comparison of the waves would have given a better idea of the differences between the stimuli.
- 'significant main effect between groups' should be written as 'significant main effect of group'.
- 'Though children with normal hearing had shorter latencies than children with LD, the latency difference did not reach significance'. Did children with LD have hearing loss? Please use the name of the groups uniformly.
- 'p' is not reported uniformly. In some places the exact 'p' is reported while in others, it reports p as <0.01. Please bring uniformity.
- The names of groups in tables and figures are not acceptable. Participants with LD cannot be termed as 'LDs'. Other groups cannot be termed as 'normal groups'.
- Figure 1 is expected to represent data of P1, but it has latency of P2.
- Giving the same data in tables as well as figures will add redundancy. Please give only one.
- The title of the figures and tables needs to be lot more descriptive and precise.
- Number of decimal points given in the table could be restricted to 2.
- Consider clubbing together all the grand average waves in one panel if the journal permits.

Discussion

- Rephrase 'While the preliminary aim of the study understands the neurophysiology of dichotic processing, the fact that monaural differences in CEAPs itself are not well understood'.
- 'CEAPs' to be changed to 'CAEPs' - throughout the article.

Conclusions

- 'The study failed to categorize learning disability subjects based on their specific learning disability'. This was not the objective anyway and no analysis was meant to do this. Why is this coming here?
- Again, avoid using the term LDs.
- Conclusion will be better if it is precise and short. Present the most salient contributions for your research here. This can be followed by caveats and limitations.
- Please write the implications of your findings.

General Comments

- The manuscript needs a thorough editing of grammar, punctuation and spellings.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Audiology, Auditory evoked potentials, Immittance audiometry

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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