A Study of Late Auditory Event Related Potentials Related to P300 Responses in Individuals with Learning Disabilities

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ABSTRACT

This cross sectional study is focused on finding P_{300} response by changing the interstimulus interval (Gross and fine discrimination of signal) in 50 subjects with learning disabilities. P_{300} recording on these ears produced long latency and reduced amplitude.

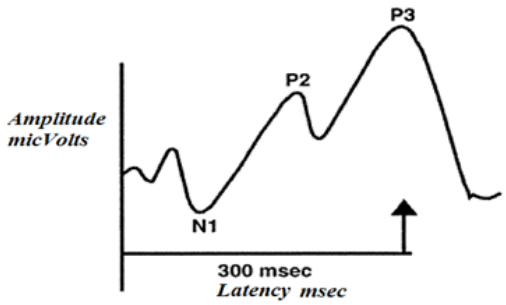
Results shows in gross and fine discrimination of signal, the latency of the P_{300} response increases and the amplitude decreases as the Inter-stimulus Interval (ISI) decreases. Among gender description, latency of both gross and fine discrimination of signal, female (Gross mean 408 with SD of 20.99 and fine mean 443.92 with SD of 31.06) appeared better P_{300} as compared to male (Gross mean 436.16 with SD of 31.99 and fine mean 459.60 with SD of 29.95). Learning disabilities individuals show auditory or cortical processing difficulty, and they needed longer inter stimulus intervals to separate two sounds than did normal individuals.

INTRODUCTION

Children with learning disabilities (LD) represent a unique challenge for audiologists. They have problem in reading, working memory, sensory motor coordination and early sensory processing. Characteristics of children with learning disabilities are many. It includes developmental dyslexia (reading difficulties) and / or problems with arithmetic calculation (dyscalculia). Soft or mild neurological signs may also be observed in children with learning disabilities. Often poor academic performance in grade school is the first indication of LD (Hall, 1992). They also have problems in working memory – sensory motor – coordination and early processing. Thus LD is thought by many to be secondary to a central nervous system dysfunction mainly due to a central processing disorder (CAPD). Children with CAPD have problems in comprehending speech. They have normal hearing sensitivity but have problems in analyzing and interpreting sensory information received by ears. The localization of the processes responsible for learning disabilities can be understood by the abnormalities of the neuronal processing system.

In evaluating CAPD in children with LD, the audiologist commonly administers a battery of behavioral tests of central auditory function. These tests seem to have less specificity in their result (Bureigh&Whileford, 1995). Thus, in an effort to enhance the objectivity in the assessment, electrophysiological tests are introduced. Of these responses the most studied has been the P_{300}component (Gollegy, Musiek&Verkest, 1998).

P_{300} is a long latency cortical endogenous potential occurring at about 300 ms(Barren, John, Sutton& Zubin, 1965). P_{300} can be taken as a measure or index of stimulus processing. It appears to have potential value in the assessment of hearing sensitivity and auditory processing abilities. Another distinct advantage of the P_{300} response is that it is less dependent on the physical characteristics of stimulus employed than are the exogenous potentials although it does require attention to task relevant stimulus items (Butcher, 1983).



The simplest of these conditions is the “odd ball paradigm”. “One stimulus” or “a frequent and predictable stimulus” (the standard signal), generates an auditory late response. The other stimulus, which is infrequent (rare) and unpredictable and different in some way from the first signal – the oddball or target signal – produce a positive wave in latency region of 300ms. However, the P_{300} may be recorded in normal subjects as early as 250 ms or late as 400ms and may not necessarily be the third major component in waveform (Jeon&Polich, 2001).

Although P_{300} is reported to be highly variable which makes the effectiveness of this index uncertain (Baran, Museik&Pinheriro, 1992) there are sufficient studies to prove that age matched

P_{300} results have high efficacy (Howard, Polich& Starr, 1985).

P_{300} is also referred to as "P3" or "P3b" (Stapells, 2002) and is usually recorded using an active listening paradigm with the subject responding to the deviant stimulus, whereas mismatch negativity (MMN) is a pre attentive response that is usually recorded with the subject ignoring the stimuli (Schroger&Wolff, 1998).

Duffy (1986) used long latency auditory and visual electrophysiological measures in the investigation of children who are Learning Disabled (LD) and children who have Dyslexia. Using the data to form topographic maps, he showed that boys with Dyslexia could be differentiated from normal control subjects. Long latency Auditory Evoked Responses were also used by Ollo& Squires (1989), in the evaluation of LD children. They found a decrease in the amplitude of the parietal slow wave in the LD subjects compared to age-matched normal control subjects.

The American Speech-Language-Hearing Association (ASHA) Task Force on Central Auditory Processing (1996) concluded that electrophysiological measures are useful for the diagnosis of central auditory processing disorders (CAPDs) but acknowledged that further research is needed to establish the clinical utility of middle and late evoked potentials.

More recently, the Bruton Conference held at the Collier Center in Dallas (Chermak, 2001; Jerger&Musiek, 2000) produced the recommendation that a minimal test battery for the diagnosis of auditory processing disorders (APDs) in school-aged children should include Auditory Brain stem Response test (ABR) and Middle Latency Response(MLR) testing.The P3 event-related response was included in the list of optional procedures that are potentially useful for strengthening the diagnosis of Auditory Processing Disorders (APD) and LD.

The cortical P1-N1-P2 evoked potentials that occur within about 300 ms after stimulus onset in adults depend primarily on the physical properties of the stimulus. Discriminative cortical potentials elicited using an oddball stimulus paradigm result from either preconscious (e.g., MMN) or conscious (e.g., P3b) perception of a change in the auditory stimulus and hence have been referred to as "processing- contingent potentials" (Stapells, 2002).

Both obligatory and discriminative potentials have been investigated as objective indices of central auditory function since they correlate well with perception and discrimination of auditory stimuli (Hyde, 1997; Stapells, 2002) and are abnormal in individuals with brain lesions affecting auditory cortical regions (Hood et al., 1994).

Cortical Auditory Evoked Potentials (CAEP) generators include primary auditory cortex, auditory association areas, frontal cortex, and sub cortical regions (Pictonet al., 1999; Stapells, 2002).Although these responses are present in infants (Stein Schneider et al., 1992), they undergo considerable maturational changes, and some cortical potentials may not be fully mature until close to adulthood (Ponton et al., 2002). In infants and young children, CAEPs are dominated by P1, which becomes earlier and smaller as N1 and P2 begin to emerge in the waveform at about 8 to 10 years of age (Ponton et al., 2002; Sharma et al., 1997).

These maturational changes complicate the use of CAEP for diagnosis of APD since more extensive normative data are required than for the earlier-maturing evoked potentials. The scalp distribution of P1, Nl, and P2 is normally symmetric with maximal amplitude near the vertex (Pictonet al., 1999), but, as for MLR wave Pa, a contra lateral hemisphere advantage (earlier latencies, greater amplitudes) has been reported in adults (Pictonet al., 1999; Pontonet al., 2002;Verkindtet al., 1995). The amplitude, latency, and scalp distribution of the discriminative cortical potential P3 depends on subject age as well as state of arousal and attention (Johnstone et al., 1996; Oadeset al., 1997;Pearce et al., 1989; Squires et al., 1975; Stapells, 2002).

Both obligatory and discriminative CAEPs have been investigated in children and adults thought to have APD. Researchers have found a variety of P1-N1-P2 and P3 abnormalities, including increased absolute and inter wave latencies (Arehole, 1995; Bruneauet al., 1999; Clontz&Jirsa, 1990; Seri et al., 1999; Tonnquist-Uhlen, 1996a, 1996b), reduced N1 amplitude (Bruneauet al., 1999; Cunningham et al., 2001; Seri et al., 1999; Wiolandet al., 2001), reduced P3 amplitude (Clontz&Jirsa, 1990), increased (Bernal et al., 2000) or decreased (Tonnquist-Uhlen, 1996b) P2 and N2 amplitudes, and increased hemispheric asymmetry (Jerger et.al, 1991; Mason & Mellor, 1984).

A number of studies have shown reduced MMN amplitudes (and sometimes increased latencies) in adults and children with speech/language, reading, or learning difficulties (Baldeweg et al., 1999; Bradlow et al., 1999; Kraus et al., 1993, 1996; Korpilahti&Lang, 1994; Schulte-Kame et al., 1998, 1999, 2001). Further research is required, however, before MMN can be regarded as a clinical tool for APD assessment owing to the small amplitude and high variability of the response (Dalebout&Fox, 2001;McGee et al., 2001; Picton et al., 2000).

Thus main focus on this study is to discuss the use of P_{300} in the diagnosis of learning disabilities in which the underlying problem may be connected to cortical or cortical auditory processing.

The recent advances in cortical event related potential has made it possible to provide the means to uncover the important aspects of neural basis of such disorders. The present study is undertaken to evaluate the auditory event related potentials and related P_{300} component in children with learning disabilities.

LITERATURE REVIEW

The P_{300} (P3) is an auditory evoked potential (AEP) referred to as a “cognitive” or “event-related response” occurring in the 300ms latency region with a large positive voltage peak, hence “P”, after an acoustic stimulus. Like most long latency potentials (LLP), the P_{300} is an endogenous response, highly dependent upon subject attention to auditory stimuli.

The P_{300} is typically recorded with the subject attending or listening for a rare, “oddball”, or target stimulus that is presented along with frequent stimuli. The stimulus that occurs, majority of the time is the “frequent stimulus” and the infrequent stimulus is known as the “oddball”. In the “oddball” test paradigm, two stimuli are presented with one occurring between 80%

and 85% of the time and the other occurring between 15% and 20% of the time. The participant is asked to respond, usually by counting out loud or by pressing a button, when the oddball stimuli are perceived. Polich (1996) pointed out that the major peak is a large positive voltage (5μV) occurring approximately 300msafter the rare or "oddball" response.

Chauvel, Halgren&Marinkovic(1998) postulated that the P_{300} is classified as an endogenous potential, meaning that it originates from within the subject and is dependent on the subject attending to or processing the stimuli.

According to Hall, 1992 P_{300} is not directly impacted by the stimulus characteristics. Attention and state of arousal are the two most important factors in eliciting a P_{300}response. In order to adequately assess the P_{300} response, the subject must actively attend to the oddball stimulus and be able to discriminate it from the frequent stimulus. If the subject is unable to discriminate the oddball from the frequent stimulus, then the P_{300} will not be present.

P_{300} amplitudes and latencies are used clinically to assess patients with Alzheimer's disease, Parkinson's disease, and dementia. Patients with these neurodegenerative disorders tend to have prolonged P_{300} latencies, believed to be related to changes in neurotransmitters (Kugler, Platt&Taghavy, 1993).

Herbst&Polich(2000) exposed that the P_{300} can be extremely valuable tool when evaluating general cognitive function. P_{300} latencies have been shown to increase, while amplitudes decrease, with decreases in cognitive function (Howard, Polich& Starr, 1983).

Some studies (Eggermont, 1988; Kurtzberg&Vaughan, 1992)postulated that the majority of Event Related Potential (ERP) waves are thought to reflect the synchronous activity of neural systems generated by excitatory and inhibitory post-synaptic potentials. Thus, the maturational changes in ERP morphology might to a large extent involve changes in intra-cortical synaptic organization and synaptic density. Kurtzberg&Vaughan (1992) suggested that the ERP amplitude is proportional to the magnitude of synaptic activation.

The Event Related Potential (ERP) peak amplitudes was observed for auditory (Kushnerenko etal., 2002) and visual modality in infants (Kurtzberg&Vaughan, 1992), for auditory modality in children (Ponton etal., 2000), and for both the visual and auditory modalities together (Courchesne, 1990). The increase in consistency of brain response with age (Crow& Thomas, 1994), resulting in decrease of the trial-to-trial latency variability also contributes to the shortening of the ERP peak latencies. The latency changes in one ERP peak might also be affected by the maturational changes in another, overlapping peak (Kushnerenko et al., 2002; Ponton et al., 2000).

The amplitude of the second major positive peak markedly decreased between 6 and 9 months, while the amplitude of the preceding negativity (N200) increased (Kurtzberg etAl., 1986;Kushnerenko et al., 2002).

The P_{300} is dependent upon stimulus probability and inter-stimulus interval (Ceponiene et al., 2002; Kurtzberg etal., 1995).

Several auditory detection components have been described in infants. In the majority of

the studies, a positivity peaking at about 300 ms was observed (Baillet&Dehaene-Lambertz, 1998; Dehaene-Lambertz& Pena, 2001; Dehaene&Gliga, 2004; Friedrich et al., 2004; Winkler etal., 2003).

A P_{300} response usually referred to as the P3a component, can also recorded with a passive measurement paradigm. That is the subject does not attend to the rare stimulus but, rather it ignores both frequent and rare stimuli. In this respect, the passive P3a component is an "automatic" response. As a rule, P3a component is shorter in latency (about 250ms), smaller in amplitude, and habituates more rapidly than the traditional P3 (P_{300}) wave. (Courchesne, Glaambos&Hillyard, 1975; Katayama &Polich, 1998; Polich, 1986; Rugg et al., 1993; Squires et al., 1975).

The P3a component appears to be related of the P_{300} response, an "alerting response that most likely originates from neural sources related to initial attention allocation" (Katayama&Polich, 1998) with engagement of memory and more attention processing and resources, the later latency and conventional P_{300} (P3b) is generated with maximum amplitude in parietal region (Katayama &Polich, 1998).

The P_{300} is a positive-going potential with parietal maximum amplitude, and a peak latency of about 300–350 ms in young adults. On the assumption that theP_{300} reflects cognitive processing, it is used as a marker of cognitive changes in a variety of clinical groups and in studies of life span development (Bauer, 2001; Fjell&Walhovd, 2001; Goodin et Al., 1978; Polich, 1986, 1996; Reinvang, 1999; Solbakk et al., 1999, 2000; Ullsperger et al., 2000; Yamaguchi et al., 2000).

The component has been assumed to be relatively immune to the effects of physical characteristics of stimuli (Donchin et.al, 1978). This line of thought partly originates from the fact that P_{300} is elicited independently of the sensory modality of the stimulus (Regan, 1989). Still, some studies have been able to identify effects of stimulus factors such as tone intensity and frequency (Roth et al., 1982).

Papanicolaou et al. (1985) addressed the question of intensity effects by systematically varying the intensities in an auditory oddball paradigm from 15 up to 65 dB. Variations in intensity had an impact on P_{300} latency, but not amplitude. This was later also reported by Polich (1989).

Some studies (Cass &Polich, 1997; Polich&Sugg, 1995; Vesco etal.,1993) found that P_{300} amplitude increased and peak latency decreased with higher stimulus intensities. Vesco et al. (1993) also observed intensity – frequency interaction effect, as the higher stimulus frequencies (1000/2000 Hz) demonstrated stronger P_{300} latency age effects than did the lower frequencies (250/500 Hz).

Covington &Polich (1996) further showed that intensity effects could be obtained for both auditory and visual modalities, and concluded that the specific nature of auditory stimulus factors contribute to P_{300} measures directly and robustly.

P_{300} is related to cognitive and neuropsychological measures, that is, measures of a type of intelligence that is applied to novel problems and is relatively independent of educational and cultural influences (Egan et al., 1994; Fjell&Walhovd, 2001; Jausovec, 2000; O'Donnell et al., 1992; Reinvang, 1999).

The relationship between P_{300} and cognitive function is robust, and has been demonstrated in homogenous samples as well as life span samples. P_{300} latency is often regarded as a measure of the relative timing of the stimulus evaluation process (Coles etal., 1995),Thereby constituting a marker of speed of processing. P_{300} amplitude depends on the synchronized firing of large numbers of neurons, and is held to index attentional resource allocation (Polich, 1996). Both processing speed and attentional allocation are crucial in cognitive performance. A relationship between cognitive functioning and P_{300} is thus expected.

Some works (Bauer, 2001; Fjell&Walhovd, 2001; Goodin etal., 1978; Polich, 1986, 1996; Reinvang, 1999; Solbakk etal., 1999, 2000; Ullsperger etal., 2000; Yamaguchi etal., 2000)revealed that the P_{300} event-related potential (ERP) is typically elicited by tasks where two types of stimuli of unequal probability are presented, and attention is to be paid to the infrequent ones.

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McPherson&Salamat (2004) recorded behavioral (pushing the button) reaction times for the presentations of frequent signals and reported a direct relation between Inter-stimulus Interval (ISI) and both behavioral reaction time and P_{300} latency values. That is, longer ISIs were associated with longer reaction times and P_{300} latency values. Also, amplitude of the P_{300} response decreased as ISI's increased.

In dual task paradigm, Doerfling, Fowler&Singhal (2002) found that the subject performance for visual task during auditory P_{300} measurement involving dichotic listening task was associated with decreased amplitude of P_{300}. As difficulty of the visual task increases and attention is allocated more to visual modality, amplitude of the P_{300} reduces. Polich (1987) demonstrated that P_{300} latency was longer and amplitude larger when the subject silently counted the target signals vs. when the subject silently pressed a button with a thumb.

Johnson (1988) and Polich(1986) postulated that the latency of the P_{300} response increases and the amplitude decreases as theInter-stimulus Interval (ISI) increases. Probability of the occurrence for the standard and the target stimuli affects P_{300} response characteristics. Within certain limits, amplitude of the P_{300} response decreases as the probability of the target stimulus increases (Donchin, Duncan & Johnson, 1977), whereas the effect of target stimulus probability on P_{300} latency is minimal (Bondurant&Polich, 1977).

There is a direct relation between latency of the P_{300} response and the speed of information processing (Courchesne, 1978). With faster information processing, including quicker recognition and categorization of the stimulus, P_{300} latency is shorter. Conversely, P_{300} latency increases

directly with complexity of the processing task and with short term memory demands (Howard, Polich&Starr, 1983).

Patient populations with progressive deficits in cognitive function characteristically show increases in P_{300} latency (Polich&Herbst, 2000). Investigations in normal subjects show clearly that P_{300} latency is directly related to the speed with which a subject classifies signals, updates memory and allocates attention. Patient populations with progressive deficits in cognitive function characteristically show increases in P_{300} latency (Polich&Herbst, 2000)

Nonetheless, changes in cognitive status (decline and improvement) for most neurological and psychiatric diseases can be tracked with the P_{300} response, and the P_{300} response has value in documenting the therapeutic effectiveness of medical management of selected central nervous system diseases.

Davies, Kelly & Purdy (2002) describe findings for variety of auditory evoked responses (ABR, MLR, LLR and P_{300}) recorded from children with learning disabilities (LD).The P_{300} response to standard and to target stimuli was significantly smaller amplitude and longer in latency for the children with learning disabilities versus control group.

Ganapathy, Heramba, Maru, Nikitha&Santhoshini (2002)studied P_{300} component in five children with learning disabilities (LD) and normal subjects with age range of 7 to 13 years. P_{300} was administered with tone burst stimuli using "oddball paradigm". Mean latency and amplitude were analyzed for both groups, the results showed significant differences in the mean latency and differences in discernibility of wave morphology and amplitude in P_{300} between children with confirmed learning disabilities (LD) and their age matched normal group.

METHOD

Goals

To find the significant difference in mean latency and wave morphology value of P_{300} component between children with LD.

To investigate significant variability within the LD group (inter subject variability).

To investigate how well the LD children can able to discriminate the Gross Frequency of signal and Fine Frequency of signal by changing the Rare and Frequent stimuli.

Study Design: Cross sectional study design

Study Centre: The study was carried out in the Department of Audiology, Mafraq hospital, Abu Dhabi.

Subjects: Convenient sampling was done for the period of March 2016 to October 2016. Randomly, participants were selected from the rehabilitation center within Mafraq Hospital and nearby private/governmental rehabilitation centers. Diagnosed Learning Disabled patients were selected from these centers and their therapists were requested to get permission from care takers and parents to contact directly. Out of all contacted, 59 subjects participated in the study and out of which, 50 subjects (50 pairs of ear) were selected for the testing (25 male and 25 female participants), based on academic performance with respect to reading, writing,

social relationship and speech and language development and below criteria.

Inclusion Criteria

Age Range: 7 – 20 (Chronological age)

Cognitive status (IQ): average IQ Level.

Visual – Spatial, Perceptual skills and auditory memory span: Adequate

Exclusion Criteria:

Peripheral hearing Loss

ENT complications

Medical associated complications.

Instrumentation: The following instruments were used in the study:

- Pure tone audiometer: A calibrated dual channel Grason-Stadler Inc-61; GSI-61 Clinical Audiometer was used to estimate the behavioral hearing thresholds.
- TDH-49 earphones
- Radio Ear B-71 bone vibrator
- Middle ear analyzer: A calibrated Middle ear analyzer (Grason-StadlerInc-Tympstar; GSI-Tympstar) was used to assess the middle ear status.
- Medelec Synergy –ULHORIE400 (Oxford Instruments) Used for assessing P_{300}.

Test environment:

All the tests were carried out in a sound treated room with permissible noise level.

Test Procedure

Preliminary Investigation:

Otoscopic examination and physical examinations were performed by ENT specialist

Pure tone audiometry

Modified Hughson-Westlake procedure (Carhart&Jerger, 1959) was used for air conduction and bone conduction hearing threshold estimation in all the participants.

Tympanometry

Individuals in this study presented with clear, unobstructed ear canals as determined by otoscopy. Acoustic Impedance testing was performed using a 226 Hz probe tone frequency using, GSI-Tympstar – Middle Ear Analyzer. Normal middle ear function was defined by tympanometry results of middle ear peak admittance within 0.3 to 1.4 mmho, middle ear pressure within -150 to +150 daPa, and ear canal volume from 0.6 to 1.7 cc (Margolis & Shanks, 1991).

These entire tests were performed to rule out any peripheral pathology in LD subjects which could possibly interact with P300 test results.

Core Investigation:

Cortical Auditory Evoked Potential (P300) will be carried out by using ***Medelec synergy ULHORIE400.***

Procedure:

P_{300} elicited in 'odd ball Paradigm' in which an rare stimulus occurred in a series of frequent stimuli and instruct the participant to mentally count the number of time rare stimuli occurred in series of frequent array of stimuli.

Settings:

Interval between the rare (Rs) and frequent (FS) stimuli frequency range will be varied by 1 octave frequency range for fine discrimination Eg.(RS 2000 Hz and FS 1000 Hz) and for gross discrimination of 2 octave frequency range been selected Eg (RS 500Hz and 2500Hz Fs). Stimulus waveform envelops will be (BACK MAN MODE) and filter setting low pass filter of 50Hz been selected.

Electrode Placement:

A Gold plate electrode would be used. The following electrode placement as recommended by Snyder, Hillyard and Galambos (1986) will be followed:

- None inverting: Cz, Fz
- Inverting : M1, M2
- Ground :Fpz

The non-inverting electrode is linked together with a jumper and care was taken to make sure that the electrodes impedance level and intra electrode impedance is less than 4 kΩ, in all the subjects.

Both ears will be tested by presenting a frequent stimulus of 500 Hz and a rare stimulus of 3000Hz tone burst and also 1000 Hz and 2 kHz for fine and gross discrimination of stimulus. The total stimulus presentation will be 200 and rare stimulus probability condition will be fixed at 20% and level will be adjusted at 80dBHL

Identification of Latency and amplitude of P300

P_{300} latency and amplitude measurements will be obtained in low pass filtering 0.1 to 100 Hz. The criteria given by Sutton et al. (1965) will be used to identify the latency and amplitude of P300. Latency measures will be made at the location of the largest slope in the peaks.

Identification of fine and gross discrimination of signal

Blackmann stimulus for frequent and rare stimulus will be used. Fine stimulus discrimination range of 1000Hz and 2000Hz will be used, and for Gross discrimination the range will be from 500Hz and 2500Hz. And identify the latency, amplitude, and also morphological changes in wave will be noted and taken for the study.

Statistical Analysis

The collected data was subjected to statistical analysis using SPSS version 17 for Windows (Chicago, Inc.) to do the descriptive analysis and to find out mean, standard deviation (SD), 'p' value to find out statistical significance from Student't' test of absolute latency and amplitude with respect to different age, gender, gross and fine discrimination of frequency to find out the relation between them.

RESULTS

P300 recording was done using in 'odd ball Paradigm' in which a rare stimulus occurred in a series of frequent stimuli and identified fine and gross discrimination of signal by Blackmann stimulus for frequent and rare stimulus used. Fine stimulus discrimination range of 1000Hz and 2000Hz will be used, and for gross discrimination the range will be from 500Hz and 2500Hz. And identify the latency, amplitude, and also morphological changes in wave noted on 50 participants with learning disabilities (25 male and 25 female participants with age ranges from 7 – 20 years) based on academic performance with respect to reading, writing and social relationships and speech and language development.

Table 1: *Represents the gender, Frequency and percentile*

Gender	Frequency	Percent (%)
Male	25	50.00
Female	25	50.00
Total	50	100.00

Mean age = 14.18, Standard Deviation (S D) =2.83, Age ranges from 7 to 19

The objectives of the present study were determining the significant difference in mean latency and amplitude (wave morphology) value of P_{300} component between children with LD.

Correlation between gross amplitude and gross latency

Table 2: *Means, Standard Deviations (SD), Minimum and Maximum ranges of latency and amplitude for gross discrimination of* P_{300}.

	Latency(ms)	Amplitude(µV)
N(ears)	50	50
Mean	422.08	2.62
SD(Std Deviation)	30.33	1.05
Minimum	378	0.12
Maximum	489	4.45

Average gross latency among the 50 subjects was 422.08±30.33 and average gross amplitude was 2.62±1.05. Latency ranges from 378 msto 489ms and Amplitude ranges from 0.12µV to 4.45µV.

Correlation between gross amplitude and gross latency using Spearman's rho Correlation Coefficient is – 0.20 (p value=0.16).There is a weak and not significant negative correlation between gross latency and gross amplitude.

Table 3: *Means, Standard Deviations (SD), Minimum and Maximum ranges of latency and amplitude for fine discrimination of* P_{300}.

	Latency (ms)	Amplitude(µV)
N	50	50
Mean	451.76	1.33
SD(Std Deviation)	31.22	0.84
Minimum	398	0.1
Maximum	498	3.17

Average gross latency among the 50 subjects was 451.76±31.22 and average gross amplitude was 1.33±0.84.Latency ranges from 398ms to 489ms and amplitude ranges from 0.1µV to 3.17 µV.

Correlation between fine amplitude and fine latency Spearman's rho Correlation Coefficient is -0.41 (p =0.003).There is a significant negative correlation between fine latency and fine amplitude.

The second objectives of the present study were determining significant variability within the LD group (inter subject variability).

Gender and age variability in fine and gross discrimination of signal.

Table 4: *Comparison of latencies in milliseconds (ms) among gender*

Male			Female	
	Gross	Fine	Gross	Fine
N(ears)	25	25	25	25
Mean	436.16	459.60	408.00	443.92
S.D(StdDeviation)	31.99	29.95	20.99	31.06
Minimum	378	399	378	398
Q_1	405.00	431.50	389.50	420.00
Median	448.00	467.00	409.00	438.00
Q_3	456.00	484.50	421.50	478.00
Maximum	489	498	448	489

Average gross latency among the males was 436.16±31.99. Grosslatency ranges from 378 to 489. 25th percentile (Q_1) of gross latency among the males was 405.00 and 75th percentile (Q_3) was 456 and Median was 448.

Average gross latency among the female was 408.00±20.99.Gross latency ranges from 378 to 448.25th percentile (Q_1) of gross latency among the females was 389.50 and 75th percentile (Q_3) was 421.50 and median was 409.

Average fine latency among the male was 459.60±29.95.Fine latency ranges from 399 to 498. 25th percentile (Q_1) of fine latency among the males was 431.50 and 75th percentile (Q_3) was 484.50 and Median was 467.

Average fine latency among the female was 443.92±31.06.Fine latency ranges from 398 to 489. 25th percentile (Q_1) of fine latency among the females was 420 and 75th percentile (Q_3) was 478 and Median was 438.

Figure 1: *Box plot diagram representing comparison of latencies in milliseconds (ms) among gender.*

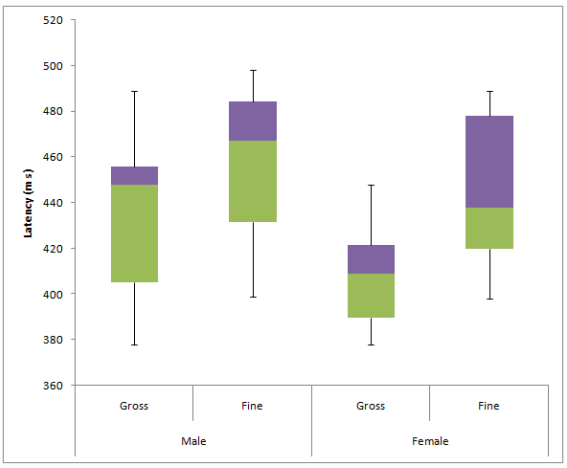


Figure 1, Box plot diagram describes gross and fine latencies among the male and female. Lower and upper end of the whisker of the box plot represents the minimum and maximum latency in each group respectively.

Lower border ofthe box represents the Q_1 (first quartile) and the upper border of the box represents Q_3 (third quartile). The line of separation of the two colored box i.e. the middle line represents the median.

On comparison, latency of both gross and fine discrimination of signal, female (gross mean 408 with SD of 20.99 and fine mean 443.92 with SD of 31.06) appeared better P_{300} as compared to male (gross mean 436.16 with SD of 31.99 and fine mean 459.60 with SD of 29.95)

Table 5: *Interpretation of comparison of gross latency between male and female*

	SEX	N	Mean	SD	t	p	
Gross Latency	Male	25	436.16	31.99	3.68	0.001	**
	Female	25	408	20.99			

** Significant at .01

Average gross latency among the male 436.16±31.99 and that among the females 408.00±20.99. The observed difference in gross latency among the male and female was statistically significant (p<.05). Gross latency among the male was significantly higher than that of females.

Table 6: *Comparison of fine latency between male and female*

SEX	N	Mean	SD	t	p	
Male	25	459.6	29.946	1.82	0.08	*NS
Female	25	443.92	31.064			

**not Significant (NS)*

Average fine latency, among the male is 459.6±29.95 and that among the females is 443.92±31.06. The observed difference in fine latency among the male and female was not statistically significant**.**

Table 7: *Comparison of amplitude according to gender*

	Male		Female	
	Gross	Fine	Gross	Fine
N(ears)	25	25	25	25
Mean	2.31	1.05	2.94	1.61
SD	1.17	0.74	0.83	0.86
Minimum	0.12	0.1	1.34	0.14
Q1	1.62	0.24	2.34	1.24
Median	2.35	1.24	2.45	1.45
Q3	2.93	1.37	3.56	2.44
Maximum	4.45	2.48	4.45	3.17

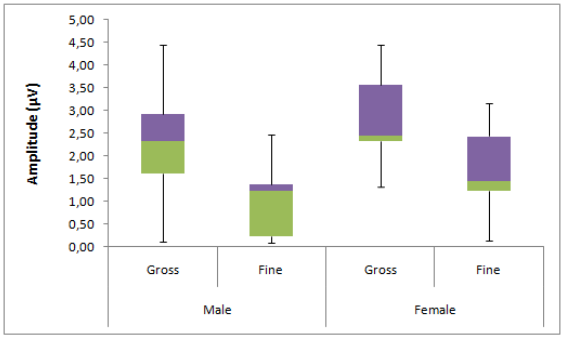
Average gross amplitude among the males was 2.31±1.17. Gross amplitude ranges from 0.12to4.45. 25th percentile (Q1) of gross amplitude among the males was 1.62 and 75th percentile (Q3) was 2.93 and Median was 2.35.

Average gross amplitude among the females 2.94±0.83.Gross amplitude ranges from 1.34to4.45.25th percentile (Q1) of gross amplitude among the females was 2.34 and 75th percentile (Q3) was 3.56 and median was 2.45.

Average fine amplitude among the male was 1.05±0.74. Fine amplitude ranges from 0.1to2.48.25th percentile (Q1) of fine amplitude among the males was 0.24 and 75th percentile (Q3) was 1.37 and Median was 1.24.

Average fine amplitude among the female was 1.61±0.86. Fine amplitude ranges from 0.14to3.17.25th percentile (Q1) of fine amplitude among the males was 1.24 and 75th percentile (Q3) was 2.44 and median was 1.45.

Figure 2: *Box plot diagram representing comparison of amplitude (µV) among male and female.*



In Figure 2, the box plot diagram describes gross and fine amplitude among the male and female. Lower and upper end of the whisker of the box plot represents the minimum and maximum amplitude in each group respectively. Lower border of the box

represents the Q1 (first quartile) and the upper border of the box represents Q3 (third quartile). The line of separation of the two colored box i.e. the middle line represents the median.

Table 8: *Interpretation of comparison of gross amplitude between male and female*

	SEX	N	Mean	SD	t	P	
Gross Amplitude	Male	25	2.31	1.17	-2.19	.034	*
	Female	25	2.94	.83			

*Significant at .05

Average gross amplitude among the male is 2.31±31.17 and that among the females is 2.94±.83. The observed difference in gross amplitude among the male and female was statistically significant (p<.05). Gross amplitude among the male was significantly higher than that of females**.**

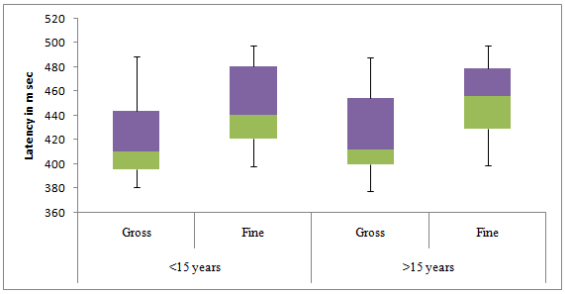
Table 9: *Interpretation of comparison of fine amplitude*

	SEX	N	Mean	SD	t	p	
Amplitude Fine	Male	25	1.05	0.74	-2.47	0.02	*
	Female	25	1.61	0.86			

*Significant at .05

Average fine amplitude among the males is 1.05±0.74 and that among the females are 1.61±0.86. The observed difference in fine amplitude among the male and female was statistically significant (p<.05). Fine amplitude among the females was significantly better than that of males.

Figure 3: *Box plot diagram representing comparison of latency according to age*



In Figure 3, the box plot diagram describes age group<15 years and >15 years. Lower and upper end of the whisker of the box plot represents the minimum and maximum latency in each group respectively. Lower border of the box represents the Q1 (first quartile) and the upper border of the box represents Q3 (third quartile). The line of separation of the two colored box in the middle line represents the median.

Average gross latency among <15 years age group 418.92± 28.55, ranges from 381 to 489, Median 410.5, Q1 and Q2 was 396, 444 respectively.

Average fine latency among <15 years age group 449.31± 33.21,ranges from 398 to 498, median 441,Q1 and Q2 was 420 and 480.25 respectively.

Average gross latency among >15 years age group 425.5±32.40,ranges from 378 to 488, median 412,Q1 and Q2 was 399.5 and 454.25 respectively.

Average fine latency among >15 years age group 454.42±29.39, ranges from 399 to 498, and median 456.5 respectively.

Table 10: *Interpretation of comparison of gross latency according to age*

Age	N	Mean	SD	t	p	
<15	26	418.92	28.55	-0.76	0.45	*NS
>15	24	425.5	32.40			

Not significant

Average gross latency among <15 years 418.92±28.55 and that among >15 years 425.5±32.40. The observed difference in gross latency among <15 years and >15 years was statistically not significant.

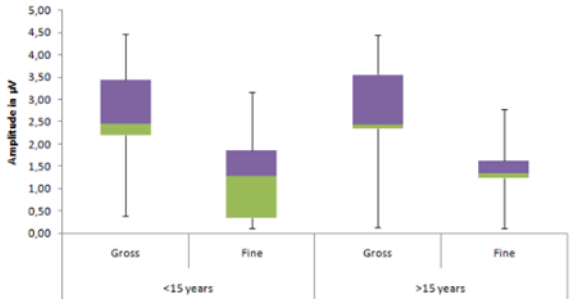
Table 11: *Interpretation of comparison of fine latency according to age*

Age	N	Mean	SD	t
<15	26	449.31	33.21	-0.57
>15	24	454.42	29.39	

*Not significant

Average fine Latency among <15 years 449.31±33.21 and that among >15 years 454.42±29.39. The observed difference in gross latency among <15 years and >15 years was statistically not significant.

Figure 4: *Box plot diagram representing comparison of amplitude according to gender*



In Figure 4, the box plot diagram describes age group<15 years and >15 years. Lower and upper end of the whisker of the box plot represents the minimum and maximum amplitude in each group respectively. Lower border of the box represents the Q1 (first quartile) and the upper border of the box represents Q3 (third quartile). The line of separation of the two coloured box i.e. the middle line represents the median.

Average gross amplitude among <15 years age group 2.55±1.02, ranges from 0.38 to4.45, median2.45, Q1 and Q2 was2.19 and 4.44 respectively.

Average gross amplitude among >15 years age group 2.70±1.11, ranges from 0.12 to4.45, median2.45, Q1 and Q2 was2.34 and 4.45 respectively.

Average fine amplitude among <15 years age group 1.31±0.92, ranges from 0.11 to3.17, median1.27, Q1 and Q2 was0.34 and 1.86 respectively.

Average fine amplitude among >15 years age group 1.35±0.77, ranges from 0.10 to2.77, median1.34, Q1 and Q2 was 1.23 and 1.63 respectively.

Table 12: *Interpretation of comparison of gross amplitude according to age*

Age	N	Mean	SD	t	p	
<15	26	2.55	1.02	-0.52	0.60	*NS
>15	24	2.70	1.11			

*Not significant

Average gross amplitude among <15 years 2.55±1.02 and that among >15 years 2.70±1.11. The observed difference in gross amplitude among <15 years and >15 years was not statistically significant.

Table 13: *Interpretation comparison of fine amplitude according to age*

Age	N	Mean	SD	t	p	
<15	26	1.31	.92	-.17	.86	*NS
>15	24	1.35	.77			

*Not significant

Average fine amplitude among <15 years 1.31±0.92 and that among >15 years 1.35±0.77.The observed difference in fine amplitude among <15 years and >15 years was not statistically significant.

The third objectives of the present study were determining how well the LD children can able to discriminate the gross frequency of signal and fine frequency of signal by changing the rare and frequent stimuli.

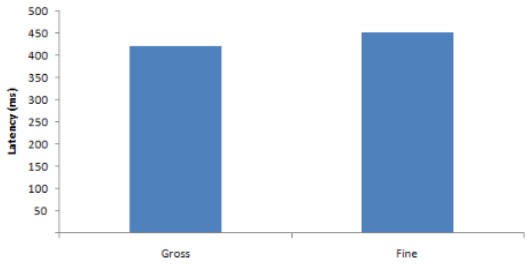
Table 14: *Comparison of gross and fine latency*

	N	Mean	SD	t	p
Gross	50	422.08	30.33	14.08	<.001 ***
Fine	50	451.76	31.22		

*** Significant at .001

Average gross latency was 422.08±30.33 and that of the fine latency was 451.76±31.22. Average gross latency was significantly lesser than that of fine latency (p<.05). Among the LD subjects gross latency was significantly better than that of the fine latency

Figure 5: *Bar Graph representing gross and fine latency among the LD subjects*



In Figure 5, x-axis represents gross and fine discrimination of signal and y-axis represents latency in milliseconds (ms).Among the LD subjects gross latency was significantly better than that of the fine latency.

Table 15: *Comparison of gross and fine amplitude*

	N	Mean	SD	t	P
Gross	50	2.62	1.05	14.38	<.001
Fine	50	1.33	0.84		

*** Significant at .001

Average gross amplitude was 2.62±1.05 and that of the fine amplitude was 1.33±0.84.Average fine amplitude was significantly lesser than that of gross amplitude (p<.05). Among the LD subjects gross amplitude was significantly better than that of the fine amplitude.

Discussion

The objectives of the present study were determining the significant difference in mean latency and amplitude (wave morphology) value of P300 component between children with LD. P_{300} was done by using fine stimulus discrimination range of 1000Hz and 2000Hz, and for gross discrimination range from 500 Hz and 2500 Hz and identified the latency, amplitude, and also morphological changes in wave noted on 50 participants with learning disabilities.

Correlation between gross amplitude and gross latency was done. Spearman's rho Correlation Coefficient obtained weak negative correlation (-0.20, p=value=0.16) between gross latency and gross amplitude. This indicates that P_{300} amplitude decreases while latencies increase.P_{300} latencies have been shown to increase, while amplitudes

decrease, with decreases in cognitive function (Howard, Polich& Starr, 1983).The latency of the P_{300} response increases and the amplitude decreases as the Interstimulus Interval (ISI) increases (Gross discrimination of signal postulated by Johnson, 1988; Polich,1986).

Correlation between fine amplitude and fine latency was done using a Spearman's rho Correlation Coefficient, and anegative correlation (-0.406, p=value=0.003).wasobtained. There is a significant negative correlation between fine latency and fine amplitude. This indicates that P_{300} amplitude decreases while latencies increase. P_{300} latencies have been shown to increase, while amplitudes decrease, with decreases in cognitive function (Howard, Polich& Starr, 1983).

The second objectives of the present study were determining significant variability within the LD group (inter subject variability).

In the present study, variability across the LD subjects, taken as among gender and age variability, in fine and gross discrimination of signal. On observation, average gross latency among the male 436.16±31.996 and that among the females 408.00±20.996. The observed difference in gross latency among the male and female was statistically significant (p<.05). Gross latency among the females was significantly better than that of males. Among learning disabilities subjects, female subjects will have better gross latency P_{300} than males. (Fleming, Hales,Ohran, Shipp,Steffensen,&Stobbs, 2008)

On observation, average fine latency among the male 459.6±29.95 and that among the females 443.92±31.06. The observed difference in fine latency among the male and female was not statistically significant. Learning-disabled children needed longer inter-stimulus intervals to separate two sounds than did normal readers. LD has also been found to be less sensitive than normal readers to changes in amplitude and latency (Menell et al., 1999; McAnally& Stein, 1997).

On observation, average gross amplitude among the male 2.31±31.17 and that among the females 2.94±.83. The observed difference in gross amplitude among the male and female was statistically significant (p<.05). Gross amplitude among the females was significantly better than that of males.P_{300} amplitude was found to be larger in females (Johnston & Wang, 1991).

On observation, average fine amplitude among the male 1.05±0.74 and that among the females 1.61±0.86. The observed difference in fine amplitude among the male and female was statistically significant (p<.05). Fine amplitude among the females was significantly better than that of males. This difference found between females and males might be in accordance with the greater allocation of attentional resources to irrelevant auditory stimuli shown by the larger P300 amplitude and better P300 latency for females as compared to males. It may also be due to differences in processing. The findings may also suggest that the P300 reflects colossal size and inter-hemispheric transmission efficacy.

In the present study, comparison of gross latency according to age, observed average gross latency among <15 years 418.92±28.55 and that among >15 years 425.5±32.40. The difference in gross latency among <15 years and >15 years was not statistically significant, (p=0.45). And comparison of fine latency, average fine

latency among <15 years was 449.31±33.21 and that among >15 years was 454.42±29.39. The observed difference in gross latency among <15 years and >15 years was not statistically significant, (p=0.57). P_{300} latency and aging suggest a general increase in latency with advanced age (Polich, 1996). In the present study among the LD children gross and fine latency were statistically not significant in <15 years and >15 years.

Comparison of gross amplitude according to age, Average gross amplitude, among <15 years 2.55±1.02 and that among >15 years 2.70±1.11. The observed difference in gross amplitude among <15 years and >15 years was statistically not significant. (p=0.60).P_{300} amplitude in adolescents has demonstrated that auditory P_{300} gross amplitude increases with age (Bauer &Hesselbrock, 2003; Hill et al., 1999; Ladish&Polich 1989; Polich et al., 1990).On observation, average fine amplitude among <15 years 1.31±0.92 and that among >15 years 1.35±0.77.The observed difference in fine amplitude among <15 years and >15 years was not statistically significant (p=0.86).

In the present study, among LD children gross and fine amplitude were statistically not significant in <15 years and >15 years. The reason may be due to increased variability in subjects P300 responses.

The third objectives of the present study were determining how well the LD children can able to discriminate the gross frequency of signal and fine frequency of signal by changing the rare and frequent stimuli.

In the present study, comparison of gross and fine latency among the LD subjects,on observation average gross latency was 422.08±30.33 and that of the fine latency was 451.76±31.22. Average gross latency was significantly lesser than that of fine latency (p<.05). Among the LD subjects gross latency was significantly better than that of the fine latency.

On observation of gross and fine amplitude, observed average gross amplitude was 2.62±1.05 and that of the fine amplitude was 1.33±0.84.Average fine amplitude was significantly lesser than that of gross amplitude (p<.05). Among the LD subjects gross amplitude was significantly better than that of the fine amplitude.

In the present study, gross discrimination of P_{300} findings reveal that, longer ISIs (Inter-stimulus Interval or gross discrimination) was associated with better P300 latency and amplitude values, as compared to fine or short Inter-stimulus Interval.(Johnson&Polich, 1988).

SUMMARY AND CONCLUSION

P_{300} is a long latency cortical endogenous potential occurring at about 300ms (Barren, John, Sutton & Zubin, 1965). P_{300} can be taken as a measure or index of stimulus processing. It appears to have potential value in the assessment of hearing sensitivity and auditory processing abilities.The simplest of these conditions is the “odd ball paradigm”. “One stimulus”, “a frequent and predictable stimulus” (the standard signal), generates an auditory late response. The other stimulus, which is infrequent (rare) and unpredictable and different in some way from the first signal (the oddball or target signal) produce a positive wave in latency region of 300ms. The P300 is dependent upon stimulus probability and inter-stimulus interval (Ceponiene et al., 2002;Kurtzberg et al.,

1995). Compare to cortical endogenous P300 response with long inter-stimulus interval holds additional advantage by providing information on cortical processing (Bondurant &Polich, 1977; Courchesne, 1978).There is limited data available on inter-stimulus interval changes in P_{300} both in normal and pathological condition.

The present study focused on finding P_{300} response by changing the inter-stimulus interval (gross and fine discrimination of signal) in 50 subjects with learning disabilities. P_{300} recording on these ears produced long latency and reduced amplitude. Results shows in gross and fine discrimination of signal, the latency of the P_{300} response increases and the amplitude decreases as the Inter-stimulus Interval (ISI) decreases (fine discrimination of signal)with decreases in cognitive function, as postulated by Johnson (1988) andPolich (1986). Latencies have been shown to increase, while amplitudes decrease, with decreases in cognitive function (Howard, Polich& Starr, 1983).It was apparent when compared to amplitude –latency function in learning disabilities individuals (Davies, Kelly& Purdy, 2002; Ganapathy, Heramba, Maru,Nikitha, &Santhos, 2002). This can be attributed to cognitive function, attention processing and memory in LD (Katayama &Polich, 1998).

In the present study, among gender description, latency of both gross and fine discrimination of signal, female (gross mean 408 with SD of 20.996 and fine mean 443.92 with SD of 31.064) appeared better P_{300} as compared to male (gross mean 436.16 with SD of 31.996 and fine mean 459.60 with SD of 29.946). Among learning disabilities female subjects will have better gross latency P_{300} than males. (Fleming, Hales,Ohran, Shipp, ,Steffensen,&Stobbs, 2008) and gross amplitude and fine amplitude among the females was significantly better than that of males.P300 amplitude was found to be larger in females (Johnston & Wang, 1991).P_{300} amplitude depends on the synchronized firing of large numbers of neurons, and is held to index attentional resource allocation (Polich, 1996). Both processing speed and attentional allocation are crucial in cognitive performance. A relationship between cognitive functioning and P_{300} is thus expected. On normal children P300 responses would be reduced in female as compare to male because of maturational changes in female (Rebecca et.al). However, as in the present study, females with learning disabilities had better P300 response than male.

In the present study, the observed difference in latency and amplitude among <15 years and >15 years was not statistically significant. P_{300} latency and aging suggest a general increase in latency with advanced age (Polich, 1996).P_{300} amplitude in adolescents has demonstrated that auditory P_{300} gross amplitude increases with age. ((Bauer &Hesselbrock, 2003; Hill et al., 1999 Ladish&Polich, 1989; Polich et al., 1990).

Individuals with learning disabilities, cognitive function characteristically show increases in P_{300} latency and reduced amplitude (Herbst&Polich, 2000).

In the present study, comparison of gross and fine latency among the LD subjects, gross latency was significantly better than that of the fine latency. And comparison of gross and fine amplitude among the LD subjects, gross amplitude was significantly better than that of the fine amplitude.Gross

discrimination of P_{300} findings reveal that, longer ISIs (Inter-stimulus Interval or gross discrimination) was associated with better P300 latency and amplitude values, as compared to fine or short Inter-stimulus Interval.

It can be concluded that, Individuals with Learning Disabilities (LD) showed evidence for poor P_{300} responses. Fine discrimination will be more exaggerated than that of gross discrimination of acoustic signal according to gender and age. As learning disabilities individuals show auditory or cortical processing difficulty, they needed longer inter stimulus intervals to separate two sounds than did normal individuals.

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