# EFFECTS OF INTENSITY DEVIANCE ON MISMATCH NEGATIVITY

**Register No. M9808**

**An Independent Project Submitted as part fulfillment**
**for the first year M.Sc. (Speech & Hearing ) to University of Mysore.**

**ALL INDIA INSTITUTE OF SPEECH AND HEARING MSORE-570006**
**MAY - 1999**

*Dedicated to*

*St. Gregorious*

# Certificate

*This is to certify that the independant project entitled "Effects of intensity deviance on Mismatch Negatioity" is a bonafied work done in part fulfillment for the degree of faster of Science (Speech and Hearing) of the student with Register No. 949608.*

Director

*Mysore*
*May 1999*

*All India Institute of*
*Speecb & .Hearing,*
*Mysore - 570006*

# Certificate

*This is to certify that the independent project entitled "Effects of intensity deviance on Mismatch Negativity" has been prepared under my supervision and guidance.*

*Mysore*

*May 1999*

Vanaja C.S.

*Lecturerin Audiology*

*Dept. of Audio/ogy*

*AIISH .Mysore- 570006*

# Declaration

*I hereby declare that this independent project entitled " Effects of intensity deviance on mismatch negativity " is the result of my own study under the guidance of Mrs. Vanaja C.S. Lecturer in Audiology, department of Audiology. All India Institute of (Speech and Hearing, Mysore, and has not been submitted earlier at any other University for any other diploma or degree.*

*Mysore* *Register:No.M9808*
May, *1999*

*A thought to prospective readers*

" *A little learning is a dangerous thing ;*

*drink deep or taste not the pierian spring :*

*There shallow draughts intoxicate the brain ;*

*And drinking largely sobers us again.* "

*Alexander Pope*

*(1688 - 1744)*

ACKNOWLEDGEMENTS

*Gratitude is the hardest of all,*

*Emotions to express*
*There is no word capable of covering all,*

*That one feels until we reach a world.*

*Where thought can be adequately expressed in words.*

*' Thankyou will have to do.'*

First and foremost i thank *God* almighty for the *countless* blessing he has bestowed on me.

Fear thou Not: for I am with thee(Isaah 41: 10)

I extend my *deepest* gratitude, reverences and heartfelt thanks to Vanaja ma'am for the excellent *guidance and ccrstart help* through out this *project.*

I am thankful to Dr. S. Nikam, Director, all India institute of *speech and* hearing, Mysore, to permit me to carryout -his project.

I am thankful to Dr. Lancy Disouza, Dr. Marutham, and Dr. Venkatesh for helping me out with my statistics analysis

To my Appa & Amma

To you I humbly owe what is today.... "Not volume of words would suffice *to say* of my pride and joy in being of you. To the very end of my existence I love you..."

To my naughty *brother,* its *great to have a younger* naughty like you for life is always on the sunny side for me when I 'm with you.

To Mami , " There is no more noble *occupation* in the world than to assist an other human being - to help some one succeed".

Words *are ncr enough* to thank you for every bit of *support and help you rendered rr,e* through out this project. Thanks for being with me in all my *tensions and* worries

To my schoolmate & *row m*y *senior* -Sadhika

Thanks a lot for your valuable ideas suggestions & comments during the *course of mis whole projec.*

To Reddy

Thanks for being c good *critic* evaluator of all my rough drafts and the kind of suggestions and help for making the *hercullan task* simpler.

*Dear peter*

I need no tell you crything by me by it is understood its nice to have a good friend and wisnes like you. I enjoyed my days with you in AIISH. Thanks for patiency listening a all my troubles, *complaints and for* sharing.my *happiness.*

To my dear seniors

Annavaru, Manager, SA's, Miss you guys next year. Thank you chandan for all your suggestions and help.

Annavaru, irs nice to have a good person known who patiently listens to my *problem and* offers veriable advises and suggestions. I Shall miss it in the forth corning year. Hats off to your patience.

Milind J.K. Thanks 'mama' for all your help and support.

Dear old *and* new classmates and juniors

*Those* who did help me know who they are and have my everlasting gratitude, especially to Krithika, Anita & *Sarah for* helping me out in adding to my literature note.

Thanx to all my *subjects* for patiently sitting through out the recording procedure.

Yoh! The 5-same group

Hia, Anjana, Srabanthi, and Prarthcna thank you guys, for your moral *support and encouragement.*

*Dear* Sunil *Ghetto,* its nice to have a person like you to *encourage,* inspire, some one you can look up *to as an* example.

Last but *not the least*

I extend my heart felt thanks to my computer expertise for the kind of neat $ expedient *processing which* actually metamorphosed the [jigsaw puzzes" into its *present form.*

TABLE OF CONTENTS

# INTRODUCTION

Concept in the mind is a pattern of action within the child's brain Computer, a pattern by which sensory information is put together into a whole unit called percept.

John Chilton pearce
Magical Child

Speech may be defined as a form of Oral Communication in which transformation of information takes place by means of speech waves which are in the form of acoustic energy ( Fant, 1960). The processing of speech signals within the existing constraints of natural language has interested and excited scientists for many years.

Ear, the versatile organ is not only for the purpose of detecting but also helps in analyzing the auditory input. The speech signal, which are long spurts of complex and constantly changing stream of sounds radiating from the speakers lips, travel in air , impinge upon the ear drum of the listener and reaches the higher cortical structures through the middle ear, inner ear and the auditory pathways.'Analysis of these speech signals, to some extent, are done at the lower centers ( below the thalamus level) while the processing of specific speech parameters and complex acoustic features of natural stimuli begins only at the level of Medial Geniculate Body (MGB), located in the thalamus (Kiedel, Kerth, Kallert and Homes, 1983). In addition to this, higher cortical centers help in adding on the linguistic components to the already analyzed signal, to reconstruct the percept intended by the speaker.

Reconstruction of this signal by the listener, (i.e. decoding and interpretation) is speech perception. Indeed, an interrelation between the hierarchy of processing levels becomes essential for this complex phenomenon of speech comprehension / perception - the initial stage of it being at the level of the auditory system.

Perceiving speech requires the discrimination of different auditory stimuli, which in turn involves comparing one stimulus to another stimulus that is presented concurrently or (more likely) remembered from some prior presentations. This process requires a comparator and in most instances, a "Memory". In recent years, research studies have considered the possibility of studying auditory discrimination with "Event Related Potentials" (ERPS), which is used to describe the many different electrical changes associated with "something" that happens at a particular time. When the "something" is a sensory stimulus, the ERP is an "evoked potential". Thus, ERPS that occur when the brain makes a decision.about whether one stimulus differs from another provides an objective measurement of auditory discrimination.

A simple approach to study auditory discrimination is to present a series of stimuli containing both high probability "standard stimuli" and low probability "target stimuli" and to record the ERP's while the subject detects the target or "oddball stimuli". If the subject can discriminate between the target and standard stimuli (and if he/she pays attention to the task) a large complex of waves occur in response to the target stimuli, the most prominent in this complex being $N_2$ and $P_3$ waves. The $P_3$ wave is also known as the $P_{300}$ wave, since its peak-latency in young adults performing a simple auditory discrimination is about 300 msec (Picton, 1995). The presence of this complex in the response indicates that the subject has discriminated between the stimuli. However, since the subject was actively attending to the stimuli he/she could have made some behavioural response to the targets (pressed a button in response to the target or kept a running mental count of the number of targets) and the electro physiological recordings were not really necessary for measuring the discrimination (Picton, 1995). Further more, the absence of an $N_2$- $P_3$ complex doesn't necessary mean that the subject could not discriminate between the stimuli: it may just mean that the subject was not attending to the task. Since it requires the subjective co-operation of the subject with the testing procedure, this test is not "objective" (Picton, 1995). This does not mean that the test is uninformative, since it may provide evidence about the timing and the location of the cerebral processes as underlying auditory perception. However it may not be helpful in evaluating patients who cannot or will not attend to the stimuli (Picton, 1995).

Wouldn't it be nice if there was an objective ERP test to assess auditory discrimination?

There is, and this procedure is referred to as "MISMATCH NEGATIVITY" or simply, the MMN.

Very early studies along these lines were performed by Butler (1968) who recorded the $N_1$ - $P_2$ vertex potential from awake but passive subjects. Naatanen(1975), however proposed that stimulus deviation per se, irrespective of its significance (or of the direction of attention) should produce a brain response that could be measured from the scalp. Evidence for this suggestion was obtained in experiments conducted on $P_{300}$ response by Naatanen, Gaillard and Mantysalos in the Institute for perception TNO, Soesterberg, The Netherlands, in the summer of 1978.

A Negativity was elicited at the 100-200 msec latency range by the deviant stimuli both in the attended and unattended stimulus, which could not be seen in response to the standard stimuli. This negativity was best visible in the deviant - minus - standard difference wave and was very similar for the attended and ignored input sequences, suggesting that attention was not required. Naatanen et al (1978) proposed that " It may well be that a physiological mismatch process caused by a sensory input deviating from the memory trace ('template'), formed by a frequent 'background' stimulus, is such an automatic basic process that it takes place irrespective of the intentions of the experimenter and the subject, perhaps even unmodified by the latter. This view is supported by the fact that the mismatch negativity was similarly observed for both the attended and unattended sides. On the basis of the relatively large MMN amplitude above the temporal areas, the authors further suggested that " the mismatch negativity reflects specific auditory stimulus discrimination processes taking place in the auditory primary and association areas.

Mismatch Negativity is elicited only by auditory stimuli whereas $P_{300}$ is a multisensory response that can be elicited by auditory, visual and somato sensory stimuli. MMN can be obtained in response to very small stimulus differences whereas the P300 requires large stimulus difference. Attention plays a major role for the elicitation of P300 but not in MMN. In addition, MMN can be elicited by a predictable oddball pattern but not a P300 wave (Kraus et al., 1994).

Despite its rather recent discovery, the MMN already holds a number of promising applications. These applications might be divided into four main categories. The mismatch Negativity might be an indicator of :

i) The functional state of cortex (studies by Lang et al, 1995; Born et.al., 1986)

ii) Sensory and perceptual abilities (Kraus et.al., 1995b; Lang et. al., 1995 Ponton and Don, 1995)

iii) Pathology of automatic processing ( Shelley et. al., 1991; Oades 1991, Schrodt et. al., 1992)

iv) Neural plasticity (Kraus et. al., 1995b, Naatanen et al 1993c)

Mismatch Negativity appears to index operations of the " echoic Memory " or auditory sensory memory system which is a system that stores and maintains brief representations of the physical and temporal properties of simple auditory stimuli for periods of seconds to tens of seconds even in the absence of directed attention ( Cowan 1984, Cowan et. al., 1993; Winkler et. al., 1993; Shroger, 1994) . Javitt et.al., (1998) opined that the generation process of Mismatch Negativity normally depends upon two discrete process. First, the auditory cortex must form representations of the physical characteristics of the repetative standard and maintain the representation until the next deviant stimulus is presented. Second, the neural structures within the auditory cortex must compare each stimulus to the maintained representations of the preceding stimuli. The main determinant of the strength of auditory sensory memory trace is the number of consecutive standard stimuli presented between each deviant. As the number of consecutive standard increases (deviant probability decreases), the strength of the representation of the standard stimulus increases , leading to an increase in MMN amplitude to subsequent deviant stimuli (Javitt et al 1998).

Mismatch Negativity can be elicited by almost any kind of discriminable stimulus change, such as a change in frequency (Naatanen et. al., 1978, Sams et. al , Alho,;Naatanen 1985), intensity (Naatanen et. al., 1989a) and Spatial location ( Paavilainen, Reinikainan , Naatanen 1989 ). MMN is specific to change in that it only occurs when there is a stimulus change i.e. the first stimulus in a sequence elicits no MMN whereas a deviating one in this sequence does ( Sams et. al., 1984 ). It has been opined by ( Javitt et al 1998) that MMN amplitude increases as a function of the degree of physical deviance between the deviant and standard stimulus- greater the stimulus deviance greater the activation of the comparator, leading to an increased current flow and MMN generation. As stimulus deviance increases, MMN latency decreases and a parallel decrease is observed in reaction time leading to the suggestion that attentive novelty detection in humans is governed by pre-attentive sensory memory, as indexed by MMN (Novak et. al; 1992, Tiitinen et. al., 1994)

A reasonably small inter-individual variation in normal population , good replicability , and short measurement time are the prerequisites for a clinical list, to make it suitable for use in individual diagnostics and follow up studies. But, before MMN can be introduced as an electrodiagnostic tool i.e.

at individual level, it has to be determined how reliable and replicable a waveform the MMN is in individuals. So far , MMN has been measured and analyzed mainly in basic research using grand averaged wave forms across healthy subjects with various parametric changes, which have been mentioned already. A majority of the investigators have used deviations in frequency or speech to study MMN.Only a few publications have described the effects of intensity deviance on MMN in healthy groups. However a majority of the commercially available electrophysiological units do not have the provision for varying the frequency in smaller steps, but intensity can be varied in ldB steps.

Naatanen et al (1989a) studied the effects of infrequent decrements in stimulus intensity on MMN amplitude and latency and concluded that larger the amplitude and shorter the latency, the softer the deviant stimulus was. But its effect on the different measures of MMN were not studied i.e. onset latency, offset latency, onset amplitude, offset amplitude, MMN duration and magnitude of MMN. The present study was taken up to investigate automatic deviance related processing, as revealed by ERPS elicited in an ignore condition when the deviant stimulus differs along a single dimension of "INTENSnY" from the standard.

Aim of the present study

1. To Study the effects of following intensity deviance on MMN
   i. 3dBnHL ii. 5dBnHL iii. lOdBnHL.

An attempt was made to study the effect of intensity deviance on

1. LATENCY - (ONSET,PEAK, OFFSET)
2. AMPLITUDE = (ONSET, OFFSET, PEAK)
3. MMN DURATION
4. MMN area / MMN magnitude = duration x Peak amplitude

2. To investigate whether reading can cause a significant difference on intensity MMN.

# REVIEW OF LITERATURE

The need to develop a neurophysiological response that indicates discrimination without the subject having to pay attention caused Butler to pioneer in this area. He recorded the N1-P2 vertex potential from awake, but passive subjects. Butler (1968) found that the peak to peak amplitude of the response, elicited by a regularly repeating "test" tone, was attenuated by inserting "intervening" tones in between the "test" tones. He hypothesized that the amplitude of the response to the "test" tone could be used to measure discriminability between the " test" and "intervening" tones: the more similar the intervening tone to the "test" tone, the smaller the response to the test tone. This works well when the tones are far apart, but when the tones are close together in frequency, the differences are difficult to measure - (Butler 1968).

However, Picton (1985) stated that when the stimuli are close together in frequency, close examination of the response to the test stimulus shows a clear wave form difference that goes undetected by simple N1-P2 measurements : a small negative deflection is superimposed on the wave form in the latency range of the P2 wave. This is the "mismatch negativity" (MMN), originally described in the ERP's recorded following unattended auditory target stimuli by Naatanen, Gaillard and Mantysalo(1978).

Kraus, McGee, Carrel and Sharma (1995) described MMN as an "automatic cortical evoked potential that signifies the brain's detection of acoustic change". In other words, the MMN reflects the neurophysiological process that underlies auditory discrimination. Sams et.al., (1985) showed that

MMN was present when the deviant stimuli were just discriminable from the standard stimuli but not when the difference was not perceptible. Thus, MMN is a prime candidate for an objective neurological test of auditory discrimination which can be recorded when the differences between the deviant and standard stimuli are close to the discrimination limen (or Jnd) and it occurs whether or not the subject is attending to the stimuli ( Sams et.al.,1985).

In the present survey of literature, the research has been classified under the following headings:

1. Historical background
2. Neurophysiological basis of MMN generation
3. Neural generators of MMN
4. Potential applications of MMN in normal and abnormal population
5. Methods of eliciting MMN
6. Variables affecting MMN
   (Factors influencing MMN elicitation)

**Historical Background**

In the 1970's, the most extensively studied component of event related potentials was P300. It was and is usually characterized as being elicited by infrequent target events, suggesting that two central factors i.e. stimulus deviation from the frequent events and the significance of this deviation underlie the $P_{300}$ generation.

Naatanen (1975), however, proposed that stimulus deviation perse irrespective of its significance should produce a brain response that could be measured from the scalp. Evidence for this suggestion was given by Naatanen et al (1978), in their study, which used dichotic stimulus presentation, the subject's task being to detect occasional deviant stimuli in the stimulus sequence presented to the opposite ear. The irrelevant stimulus sequence included deviant stimuli that were physically equivalent to the deviant stimuli (targets) of the attended input sequence. The deviant stimuli were either tones of a slightly higher frequency or tones of a slightly greater intensity than the standard tones. It was found that the deviant stimuli both in the attended and unattended stimulus sequence elicited a negativity at the 100-200msec latency range which could not be seen in response to the standard stimuli. This negativity, best visible in the deviant minus standard difference wave, was very similar for attended and ignored input sequences suggesting that attention was not required.

Naatanen etal (1978) proposed that a memory trace template is formed by a frequent "background" stimulus. When a sensory input deviates from this memory trace, a physiological mismatch process is caused. This is an automatic process and takes place irrespective of the intentions of the experimenter and subject, perhaps even unmodified by the latter. This view is supported by the fact that the mismatch negativity was similarly observed for both the attended and unattended conditions. On the basis of relatively large MMN amplitude above the temporal areas, Naatanen et.al.,(1978), suggested that the mismatch negativity reflects specific auditory stimulus discrimination processes taking place in the auditory primary and association areas.

**NEUROPHYSIOLOGICAL BASIS OF MMN GENERATION**

On the basis of the experimental research Naatanen and Michie (1979) proposed two intracranial generators for the MMN, one in the auditory cortex and other in frontal areas. They further suggested that the sensory-specific cortex perceptually detects stimulus change, whereas the subsequent frontal actuation might be associated with attention switch (orienting response) to stimulus changes. The MMN generator activation however, may not necessarily lead to a (full) orienting response but, according to Naatanen (1986) could result in a brief correct attention switch that may be the central element of the orienting response. Consistent with this hypothesis, Lyytinen, Blomberg and Naatanen (1992) showed that an MMN can be elicited without skin conductance response and heart-rate decrease indicants of the orienting response.

The hypothesis in which the MMN generation plays a role as an involuntary attention trigger is strongly supported by the recent results of Schroger (1994b). In a selective dichotic- listening experiment, he found that the reaction time (RT) to an infrequent softer-intensity stimulus in the right ear increased and the hit-rate attenuated when this target stimulus was preceded (with a 200msec lead time) by a frequent deviant in the left ear. In addition, when the frequency deviation was 50 Hz (standard 700 Hz), the reaction time increased by 12 msec, when the deviation was 200 Hz, the RT prolongation grew to 26 msec. Both frequency deviants elicited MMN's while the wider frequency deviant also elicited $N_{2b}$ - $P_{3a}$ waves. According to Schroger (1994b) " this performance decrement was probably due to attentional capture to the to be ignored channel triggered by the deviants of this channel". He further proposed that the data pattern obtained supports the hypothesis that ,"the neural processes generating the MMN may be involved in a mechanism of passive attention switch".

Further evidence for the MMN being associated with involuntary attention switch is provided by the fact that the MMN is followed by a relatively sharp, central positivity $P_{3a}$ (Squires and Hillyard, 1975), which might indicate the occurrence of a brief attention switch (Sams et.al., 1985b ; Lyytinen et.al., 1992). It has been opined that the more or less regular physiological concomitants of the MMN might be due to a phase advance of the steady state response elicited by a continuous background stimulation around 40 Hz (Makeig, 1995) and some late, slow frontal activity (Naatanen et.al., 1982, 1983 ; Alho, Woods, Algazi, knight and Naatanen, 1994b).

**NEURAL/CEREBRAL GENERATORS OF MISMATCH NEGATIVITY**

It has been suggested that MMN is generated by a neuronal mismatch between the deviant sensory input and a sensory memory trace representing the standard stimuli (Cowan, Winkler, Teder & Naatanen, 1993 ; Naatanen, Paavilainen, Alho, Reinikainen & Sams, 1989a ; Naatanen, Paavil'ainen, Reinikainen, 1989b). It has been further proposed that this automatic mismatch process might have an important role in initiating involuntary switching of attention to an auditory stimulus change occurring outside the focus of attention (Giard, Perrin, Pernier & Bouchet, 1990; Lyytinen, Blomberg & Naatanen, 1992 ; Naatanen, 1979,1990)

Thus, localizing cerebral generators of MMN will help us to identify brain mechanisms of auditory sensory memory and involuntary attention (Alho, 1995). Various methods have been applied to determine the MMN generation including localization of these generators on the basis of:

1. MMN scalp distribution
2. Magnetoencephalographic (MEG) studies
3. Intracranial MMN recordings in animals and humans, and
4. Effects of local brain lesions on MMN (Alho, 1995)

A major contribution of supratemporal activity to MMN's elicited by different kinds of stimulus changes was indicated by source localization of scalp recorded ERP's and magnetic fields recorded outside the head. Alho et.al., 1993; Aulanko et.al., 1993 ; Csepe et.al.,1992 ; Giard et.al., 1990 Huotilainen et.al., 1993 ; Hari et.al., 1984 ; Kaukoranta et.al., 1989 ; Lounasmaa et.al., 1989; Sams et.al., 1985a; Tiitinen et.al., 1993). However, it appears that there actually are several MMN generators in the auditory cortex, especially in the right hemisphere ( Levdnen et.al., 1996 ; Paavilainen et.al., 1991 ). Direct evidence for contribution of auditory cortex activity to MMN has been provided by intracranical MMN recordings in the guinea pig (Kraus et.al., 1994), cat (Csepe et.al., 1987) and monkey (Javitt et.al., 1994). These animal recordings have also provided valuable information on neural mechanisms generating MMN. Recently, MMN has also been recorded directly from the human auditory cortex (Kropotov etal., 1.991). Furthermore, contribution of auditory-cortex activity to the MMN is also suggested by attenuation of MMN's in patients with temporal lobe lesions (Aaltonen et.al., 1993;

A somewhat controversial issue appears to be whether activity of the primary auditory cortex contributes to MMN. Javitt et.al., (1992) reported that intracortical recordings of MMN's to frequency and intensity changes in the monkey indicate an MMN generator in the primary auditory cortex. Moreover, recordings of frequency change MMN's from the auditory cortex of cat have shown that in addition to responses of the primary auditory area AI, an MMN is also observed in recordings from area AII (Csepe et.aL, 1987, 1989 ; Karmos et.al, 1993). However, Kraus et.al., (1994), observed no MMN's in responses of the primary auditory cortex of the guinea pig, whereas MMN's to changes in tone frequency and phonetic stimuli occurred in responses apparently generated in the non primary auditory cortex.\A number of MMN / MMNm (magnetic counterpart of MMN) recordings in humans indicate that the supratemporal MMN/MMNm sources acivated by different kinds of sound changes are anterior to the supratemporal Nl/Nlm source. (Csepe et.al., 1992 ; Hari et.al., 1992 ; Huotilainen et.al., 1993 ; Levanen et.al., 1993 ; Sams et.aL, 1991 ; Scherg et.al., 1989 ; Tiitinen et.al., 1993 ; Woods et.al., 1993b). These findings suggest that MMN to different sound changes get a major contribution from the areas anterior to the primary auditory cortex, where the supratemporal N source is presumably located, judging from the topographic organization of this source (Bertrand, Perrin & Peraier, 1991/; Elberling et.al., 1982 ; Panter et.al., 1988 ; Tiitinen et.al., 1993; Woods, Alho & Algazi, 1993 a); However, a contribution from primary auditory cortex to MMN in these studies cannot be ruled out due to limitations in spatial resolution in localizing sources of scalp-recorded MMN's or MMNm fields recorded outside the head (Alho, 1995).

MMN has been suggested to be generated by a neuronal mismatch between a deviant sensory input and a sensory memory trace representing a preceding repetitive sound (Naatanen, 1995). Therefore, localization of MMN generators will make it possible to identify brain mechanisms of auditory sensory memory. 4lMN / MMNm recordings also have provided evidence that simple and complex sounds are processed or represented by different neuronal populations in auditory cortex (Alho, 1995). Furthermore, the MMN m elicited by a change in one frequency element of complex sounds (a chord or a sound pattern) was found to be generated in a different region of the supratemporal auditory cortex than the MMNm to an identical frequency change in a simple tone (Alho, 1995). He further hypothesized that the activity of brain areas outside the auditory cortex also may contribute to MMN. An MMN subcomponent generated in the frontal lobe was suggested by the Scalp Current Density (SCD) maps (Giard et.al., 1990). This is supported by an MMN attenuation in patients with lesions of dorso-lateral prefrontal cortex (Alho et.al., 1994b).

Alho (1995) suggested that the frontal activity contributing to the MMN might be associated with an involuntary switching of attention to a change in the acoustic environment (Alho, 1995).

Earlier r. Alho et.al., (1994b), suggested that the MMN attenuation in frontal lobe affected patients also might be caused by attenuation of the auditory cortex MMN, resulting from reduced input from frontal to auditory cortex. Thus, sustaining input from other brain areas might be important for sensory memory functions in the auditory cortex (Alho et.al., 1994b).

At least in some species, very early MMN subcomponents may be generated in the thalamus, as indicated by intracranial recordings in the cat (Csepe et.al., 1989) and guinea pig (Kraus et.al., 1994b,1995b). In addition, Csepe- et.al., (1989), observed a very early MMN subcomponent in hippocampal recordings in the cat, which is consistent with the comparison of different stimuli in the hippocampus, as had been previously suggested by Sokolov (1975) on the basis of hippocampal recordings in the rabbit (Vinogradova, 1975). Kropotov et.al., (1991) observed no MMN in intracranial recordings from the ventrolateral nucleus of the thalamus, hippocampus, amygdala and basal ganghia of the human brain.

Alho (1995) concludes in his review about cerebral generators that localization of MMN generators helps in the identification of neural mechanisms involved in auditory sensory memory and involuntary switching of attention. MMN recordings provide an objective method to investigate the above mentioned mechanisms and their dysfunction's (Alho, 1995). Moreover, it helps to study more general principals of representing sensory information in the human brain.

Based on a review, Naatanen et.al., (1995) summarized that MMN probably has

i. A bilateral cortex generator
ii. A frontal cortex generator and
iii. Sub-cortical sources

## CLINICAL APPLICATIONS OF MMN

Various applications that the MMN provides yield feature specific conformation about the sound representation (Winkler, 1996), which develops rather early in comparison to other ERP waves (Naatanen et.al., 1996). Further more there are two characteristic features of the MMN, namely its attention insensitivity and its recordability, in a broad range of consciousness which makes this component a unique candidate for clinical application (Csepe et.al., 1997). Of these factors, the relative attention independence is one of the most important in applications and/or application-oriented research. Several features make MMN a specially attractive tool for auditory research and clinical practice.

Naatanen (1995) summarizes the clinical applications of the MMN as follows.

(i) The MMN is elicited by any discriminable change of a repetitive sound and can be elicited by stimulus differences that approximate the behavioural discrimination threshold. Therefore it provides an objective measure of an individuals discrimination ability for different simple and complex (such as phomenic) sound features.

(ii). As it can be elicited without attention, the MMN is free from attentional variations that contaminate behavioural measures and attention dependent physiological measures of auditory function. In addition, auditory function can be studied even in individuals unable or unwilling to cooperate.

(iii). MMN provides a unique window to view the neurophysiological processes underlying normal hearing.

(iv). MMN also provides a means for studying auditory short-term memory which is of crucial importance for correct speech processing and understanding . Consequently, MMN opens a view to the temporal dimension of auditory function which in contrast to vision, is to a great extent sequential in nature.

**MMN AS A MEASURE OF CONCIOUSNESS**

MMN can be elicited in a range of levels of consciousness, it is not clear what quality and quantity of stimulus deviations are sufficient for its elicitation (Csepe et.al., 1997). In disturbed states of consciousness also, there are very promising clinical trials for using MMN for clinical predictions. In an extensive study done by Kane etal (1996), a large number of coma patients were investigated by using MMN elicited by pitch- deviation. The presence of MMN was highly related to the emergence of the coma. They concluded that the MMN, having an all-or-none character, can be used as an early neurophysiological indicator of recovery from coma caused by traumatic brain injury( TBI).

However Csepe etal (1997) recommended that though the sensitivity and specificity of the MMN was high, one had to be careful when using MMN as a diagnostic tool .As reported by Kane etal (1996), absence of MMN does not mean impeding death in all cases but the presence of MMN may help manage TBI patients and counsel their relatives.

The study done by Kane etal (1996) used large deviation (800 vs 1600Hz) between tones of 110 dB, which elicted large MMN in awake subjects and hence an expected appearance of MMN even in coma. This huge deviation could explain why MMN was demonstrated in coma, which contradicts the MMN results in sleep (Csepe, 1997). In non REM sleep, no MMN has been demonstrated up to now, even for large deviations like 1000 VS and 2000 Hz. (Loewy etal, 1996). One of the possible reasons according to Loewy etal (1996) for the absence of MMN in slow-wave sleep, is that the largest deviation without an awakening effect is not enough for MMN elicitation.

Another study was done by Rockstroh etal (1995) to predict recovery from coma. Some patients described as in a persistent vegetative state(apallic syndrome) were also investigated (Jennet etal., 1972). The depth of the coma was measured by the Disability Rating Scale and was correlated with the ERP measurements focussing on the N1-P2 complex and the pitch deviation elicited MMN.The MMN seemed to be less predictive than the presence of the vertex recorded Nl.lt was hence concluded that the comparison processes reflected by the MMN needed a 'functional effeciency of the cortex'. (Rockstroh et.al, 1995) that failed in most of the patients investigated. Another possible explanation for the lacking MMN is that the tone deviation used was not an optimal one for these patients (Csepe, 1995). In these studies, the all-or-none nature of the MMN was exploited, and the cautions conclusions drawn, may correspond to the questionable reliability of MMN in various clinical populations.

**MMN AS A MEASURE OF MEMORY TRACE EFFICIENCY.**

A part of clinically oriented MMN research is based on the memory trace concept that the MMN is the product of a comparison of the incoming signal against the neuronal trace built up by the frequently repeated stimuli (standard) (Csepe etal., 1997). Csepe et.al., (1997) further hypothesizes that the trace occupying the sensory memory is strengthened by the stimulus repetitions, and the trace has a rather short decay time.

This correlative nature of the MMN appearance, magnitude and strength of memory trace gave a big impetus to those studies in which patients whose sensory memory was assumed to be impaired were investigated. (Molnar et al, 1995). An experiment by Pekkonen et al (1993), measuring pitch and duration MMN at different inter-stimulus intervals revealed a faster trace decay. They concluded, after a detailed analysis of the MMN characteristics, that while the automatic stimulus comparison process was not affected by aging, the functional limits of the trace were influenced. This may lead to processing problems such as involuntary attention switching and becoming less sensitive with age.

In an earlier study by Pekkonen et al (1993), where area measures on the MMN resulted in significant differences between young and aging subjects, a similar effect was shown. In another study by Woods (1992) significant changes in MMN distribution were found in aging subjects when compared to young subjects, while serious attenuation was not reported. Contrary to their results, Gunter et. al (1996) reported that MMN was not affected by aging and the sensitivity of the processing was even enhanced with aging. This discrepancy may be due to the use of experimental parameters differentiating sensitivity and aging, (Csepe 1997). The knowledge on MMN in the elderly is substantial and of extreme importance to make a valid distinction between changes affected by age and those affected by pathological processes like Alzheimer's or Parkinson's disease appearing often in aging persons.

By measuring MMN in the same paradigm as in that of aging studies, Pekkonen et.al., (1994) found an MMN amplitude decrease as a function of the ISI. The conclusion was that the memory trace decays faster in Alzheimer patients than in the age-matched group (degree of MMN attenuation was more expressed). Another study by Yokoyama et al (1995) on dementia patients showed no significant amplitude change and longer MMN latency, an effect not found in patients suffering from vascular dementia. They concluded that MMN latency is useful for differential diagnosis.

## MMN AS A MEASURE OF THE LACK OF EXISTENCE OF THE PRE PERCEPTUAL PROCESSING.

### Parkinson's Disease.

In Parkinson's disease, an impaired change detection was supposed in general. A study done by Pekkonen et.al., (1995), revealed that the pitch MMN was smaller in non demented patients with Parkinson's disease than in age-matched controls. In this study, the MMN area was measured and the MMN attenutation was interpreted as a consequence of dopamine deficiency in these patients.

The experiments done by Karayanidis et.al.,(1995) showed an MMN amplitude reduction in Parkinson's disease. The MMN among other components such as $P_{3a}$ , $P_{3b}$ and $N_{2b}$ showed a conspicous amplitude reduction with age and a little more attenuation due to Parkinson's disease. Also the late part of MMN, called the 'late Nd' showed a significant increase.These results are in agreement with the results of Vieregge et al (1994) which provided evidence for a distinctive impairment of the controlled processing, that is a disturbed auditory selective attention, as revealed by a significantly smaller processing negativity and unchanged P3.

Csepe et.al., (1997) states that it is possible that only the all-or-none nature of the MMN can be used for drawing conclusions about these group of patients whose automatic comparison ability was not disturbed in general. He also says that it seems to be too early to judge the qualitative features of the MMN and the underlying processes before we know what is shown by the area and amplitude changes in normal and especially in aging subjects.

Schizophrenia

In understanding the neurophysiological deficits in this disorder, MMN was used to find whether the neuro cognitive dysfunction is so pervasive that it extends even to the levels of the peperceptual processing of auditory events (Csepe, 1997).

In an experiment performed by Javitt et.al., (1995) on 20 medicated and 11 un-medicated patients with MMN and $P_3$ waves measured in passive and active oddball paradigm respectively, it was found that the MMN was severely impaired in schizophrenics both in medicated and non medicated groups. The peak amplitude of the MMN and that of the two cognitive components (N2 and P3) showed a significant decrease. The reduced MMN was rather similar in medicated and non medicated groups.

Kirino and Shinomiya(1996) grouped patients according to amplitude variations of MMN and P3 .Patients in group A had a higher MMN and an amplitude increase in P3. Group B's MMN amplitude slightly increased, but no P3 changes appeared. This result seems to contradict the correlation of MMN and $P_3$ found by Javitt et.al., (1995) but this was probably affected by the persistent neurocognitive dysfunctioa

Recent data of Oades etal (1996) showed a symmetric MMN on the frontocentral sites in paranoid schizophrenics when compared to non paranoid schizophrenics whose MMN peaked over the parietal sites. Studies of O'Donnel (1994) did not find any differences in pitch deviation elicited MMN between normal subjects and medicated schizophrenic patients.

Though these results are equivocal, they are relevant to schizophrenia in both the basic and clinical research. Impairments or lack of the MMN generation in schizophrenia may contribute to the observed disturbances in shifting attention toward novel stimuli or inadequate processing of relevant versus irrelevant stimuli (Csepe etal, 1997). However it is not fully clear yet which components of the processing reflected by the MMN are assumed to be characteristic of schizophrenia.

## MMN AS A MEASURE OF PROCESSING DIFFERENCES

### Obsessive-Compulsive Disorder (OCD)

In OCD's, unlike Schizophrenia, an over focused attention is assumed. Although a frontal generator of MMN was demonstrated by Giard et.al., (1990), they showed that the hyperactivation of this region, indicated by a significantly larger processing negativity (PN), did not contribute to MMN generation. ERP data of Oades et.al., (1996) have shown distinctive differences between MMN and PN. The OCD showed a right side predominance of the MMN and an extreme regional allocation of the PN. However, it is still not known to what extent the frontal lobe is affected in OCD's.

## EFFECT OF ALCOHOL AND THE FRONTAL LOBE

Grillon et.al., (1995) stated that the automatic change detection, attention control and allocation of attention to novel stimuli are affected to a different degree by ethanol intake. A low dose of ethanol, used by Jaaskelainen et.al., (1995) resulted in a dramatic amplitude reduction and significant latency delay. They concluded that the disturbed pre-perceptual processing of the environmental cues due to the effect of alcohol, may account for an increased risk of accidents. In the study done by Grillon et.al., (1995), low dose ethanol did not affect the MMN but changed the P3 which has a strong frontal component, implying the impact of alcohol on the frontal processing of task irrelevant stimuli. Jaaskelainen et.al., (1995) investigated the dose effect of alcohol elicited by different deviance magnitudes (frequency only). The MMN was suppressed by 'larger dosage' of alcohol. In a recent study of his in 1996, Jaaskelainen reported that at longer ISI (2.4 sec) even the low dose attenuated the MMN, while the higher dose suppressed the MMN at both low and high ISI used . These findings and changed scalp distribution of MMN suggested the strong impact of alcohol on the frontal generator.

**Aphasia and the Assumption of Different Generators in Tone and Speech Processing**

A genuine application of the knowledge of bilateral generators of tone deviation elicited MMN showing a right side preponderance and that of the language sub-centers in the dominant left perisylvian region was used in the first study of aphasia patients. Aaltonen et.al., (1993) in his study of aphasic patients, found that patients with predominantly anterior lesions have intact MMN to both pure tone and vowel deviations while those with posterior lesions showed a different pattern. Both the groups lacked MMN to the vowel contrast and had normal MMN to the tone deviation.

In a recent study, Csepe et.al., (1997) demonstrated the abnormalities of MMN to speech sound differences and found results that were not fully compatible with those of Aaltonen et.al., (1993). However, it was stated that the dissociation unquestionably suggested that different areas were active in generating MMN to vowel and one deviations (Csepe et.al., 1997)

## MMN AS A MEASURE OF DEVELOPMENTAL LAG

The typical condition of MMN recording, that is the passive elicitation is a considerable advantage when children are studied (Csepe et.al., 1995, Naatanen et.al., 1995). Because of its early maturation (Kraus et.al., 1994&

Csepe et.al., 1995) MMN was investigated in the following assumed disturbances or developmental lags :

- In attention deficit and hyperactive disorder (Kenner etal., 1996, Oades etal., 1996)
- In autistic children (Kenner et.al., 1995)
- In dysphasic children (Karpilahti et.al., 1994)
- In children with learning disabilities (Kraus et.al., 1996)

All these studies showed significant changes in MMN duration, peak amplitude and latency measures.

MMN AS A MEASURE OF PROCESSING ACCURACY

One of the most exciting applications is the use of MMN in patients with cochlear implants (CI) (Csepe etal., 1997). In the study done by Kraus et.al., (1993) recording MMN's to speech stimuli of differently dissimilar spectral components, it was found that MMN was present in all good CI users and was very similar to that recorded in normal listeners. They opined that the speech perception abilities of the CI users depend on the central auditory processing reflected by the MMN. The usefulness of MMN in assessing the discriminability of CI produced stimulation patterns, was suggested by Ponton and Dons (1995). In their study, they recorded MMN's to changes in stimulus train duration and pitch. They found that the MMN recorded in CI users resembled that of normal hearing individuals. Their suggestion for using MMN in developing rehabilitation programs fulfills the hopes for a relevant clinical application of the MMN.

Hence, we see, that despite its rather recent discovery MMN already holds a number of promising applications.

To summarize:

MMN can be used as a measure of:

1. Conciousness (Kane et.al., 1996) eg. Coma patients.
2. Memory trace efficiency (Pekkonen et.al., 1993, 1996) eg. Aged and dementia patients.
3. Lack or existence of the perceptual processing (Pekkonen et.al., 1995) eg. Parkinson's disease, Schizophrenia (Javitt et.al., 1995)
4. Processing differences eg. Obsessive Compulsive Disorders, alcoholics, aphasics (Giard et.al., 1990 ; Tovey et.al., 1994 ; Jaaskelainen et.al., 1995; Kraus et.al., 1994)
5. Developmental lag eg. ADHD, Dysphasic children (Kraus et.al., 1995)
6. Processing accuracy eg. In cochlear implant users (Kraus et.al., 1993)

## METHODOLOGICAL ASPECTS OF MMN STIMULATION AND RECORDING.

### Methods for Eliciting Pure MMN Responses.

The MMN wave form is elicited as a response to deviant (rare) stimuli in a relatively homogenous stream of standard (frequent) stimuli using an oddball paradigm.

In an oddball paradigm we present a series of high probability standard stimuli and in the interval between the standard stimuli predictably or un-predictably we present a low probability deviant stimuli (i.e) a series of about 5-6 identical stimuli and a oddball stimuli will be presented.

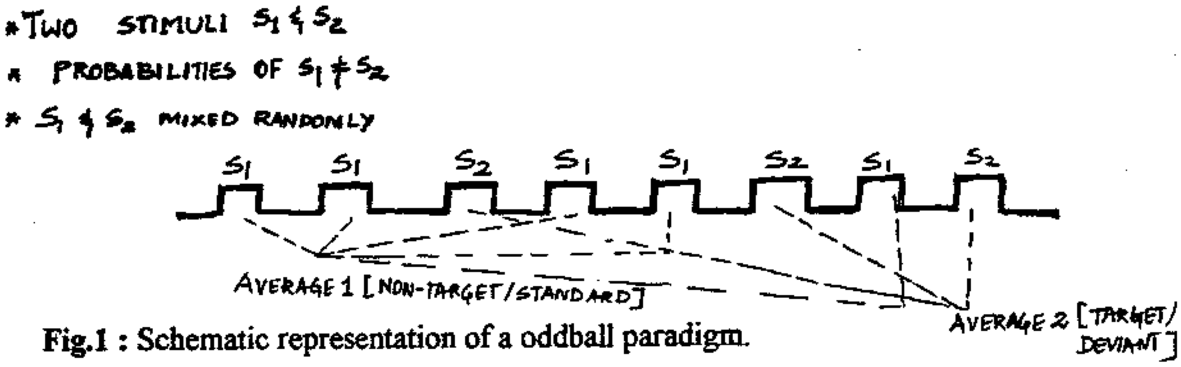



**Fig.1 : Schematic representation of a oddball paradigm.**

MMN can be elicited only in the deviant stimulus train both in ignore or attended condition indicating that MMN indexes largely preattentive stage of auditory information processing (Javitt et.al., 1998).

The oddball stimuli may differ in

a) Frequency (Sams et. al., 1985)
b) Intensity (Naatanen et.al, 1989 a)
c) Duration (Naatanen et.al., 1989 b; novak et.al., 1992)
d) Spatial origin (location) of the sound (Paavilanen et.al.,1989)

In addition, changes in more complex Auditory stimulus attributes such as phonetic (Aaltonen et.al., 1987; Sams et.al., 1990) temporal changes in the stimulus presentation i.e. on occasionally to early stimulus in a block with a constant inter stimulus intervals (ISIs)(Nordby et. al, 1991; 1988) can elicit MMN.

MMN can also be elicited even when the deviant stimuli occur in a task irrelevant input sequence (for instance among right-ear stimuli when left-ear stimuli are attended) (Naatanen et.al.,1978).However MMN cannot be elicited only by stimuli with deviant stimulus parameters when they are presented with out the intervening standard ; suggesting that MMN reflects a change in detection when a memory trace representing the constant standard stimulus and the neural code of the stimulus with deviant parameters) are descrepant (Naatanen et.al, 1988).

**Recording of MMN**:

The same principles apply to recording of the MMN as for any other long-latency ERP.

**Time Window**:

The peak latency of the MMN varies even in normal adults within the range of 80-250 msec, the recording time window has to be atleast 300 msec (Lang et. al., 1995). However in children and when using stimuli of long duration such as syllables, the MMN peak latency can even exceed the limit of 300msec (Lang et. al., 1995). The " Tail" of the MMN should be included in the window to show whether the negative MMN waveform is followed by a P3a waveform indicating obtrusiveness of the stimulus and efficacy of the passive paradigm (Lang et. al., 1995). Lang et. al., (1995) state that the window should begin about 50 msec before the triggering time to allow measurement of the pre-stimulus base line and noise level. Thus a time window of about 50 msec to 350-500 msec is recommended for the on-line averaging of standard and deviant responses ( Lang et. al., 1995).

Amplifier setting and sampling rate:

Lang et. al., (1995) recommended that a frequency band of 0.1 to 30 Hz is sufficient for the MMN recordings. AC power frequency can be further filtered by using a 50 (60) Hz notch filter, although it is preferable to eliminate noise with shielding in case there are sources of strong noise in the vicinity

(Lang et. al., 1995). Sampling rates higher than 100 Hz and analog to digital conversion of atleast 10 to 12 bits are recommended for data acquisition (Lang et. al., 1995)

Recording electrodes, Number of channel, Derivation :

In a majority of the psychophysical MMN studies, three midline electrodes (Fz,Cz,Pz), referred to the linked ear or mastoid electrode plus two Electro OcculoGraphic(EoG) electrodes have been used (Lang et. al., 1995). The scalp location of the MMN with maximum amplitude seems, however, to be center more often parasagitally than on the mid line. Further-more, the diagnostic sensitivity of MMN appears to increase if the electrode yielding the largest amplitude is used. Lang et. al., (1995) suggested that it is beneficial to use at least seven scalp electrode (Fpz, Fz, Cz, $F_3$ , Gt, C3) plus the reference and EoG electrodes. To achieve more complete scalp distribution for "brain mapping " which also improves identification of ambiguous MMN responses, all 21 electrodes of the 10 to 20 system are needed (Lang et. al., 1995. For source localization, " dipole analysis" of the MMN an extra temporo basal electrode row is essential ( Scherg, Vajsar, picton, 1989).

Recording conditions, instructions, duration of the session :

Lang et. al., (1995) stated that MMN recordings should be performed in a room with sufficient protection against noise and disturbances. Complete noise isolation is not required because the stimulus are delivered via earphones and moreover,the testing is done at threshold level (i.e. the stimuli need to be audible and at a comfortable level). If free field stimulation is used the standard and deviant might attenuate differently, thus generating an extra unintentional deviance (Lang et. al., 1995).

The subject is instructed to pay attention to a movie or to read a book and to ignore the sound stimulus. Lang et. al., (1995). Suggested screening voiceless movies with subtitles during the recording procedure.

Lang et. al., (1995) stated that watching a video movie or some other visual task is necessary not only to direct the subjects attention away from the test stimuli and to maintain the activity level and vigilance but also to attenuate the alpha rhythm and slow activity of the background EEG. Excessive background EEG activity is a major factor in distorting the MMN responses. Lang et. al., (1995) recommended that if both active and passive listening are needed it is best to first record the passively elicited MMN and then to record the active (P3) paradigm.

MMN recording takes about 8-10 minutes to record the necessary number of responses. Preparations and electrode application take about 20 minutes, it is not possible to record more than five to six blocks ( including 200 deviant and 1000 deviant with repetition rate of 3Hz) in a 1-hr session (Lang et. al., 1995).

Lang et. al., (1995) also found that when recording time exceeded 1 or 2 hrs, the MMN amplitude began to attenuate, even in young adults. Hence a maximum duration of an hour (hr) for each test session has been suggested for the elderly and school aged children and for younger children, the test session must be even shorter, for efficient MMN recording.

**Repetition Rate and Probability of Stimuli**:

In practice, an ISI of about 300 msec has been used for MMN application when using simple or vowel stimuli ( Lang et. al., 1995 ). Lang et. al., (1995) opine that good results can be obtained if every $5^{th}$ to $10^{th}$ stimulus is a deviant (p.= 0.1 to 0.2) in a" pseudo random" stimulus sequence.

**Visual Recognition of MMN and waveform Parameters**

The MMN waveform is usually superposed on by other exogeneous ($N_1P_2$) or endogeneous (N2P3) waveforms (Naatanen, 1995). Naatanen et. al., (1982) suggested that $N_{200}$ elicited by the detected deviant stimuli in the oddball paradigm is composed of two components peaking within the same time window. They were labeled the mismatch negativity and $N_{2b}$ by Naatanen et. al., (1978). Naatanen (1995) reports that when the subject attends to the auditory stimuli (in one-channel) oddball situation, MMN is partly overlapped by $N_{2b}$ .

The separation of MMN and $N_2$b in the auditory modality has mainly been based on the longer latency of $N_{2b}$ and its most posterior midline scalp distribution (Naatanen, Gillard , 1983). Earlier studies by Squires et. al., (1975) showed that $N_2$oo is followed by a positive wave ($P_{3a}$) even in ignore conditions. However, there are MMN data with no subsequent $P_{3a}$ (Naatanen, 1980, 1982). Renault and Lesevre (1979) reported on the other hand, that only $N_{2b}$ appears to be invariably followed by $P_{3a}$.

**Difference Waveform** :

It is evident from Fig-2, that MMN is apparent in the deviant and in the difference waveform (Naatanen et. al., 1988), but not in the standard waveforms. Lang et. al., (1995) suggested that if there is a common ERP waveform e.g. N1P2 in the responses evoked by the standard and deviant stimuli it can be eliminated by generating a difference waveform of these responses. A difference waveform is generated by subtracting the averaged response to the standard stimuli from that to the deviant stimuli Naatanen et. al., (1975) concluded from their initial study that MMN peaks within the range of 120-250 msec after stimulus onset. However, Kraus et. al., (1997) reported that the MMN can be identified visually as a relative negative peak occuring with a 300 msec window following the $N_1$. Mcgee et. al., (1997) suggested that the MMN can be identified visually as a relative negativity occuring with in 350msec following the $N_1$. Generally the most common parameters studied from the waveform are the latency and amplitude measures (Lang et. al., 1995).

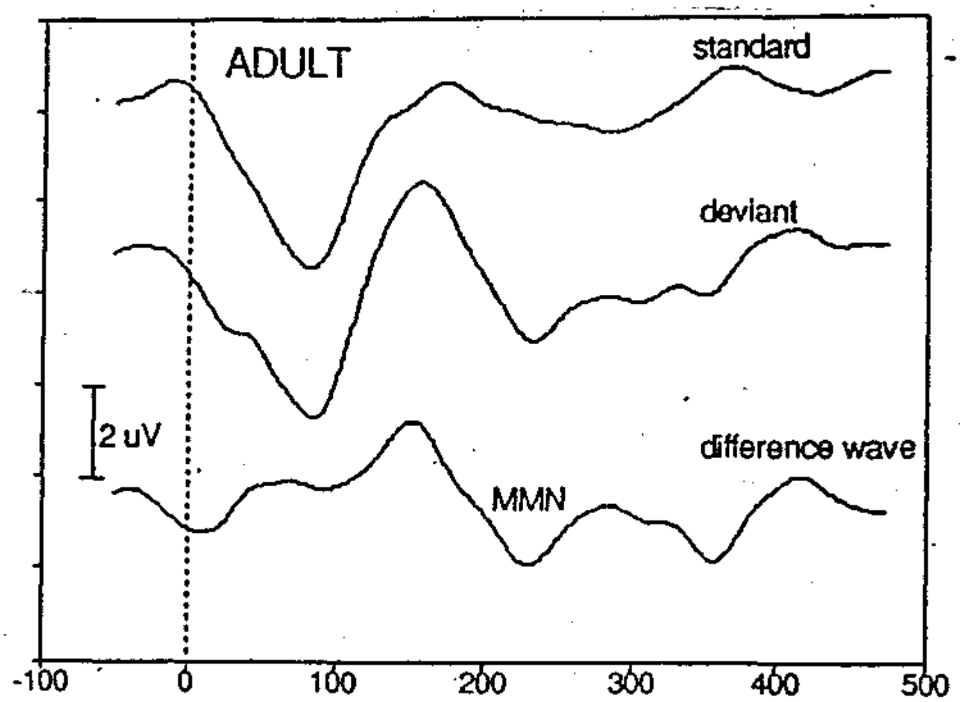



Fig-2 : MMN in representative adult in response to a standard and deviant tone of 1 KHz with an intensity deviance of 5dB.

Lang et. al., (1995) state that the latency is measured from the stimulus onset to the negative peak of the MMN. Due to a floating base line it is also necessary to determine the onset point for amplitude measurement.

This allows the calculation of the MMN risetime ( = Onset to peak ), In addition some studies also determined the offset point, enabling the measurement of the total duration and fall time (peak to offset) of the MMN. (Lang et. al., 1995)

Lang et. al. (1995b), Lang et. al., (1995c) opined that the various MMN measures such as amplitude, latency, duration of the MMN represent different central mechanism.

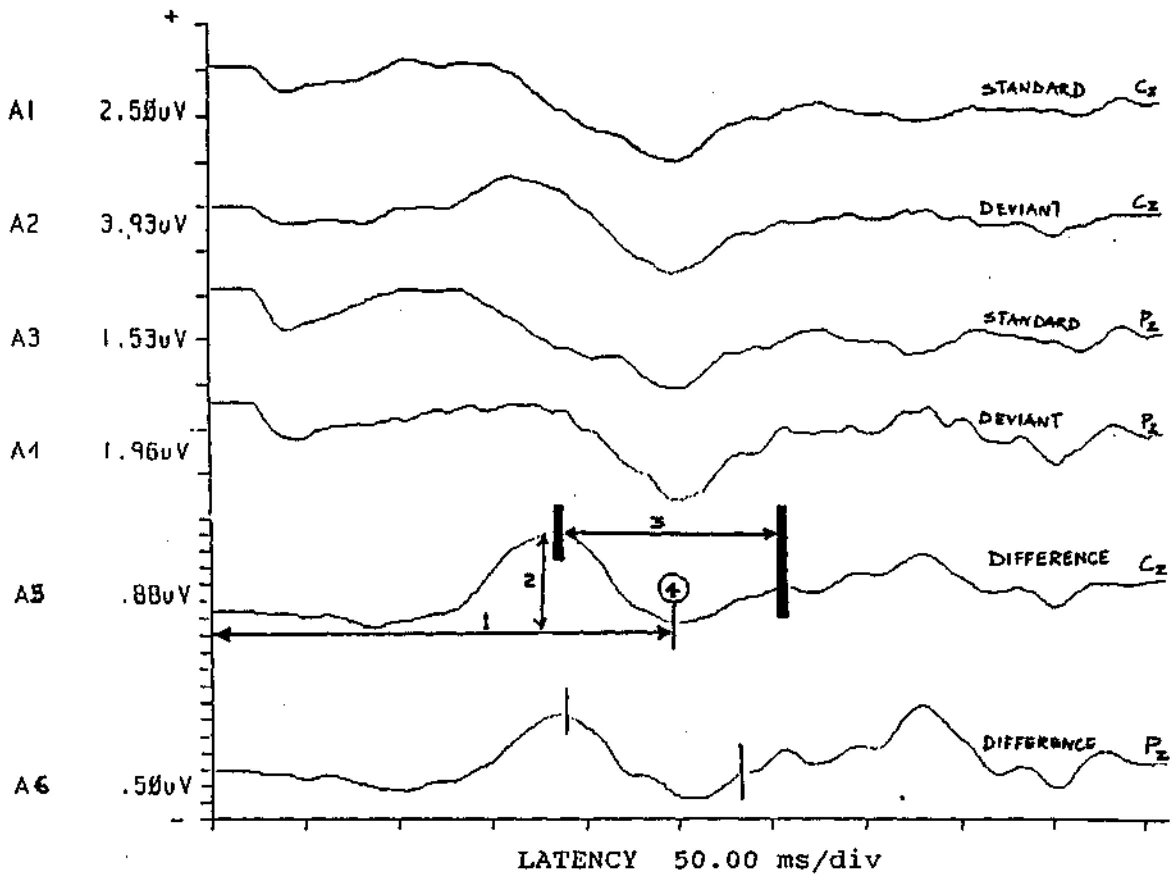



Fig - 3 : The standard stimulus was 1000Hz and deviant stimulus was 1000 Hz line with intensity deviance of 10 dB measure of MMN quantity are indicated in the difference waveform.

1. Peak Latency
2. Peak amplitude
3. Total duration
4. MMN area = Duration X Amplitude

To summarize the several MMN waveform measurements studied are

1. Latency (Onset, Offset, Peak)
2. Amplitude ( Onset, Ofset, Peak)

In case of symmetrical / Double peaks it is reasonable to measure the MMN amplitude from the highest peak (Lang et. al., 1995)

3. MMN duration (ie) duration between the zero crossing.
4. MMN magnitude (area of the MMN waveform) determined by multiplying the MMN duration with MMN peak amplitude (Groenen P. et. al. 1996)

These various measures can be inferred from fig - 3.

Identification of an Uncertain Response :

A crucial problem in the ERP data analysis is determining the existence and significance of a response (Lang et.al., 1995). Visual scoring is still the most common way to identify the response although automatic and wave form detection algorithm can be applied. A complete MMN mapping i.e. with at least 20 channels or more is valuable not only for such special examination as dipole analysis but also in routine examinations of MMN identification in uncertain cases (Lang et. al., 1995).

The t-test has been used to compare the significance of differences between two corresponding amplitude values taken from the same time incidence of two ERP wave form(Lang et. al., 1995). Lang et. al., (1995) further opines that by averaging 100 deviant responses the standard of the mean amplitude was 1.5 μv, which can be taken as the "first approximation" when planing experiments for comparing MMN responses with different stimulus pairs (e.g. when increasing frequency difference of standard and deviant stimuli. Determination of negative peak may be problematic for bifurcated or noisy waveforms which are relatively common (Lang et.al., 1995). In these cases, the area can be used as a less varying variable representing the intensity of the response (Pekkonen et.al., 1993).

McGee et.al., (1997) collected MMN responses from 86 normal school age children in response to synthesized speech syllables / wa / and two variants of / ba / in order to assess methods for determining response validity in individuals. The methods used were compared using signal detection theory techniques. They stated that visual recognition of waveforms is insufficient to adequately judge MMN validity.Consideration of other waveform measurements greatly improves the assessment of MMN validity. They concluded that criteria based on measurement of response area, Onset latency, and duration as the best indicators of response validity.

## FACTORS CAUSING VARIATION IN THE MMN.

Tracing back literature, MMN elicitation is affected by many number of factors leading to greater amount of both intraindividual and inter individual variations.

### Intra individual Variation of the MMN:

There is variation in individual MMN amplitude and latencies from one block or session to another even when the stimulation parameters are not changed. Lang et.al., (1995a) examined the relability of the MMN measurements by recording MMN responses of three male subjects on 5 consecutive days by using four different stimulus blocks. The coefficient of variation(C. V) of the MMN amplitudes and latencies were found and was seen that the coefficient of variation(C.V) for the MMN amplitude was considerably higher than that for the MMN latency. Thus, Lang et.al., (1995) concluded that the MMN amplitude is more unreliable variable than the latency.

Sleep:

The MMN disappears in sleep, although minor responses simlar to the MMN have been elicited in early morning recordings (Campbell, Bell, Bastien, 1991) or when stimuli preceding K-complexes were used selectively to sum the MMN (Sallinen, Kaartinen and Lyytinen,1994).However the MMN varies Strongly with alertness even if the subject is not allowed to fall asleep (Lang et.al., 1995). Lang et.al., (1995) reported that in various states of vigilance the MMN amplitude and Latency behaved in different ways.

Sallinen et.al., (1997) also reported that MMN is attenuated due to decrease in alertness even before an actual Sleep state is reached. In contrast, intracranial recording from anaesthetized cats (Csepe et. al., 1989) and guinea pigs (Kraus et.al., 1994a, 1994b) provide evidence for the occurrence of the MMN even during sleep or anesthesia. Thus the results of above studies are equivocal and not all of them have found an MMN in sleep (Paavilainen et.al., 1987).

**ATTENTION**:

The use of MMN as an objective measure of auditory function is to a large extent based on the assumed full or partial independence of the MMN from attention. If the MMN were elicited only in the presence of attention, then it could not be regarded as being free from attention related variations that affect behavioural measures of auditory function. Moreover, it would not be possible to associate the MMN with attention switch to change in an initially unattended sound (Naatanen, 1985).

Several studies have shown that the MMN elicited by deviant stimuli when they are targets of the attended sound sequence or when the sounds are ignored are of very similar amplitude (Naatanen et.al., 1982). Deviants in attended stimulus sequence usually elicit a large negativity (revealed by the difference wave) than when the auditory stimuli are ignored, but this difference is due to superimpositons of the $N_2b$ component on the MMN (Naatanen et.al., 1982; Naatanen, Sams and Alho,1986; Naatanen et.al., 1983).

Comparisons with the Magnetic counterparts of MMN (MMMm) between active and passive conditions have yielded very similar amplitudes (Kankoranta et.al., 1989; Lounasmaa et.al., 1989). Consistently with this the magnetocephalography (MEG) does not register the $N_2b$ generator process (probably due to the radial orientation of the generator)(Naatanen,1995).

In contrast to results suggesting attentional independence of the MMN amplitude, the MMNm recorded by Aulanko et.al.,(1993) for phonetic change

(/b/-/da/, or vice versa) has larger in amplitude when when phonetic stimuli were attended than when they were ignored. However a subsequent study by Aulanko, Ilmoniemi and Sams(1995) failed to replicate this effect.

Attention is more strongly focused during concurrent presentation of the to be attended and ignored stimuli streams, most typically when they are presented dichotically with a rapid rate (Hillyard et.al., 1973; Nāātānen 1990,1992).Under such conditions, the amplitude of the frequency change MMN seems to be unaffected by the direction of attention(Naatanen et.al., 1993b; Paavilainen et.al., 1993). Woods et.al., (1992) found larger MMN's to slight frequency deviation during attention to auditory stimuli than to visual stimuli. The studies conducted by Naatanen etal., (1993) indicated that although the frequency MMN is elicited even in the complete absence of attention, its amplitude might some times be attenuated. Thus, the threshold of the frequency MMN is not affected by attention whereas the amplitude in these cases is affected (Naatanen 1993).

In contrast, the MMN for intensity reduction is strongly attenuated though not fully eliminated, in the absence of attention (Woldorff et.al., 1991; Naatanen et.al., 1993b). Naatanen et.al., (1993b) postualated that the intensity MMN is very much vulnerable to attention i.e. when attention is very strongly focused on the input delivered to the opposite ear in a dichotic condition, minor decrements in stimulus intensity seemed to elicit no or only a very small MMN, where as MMN's were elicited when attention was focused elsewhere is less intense (reading) in other words, the MMN to intensity deviation is clearly attenuated in the absence of attention. Nevertheless, no data have demonstrated a total disappearance of the MMN in the absence of attention. Naatanen (1991) therefore suggested that the sensory analysis resulting in neural sound representations is not affected, but that the excitability of the MMN process trigered by a deviant stimulus might be dampened in the absence of attention. He proposed a division of neurons involved in the MMN process into 1. Computational and 2. Amplifying ones , suggesting that it is the latter neurons that might be modulated by attention. However. Naatanen (1995) suggest that a passive condition is preferred to avoid mixed waveform caused by the N2/P3 waves typically of active condition. Ignoring can be achieved by focussing the subject attention away from the test stimuli. Watching a video movie , instead of reading has proven useful with children and aphasic patients (Lang et.al., 1995). In watching a T.V. screen , the eye movements (with related electro occulographic artifacts) are smaller than when the subject is reading a book.

On the other hand, the reading saccades provide an objective measure of the efficiency of ignoring (Lang et. al., 1995). Naatanen et. al., (1995) recommend the use of dichotic paradigm to direct attention away from the MMN stimuli, by this procedure attention is controlled, and total time is shortened (Lang & Mikola 1994).

In summary, it appears that the MMN to frequency change is strongly attention independent in most conditions. However the MMN to intensity change is attenuated but not fully abolished in absence of attention. In general the degree of attention independence of the MMN is sufficient to justify its use as an objective measure of sensory analysis in audition as well as its interpretation in terms of a cerebral mechanism of attention switch to a change in an unattended sound sequence (Naatanen, 1995).

These views have recently received strong support from the dramatic results of Kane, Curry, Butter and Cummins (1993), which demonstrated the emergence of a well defined MMN in coma patients 1 to 2 days before they regained their consciousness and a continuous absence of the MMN in those patients who later died.

**THE INTER INDIVIDUAL VARIATION OF THE MMN :**

The inter individual variation of the MMN can be mainly attributed to the following factors.

1. Auditory discrimination ability of the subj ect
2. Age
3. Gender
4. Acquisition Characteristics
5. Stimulus Characteristics

Auditory discrimination ability of the individual:

Lang et. al. (1990) have shown that there exists a significant positive correlation between the MMN amplitude recorded in a passive condition and the pitch discrimination performance in an active condition. In a study conducted on 26 young adults with normal hearing by Lang et. al. (1990), 6 subjects showed poor, 9 moderate and 11 very good discrimination performance. Six subjects with poor performance it was not possible to elicit the MMN with a 50 Hz difference (at 698 Hz center frequency). In contrast, in the 11 subjects with good performance, the MMN was seen in the grand average even with a 19 Hz difference. Lang et. al. (1990) opined that for individuals with the good discrimination performance, an MMN can be elicited by a 12 Hz difference (the smallest difference used). However, the MMN amplitude for the nine individuals with moderate discrimination was between these two groups.

The correlation between pitch discrimination and the MMN amplitude has been recognized also in other studies (Kraus et. al., 1993; Naatanen et. al., 1993; Winkler and Naatanen, 1992).

Similar correlation has also been shown by using synthetic vowels as stimuli (Aaltonen et. al., 1995). Thus, there is an association between the pitch discrimination performance and the MMN amplitude in healthy individuals (Lang et. al., 1995) however, the correlation exists only with relatively small pitch differences. With increasing differences, other ERP components are superposed on the MMN waveform causing the difference in the ERP amplitude between the groups to disappear (Lang et. al., 1990).

Lang et. al. (1995) suggested that this association between the MMN amplitude and the discrimination of the frequency contents of a sound makes it possible to study the pre attentive processing of at least the frequency variables of sound stimuli and more complex speech signals (eg. Vowels).

Kraus et. al.(1994), Naatanen et. al. (1993) reported that when the discrimination performance was improved with training it would subsequently lead to an increase in MMN amplitude. However, it is not yet clear whether all individuals who repeatedly show a small MMN with frequency deviation (ie. It does not depend on physiological or technical variation factors) also have poor pitch discrimination (Lang et. al., 1995). Lang et. al. (1995) further opined that, it is still uncertain that whether individual differences in the MMN amplitude in subjects of the same age can be explained entirely by the difference in the pitch discrimination performance, or it may be because of individual differences in discrimination of the stimuli eg. sound duration or inensity differences would lead to variation of the MMN amplitudes.

**Age** :

According to Lang et. al., (1995), MMN can be without exception elicited in infants, children and adults and its peak latency shortens with increasing age. A complicated interaction seems to exist between age and amplitude. Lang et. al.(1995) opine that with increasing age, the MMN amplitude decrease especially if a long ISI between the standard stimuli is used. Further more, the number of Biphasic responses increases and the signal-to-noise ratio deteriorates with age. (Lang et. al., 1995; Woods, 1992).

**Gender** :

Gender also has an influence on the MMN latency. Aaltonen et. al. (1994) reported that with complex stimuli, the MMN latency is significantly longer in females than in males.

**Acquisition Characteristics**

**a. Electrode placement** :

The MMN distribution over the scalp may convey some valuable information. (Lang et. al., 1995). They opine that it is useful to measure the MMN parameters at all of the seven electrodes in which the maximum amplitude of the wave form may occur (Fpz, $F_4$, Fz, $F_3$, $C_4$, Cz and $C_3$) (Lang et. al., 1995). Naatanen (1972) recommends use of nose as reference to identify the MMN topographically.

Kurtzberg et. al., (1995) reported that MMN amplitude was larger at the frontal electrode (Fz) in majority of the subjects participated in their study secondly over the Cz however, in few subjects they found no MMN at Cz. Naatanen et. al. (1978) reported of larger MMN amplitude above the temporal areas. More sophisticated methods can take advantage of the spatial redundancy in the MMN scalp distribution to enhance its SNR (signal-to-noise ratio) (Kurtzberg et. al., 1995).

**b. Total Number of Standard and Deviant Stimuli**

Lang et. al., (1995) opine that Background EEG will not be totally cancelled in the averaging since the frequency band of the MMN response is very close to the alpha band . They suggest that a rough estimation of the number of trials for achieving the ultimate detection limit (0.3 /μv) can be obtained from the equation

$$SNR = \frac{U_{srms}}{U_{Nrms}} \sqrt{N}$$

Where, SNR- Signal to Noise ratio

Usrms - Signal Amplitude (rms)

UNrms- Noise Ampltude (rms)

N- Number of trials in the average.

In practice however, the duration of the recording session is limited and it is seldom possible to collect more than 200 to 300 deviant and 1200 - 2700 standard responses. (Lang et. al., 1995).

**c Repetition Rate and Probability of stimuli**

If simple stimuli are used, MMN amplitude increases when the IsI ( inter stimulus interval from the stimulus onset to the onset of the next stimulus) is shortened , provided that the intervals between the deviants are of the same duration (NaStanen et. al., 1987). This result is in contrast to the fast decrement of the amplitude of the $N_1$ and $P_3b$ component (Mantysalo & Naatanen, 1987; Sams et.al., 1993). Naatanen, (1995) opined that this phenomenon is due to the fact that when the repetition rate of the standard stimuli increases the memory trace evoked by it becomes more intense which in turn strengthens the MMN response generated by the comparison process. In addition to the selective increase of the MMN, a higher repetition rate shortens the recording session thus contributing to an improved recording quality (Lang et. al., 1995).

In practice an ISI of about 300msec has been used for MMN applications when using simple or vowel stimuli (Lang et. al., 1995). However, short ISI may lead to the following problems

1. if the decay speed of the memory trace contains any essential information, this information may be lost.

2. In the case of long latency response, the "tail" of the response may be lost, including the $P_3$a waves which signals the obtrusiveness of stimuli. (Lang et. al.', 1995).

The MMN amplitude also is effected by the probability of the deviants in the stimulus sequense. When the probability is lower, the MMN amplitude increases. (Lang et. al., 1995). However, the total time of recording increases which again reduces the quality of the response (Lang et. al., 1995). Lang et. al. (1995) suggested that good results can be obtained if every 5$^{th}$ to 10$^{th}$ stimulus is a deviant (P= 0.1 to 0.2) in a "pseudo random" stimulus sequence. It is imperative that the stimulation program does not generate low or more deviants one immediately after the other, because then those deviant function as new standards and MMN response in the difference waveform is attenuated (Sams et. al., 1983).

d. Large stimulus differences

When the physical differences between the standard and deviant stimuli is small it is easier for the subject to ignore the test stimuli (Lang et. al., 1995). With a small difference, however the MMN amplitude is low and the signal to noise ratio is poor. (Lang et. al., 1995). When the deviance exceeds **a** certain critical limit, the highly deviant obtrusive stimulus causes a passive switch of attention (Naatanen, 1995). In that situation, a large $P_3a$ component is superposed on the deviant waveform.

Lang et. al. (1995) suggested that with a large frequency difference between the standard and the deviant stimulus, the neurons in the primary auditory cortex activated by the deviant are different from the activated by the standard . In addition with larger ISI between deviants, the activation of Nl caused by the deviants may be significantly larger than that caused by the standards. (Lang et. al., 1995).

Currently, it is unknown what the "safe" upper limits are for the deviance of duration and intensity stimuli as well as for complex stimuli (Lang et. al., 1995). A positive waveform ($P_3a$) following the MMN waveform, however, implies that the stimulus difference is too large.

**e. Interaction and Variance of Difference Stimulus Parameters**

The selection of stimulation parameters is primarily determined by the experimental question. However, the MMN response is generated by any psychophysical (subjective) difference between the standard and deviant stimuli (Lang et. al., 1995). Although the stimulation parameters are physically (objectively) independent of each other, a psychophysical interaction may exist between them (Lang et. al., 1995).

Lang et. al. (1995) *farther* state that due to the non linear behaviour of hearing, the interactions between the different stimulus parameters should be taken into account. For example, the frequency and loudness of a tone are related via equiloudness contours (Rabinson & Dadsen, 1956) and the duration of the tone also effect the loudness level sensation. Hence if the duration of a short (less than 50msec) stimulus is increased, the intensity experienced also increases making it an unwanted additional variable, if the intention is to study only the influence of duration difference on the MMN (Lang et. al., 1995). Use of complex stimuli is the study of speech processing requires sufficiently invariant stimuli (Lang et. al., 1995). Computer programs for waveform synthesis and parametric speech synthesis (Klatt, 1980) can be used for generating these complex stimuli in a controlled way (Lang et. al., 1995).

The physical properties of the auditory stimuli (Sound pressure level, frequency spectrum) are normally fixed in the stimulus generation phase and they should not be affected by the presentation deviance (Lang et. al., 1995). In practice, however, a careful calibration of the whole stimulus delivery system by means of a precision sound level meter and an artificial ear is needed each time a new stimuli is introduced (Lang et. al., 1995).

Stimulus Characteristic :

Within the oddball paradigm, the MMN quality varies according with the dimension of deviance between standard and deviant stimulus. The MMN is reportedly produced even when the deviations are very slight atleast for changes in pitch (Sams et. al., 1985) and intensity (Naatanen, 1986). In general, it has been reported that the amplitude of the MMN is directly proportional to the magnitude of stimulus deviation (upto a plateau of about 10% deviation), where as its onset latency and duration have been reported to be inversely related to the degree of deviation (Naatanen, 1985).

Naatanen and Associates (1985) have suggested that the sensitivity of the MMN to slight physical deviations together with its putative independence from attentional influence indicate that the physical features of auditory stimuli are fully analyzed even when the stimuli are unattended. According to this view (Naatanen, 1985) a template or neural trace is established by repetition of the standard stimuli and the MMN is elicited when the deviant stimulus fails to match this trace. In order to accomplish this template-matching operation, it is postulated that the brain must have performed a " full analysis " of the physical features of both the standard and deviant stimuli (Naatanen, 1988). Recordings of the magnetic counterpart to the MMN (Hari et. al., 1984; Sams et. al., 1985) and dipole source localization of the electrical MMN (Scherg, Vajsac & Picton 1989) suggest that these analysis and comparison processes may take place in the auditory cortex.

Frequency Deviance :

Cs'epe (1995) studied the effect of frequency deviance from 25% to 5% on MMN and found that smaller the difference, the larger the latency range and cortical area showing a significant MMN. The amplitude however showed significant enhancement with the increasing frequent deviations reaching a plateau at difference of 15% (Cs'epe 1989):

Cs'epe (1989) in his study observed that no MMN was elicited with deviants with frequency decrements less than 5% . However, paavilainen et. al. (1993) postulated that MMN can be even elicited by frequency increments of 5%. The difference between the two studies was the difference in the stimulus duration used. The former used a duration of only 5 msec, whereas the later used 30msec. Paavilainen et. al.(1993) opined that a interplay between the two parameters ie. frequency and duration influence the time needed for forming a better memory trace which inturn results in the better generation of MMN.

Naatanen, (1995) opine that the difference in frequency is more important than the individual frequency of the stimuli, with a small difference. MMN amplitude is small and S/N ratio is poor.

**Intensity Deviance** :

When there is very small difference in the intensity of the two stimuli MMN amplitude is low and S/N ratio is poor (Naatanen, 1995). Currently the 'safe' upper limits for deviance of intensity is not known.

Naatanen et. al. (1989a) opined that infrequent decrement in stimulus intensity elicited the mismatch negativity (MMN) which was larger in amplitude and softer in latency, the softer, the deviant stimuli was. Synder and Hillyard (1976) postulated that changes in the intensity of even an extremely brief stimulus such as click, might produce an MMN. Paavilainen et. al. (1993) found that the intensity MMN can be elicited even with stimulus duration of 10msec and its amplitude increased as a function of stimulus duration in contrast the frequency MMN required a stimulus duration of about 30msec and the amplitude did not increased when the stimulus duration was prolonged.

**Duration :**

The time dimension is one of the critical aspect of the memory traces involved in MMN generation (Naatanen, 1995). Eliciting an MMN response by shortening ISI duration as the target has been extensively study (Ford et. al., 1981; Naatanen, 1995; Naatanen et. al., 1993; Nordby et.al., 1988). Naatanen et. al. (1981) concluded that using simple stimulus ISI duration decrements resulted in increased amplitude provided that the interval between deviance are of the same duration. On the basis of durational decrement studies Bottcher-ganelor et. al. (1992) suggested that the duration of neuronal representation is about 10 sec.

Spatial location :

Sound localization plays an important role in auditory information processing. This ability is necessary for instance in attending selectively to one sound source in the multitude of other sounds originating from different spatial loci. The human auditory system is capable of performing very fine discrimination between loci of sound origin mainly on the basis of inter aural phase and intensity differences (Schaef and Houstna, 1986). Paavilainen et. al. (1989) conducted a study to determine whether a change in spatial location produce an MMN. Auditory stimulus blocks were presented to 12 reading subjects. The standard (p = 90%) were presented in straight at 0° azimuth and the deviants from an angle of either 10, 45 or 90° to the right of the standard. The spatial locations were produced via earphones by introducing for low frequency (600Hz) tone an inter aural difference and for high frequency (3000Hz) tones an inter aural intensity difference. Standard and deviant stimuli were also delivered in more natural, free field condition via differently positioned loud speakers. They found that the deviant tones elicited MMN followed by a P3a component. They concluded that the spatial localization of a sound source is coded in the neuronal stimulus traces reflected by the MMN and that a change in this location is automatically detected by the brain by means of the MMN generator process.

Temporal Order :

Schuruger, Naatanen, Paavilainen (1992) opined that the temporal order reversals elicit an MMN when successive sound elements differ either in frequency, intensity or duration. They conducted a study to investigate whether MMN is time - locked to the temporal occurance of the deviation within the complex stimulus. Event related potentials to complex auditory sound pattern consisting of eight 50msec segments differing in frequency were recorded from human scalp while the subject was performing a visual search task. They concluded that MMN to frequency deviance can be elicited at different positions within the complex spectro-temporal sound pattern and was consistent with the hypothesis that sensory memory representation of unattended auditory events contain precise information about their spectral features. Additionally their finding that the MMN is time-locked to the temporal occurance of the deviation within the sound pattern supports the hypothesis that sensory representations contains precise temporal information about the sounds.

**Complex Stimuli** :

Complex stimuli like phonemes can be used to elicit MMN (Aaltonen et.al.,1987). Investigations by Sharma et.al., (1993) have revealed that, in adults, an MMN can be elicited by speech stimuli that are even difficult to discriminate psychophysically. MMN can be obtained to stimuli that lie within as well as across phonetic category boundaries (Sams et.al., 1990). The complex stimuli generally used are synthesized speech token in order to control the acoustic features (Rraus et.al., 1995).The stimuli consists of five formants and the pitch, contouring, fundamental frequency jitter and presentation rate are adjusted to create natural sounding phonemes.

The commonly varied parameters in this oddball paradigm using speech stimuli are interdeviant internal (EDI), interstimulus internal(ISI), stimulus onset asynchromy [interval between stimulus onsets,SOA(temporal order)] and the probability of occurance of the deviant stimuli (Naatanen, 1992). The combination of parameters that yield a robust MMN in response to., tonal difference does not necessarily yield the best MMN to complex stimuli (Kraus et.al., 1995).Kraus et.al. (1995) opined that even within complex stimuli, the combination of optimal parameters is not uniform. Moreover the parameters inherently covary making it difficult to assess specific parameters (Imada, Hari,Loveless, McEroy and Sams, 1993; Ritter et.al., 1992). In addition there are the practical issues of determining what stimulus and recording parameters will most parsimoniously yield interpretable information for a particular stimulus contrast (Kraus et.al., 1995).

MMN has been recorded in atypical oddball paradigm i.e. where several deviants or standards are present, (Ritter et.al., 1995;Winkler etal., 1992). Thus the MMN is not necessarily limited to a simple oddball paradigm in case of complex stimuli.

Although it is generally thought that MMN magnitude increases with shorter ISI.(Groneig et.al., 1996), Kraus etal., (1995) reported that MMN size decreases with a shorter ISI when elicited by /ga/-/da/ (Speech Stimuli).

**Multidimensional Deviance.**

Until recently, MMN research foccussed on one-dimensional changes, leaving open the question whether similar MMN patterns can be elicited by deviants that differ from the standard stimulus on multiple dimensions (Schroger, 1995). In the case of a multidimensional stimulus change, each deviant feature would elicit its own MMN (Schröger, 1995). In addition, these independently and simultaneously activated MMNs may lead to an additive MMN in the case of a multidimensional deviant (Schroger, 1995).

Very recently the hypothesis of additive mismatch responses was tested in the magnetoencephalographic study by Levdnen et. al. (1993). They measured the mismatch fields (MMFs) for one and two-dimensional deviants.

The two dimensional deviant consisted either of simultaneous changes in inter-stimulus interval and frequency or change in duration and fequency. The MMFs for two dimensional deviants were very similar to the sum of the MMFs for the corresponding one -dimensional deviant (Levdnen et. al., 1993).

Schroger, (1995) conducted a study to test the hypothesis of an additive MMN by employing a frequency deviant, a location deviant and a two dimensional deviant differing from the standard in both frequency and location. The testing was carried out both in ignore and attended condition. Schroger, (1995) concluded that in the ignore condition the two-dimensional deviant elicited an enhanced mismatch negativity as compared with the MMNs elicited by the one-dimensional deviants. Thus proving the additive hypothesis of MMN elicitation as the temporal and the topographic distributions of the two-dimensional MMNs can be modelled by adding the one dimensional MMNs. He postulated that this additivity of the MMNs probably results from the independent activity of separate neural populations generating the frequency and the location MMN. However in the attend condition, the deviance related-related ERPs effects were not additive in the $N_2$b and $P_3$ range implicating that the neural processes involved in the conscious detection of changes in location and frequency are not independent.

From the brief survey of literature it is evident that relatively few studies have been carried out in terms of studying the effects of intensity deviance on the various MMN waveform parameters like latency, amplitude, duration and magnitude. However on the basis of earlier studies it has been reported that very with small differences in the intensity of two stimuli MMN amplitude is low and S/N ratio is poor. Moreover, Naatanen et. al. (1993b) and Woldroff et. al. (1991) reported the effect of attention on intensity MMN. Considering these the present study, was designed to investigate the effects of intensity deviance on the following parameters of MMN waveform

1. Latency (onset, offset, peak)
2. Amplitude (onset, offset peak)
3. Total duration
4. MMN magnitude

Further, an attempt was made to investigate whether reading causes significant change on intensity MMN.

# METHODOLOGY

This study was taken up with the aim of investigating the effects of intensity deviance on mismatch negativity and also to see. whether reading can cause a significant difference in intensity MMN. The methodology is described under the following headings

1. Subjects
2. Instruments
3. Test environment
4. Procedure

## SUBJECTS

30 volunteer's (15 male &15 female) from neighboring colleges and the graduate students of AIISH in the age range of 18-23 years were taken up for this study.

### SUBJECT SELECTION CRITERIA

1. Subject should not have any history of biological, psychological, or Neurological problems.
2. Subject should be able to relax in the presence of electrodes placed for the duration of testing and impedance values were within normal limits.
3. Subjects should have hearing within normal range, (pure tone average better than 25 dBHL, reference ANSI 1969).

## INSTRUMENTATION

The following equipment were used in this study.

a. Pure tone audiometer- a single channel diagnostic audiometer (Beltone model 112) with TDH-50p earphones lodged in MX-41/AR ear cushion was used to estimate the behavioral thresholds of all the subjects. The audiometer was calibrated prior to the study as per recommendation of the manufacturer.

b. Immitance meter - A microprocessor based automatic immittance meter with a visual display ( Grason - Stadler GSI-33,Verson-I middle ear analyzer) was used to access middle ear function of subject. The immitance meter was calibrated as per recommendation of the manufacturer.

c. Electrophysiological unit -

Biological Navigator, an auditory evoked potential system was used to record waves in the subjects. The following accessories were used:

1) Electrodes - 5 silver chloride electrodes were used for recording the potentials.
2) Earphones - TDH-39 earphones mounted on supraaural MX-41/AR ear cushion was used to present the stimuli.

## TEST ENVIRONMENT

Pure tone audiometry was conducted in portable sound treated booth. Immittance evaluation and electrophysiological testing was carried out in a quiet room.

## TEST PROCEDURE

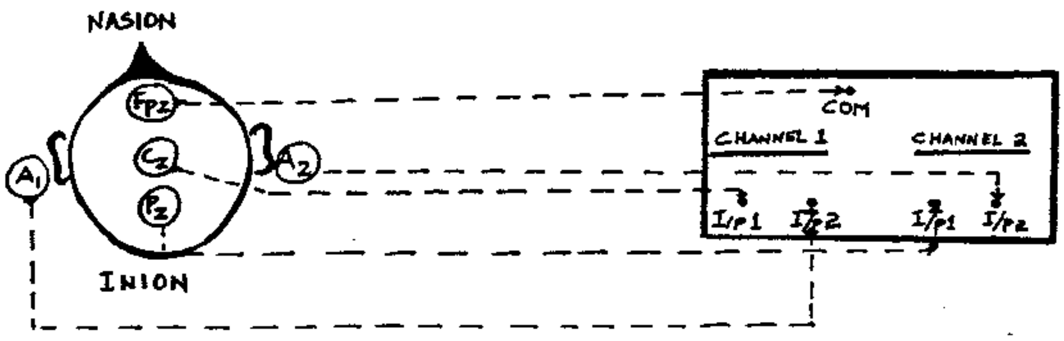
All volunteers were screened for their puretone thresholds in both the ears using single channel clinical audiometer. The frequencies tested were from 0.25-8 kHz. If the thresholds in any one ear exceeded 25dBHL, the subject was not taken up for further testing. Subjects who had thresholds within 25dBHL were tested for tympanograms and reflexes in both the ears using an immittance meter GSI-33. Subjects who passed both the tests were taken up for this study.

### PATIENTS SETUP

The subjects were seated in a comfortable posture with the head fully supported to ensure noise free recordings. Neck and Jaw muscles were relaxed to ensure a minimum rejection rate.

### ELECTRODE PLACEMENT

The electrode site for the two channel mapping recordings was selected as Cz and Pz as positive, the FPz as common and $A_1$ (left ear mastoid) and $A_2$ (right ear mastoid) as negative.




| POSITION | CONNECTION IN ELECTRODE BOX |
|---|---|
| Forehead (FPz) | Common |
| Vertex(Cz) | Channel-1, Input-1 |
| Parietal(Pz) | Channel-2, input-1 |
| Mastoid(Left)($A_1$) | Channel-1, Jnput-2 |
| Mastoid (Riqht)($A_2$) | Channel-2, input-2 |

Schematic representation of electrode site and its connection in the electrode box

Silver cup electrodes were fixed at the sides after thorough skin surface cleaning with surgical spirit and skin preparing solution and later filled with standard EEG electrode paste, suitably secured in place with surgical tape.

**MEASURING IMPEDANCE**

The impedance of the electrodes were measured for each electrode for the 2 channels. All electrode impedance were less than 5k ohms, and within 3k ohms of each other (inter electrode impedance). If the impedance increased beyond 5kohms, the electrodes were removed and the sites were properly cleaned again, patient was asked to relax and the electrodes were resettled. The negative electrode $A_1$ and $A_2$ was interlinked using a jumper to obtain a clear waveform.

**STIMULUS PARAMETERS :**

MMN measurements were carried out with alternating tone bursts, using an oddball paradigm. A 1000 Hz tone burst (with 10-ms linear rise and fall time, 30-ms plateau) was used as the standard stimulus while a 1000 Hz with various intensity deviance from the standard stimulus (ΔI) 3dBnHL; 5dBnHL; lOdBnHL corresponding to deviant intensities of 63dB, 65dB, 70dB (with the same envelop) was used as the deviant stimulus.

The test protocol used. for recording MMN are summarized in Table 1.

**Table - 1: Test Protocol for Recording**

| | |
|---|---|
| Stimuli | Alternating tone burst |
| Frequent stimuli | 1000 Hz |
| Infrequent stimuli | 1000 Hz |
| Intensity Deviance | 3 dBnHL; 5 dBnHL; 10 dBnHL; |
| Intensity of frequent stimuli | 60dBnHL |
| Intensity of infrequent stimuli | 70 dBnHL / 65 dBnHL / 75 dBnHL |
| Rise time | 10 msec |
| Fall time | 10 msec |
| Plateau | 30 msec |
| Filter | 1.1-30 Hz |
| Repetition rate | 1.1/Sec |
| Gain | 50,000 |

**RECORDING PROCEDURE**

Recording was done in two conditions

1. Condition I : Without Reading

2. Condition II : With Reading

In Condition I recording was done with 3dB; 5dB; lOdB deviance and for Condition II recording was done with 5dB deviance only.

The instructions given to the subjects were as follows :

Condition I : To be relaxed while recording

Condition II : They were instructed to read a book of their choise

Stimuli were presented through earphones placed on subject's ear with caution not to dislodge any electrodes. The blue and the red earphones were placed over the left and right ears respectively. The center of the earphone diaphragm was placed over the earcanal opening for delivery of accurate stimulus intensity. The earphones TDH-39 were used to deliver the alternating tone bursts in three separate blocks each incorporating 100 deviant stimuli and appropriate number of standard stimuli. All tones were presented pseudo randomly ( at a ratio of 5:1 for standard:deviant) at a rate of 1.1 / sec. The amplifier filter was set to a band pass of 1.1 - 30Hz with a 12 dB per octave roll off All averaged ERP's were stored in the computer for further analysis.

**ANALYSIS**

MMN was obtained by subtracting the waveform for frequent stimuli from the wave of infrequent stimuli of the Cz wave / Pz wave. From the difference wave the MMN waveform parameters, Latency, Amplitude, Duration, Magnitude (area) were measured .

## RESULTS AND DISCUSSION

The aim of the present study was to investigate

1. The effect of intensity deviance on mismatch negativity
2. The effect of reading on intensity MMN.

**CHANGES IN WAVE MORPHOLOGY:**

MMN were judged to be present by visual recognition for all the subjects both in deviant and the difference waveform .Mcgee et. ai,(1997) reported that MMN can be identified visually as a relative negativity occuring with in a 350msec window following the NI. In the present study MMN was apparent for all subjects both in deviant and the difference waveform but not in the standard waveform. At 3dB deviance the MMN was identified visually as a relative negative peak in the difference wave with peak latency falling in the region between 225-300msec which is evident from fig5. It can inferred from fig7 that for 5dB deviance difference waveform the peak latency fell in the region between 217-277msec. However at l0dB deviance the MMN was identified as a relative negativity in the difference wave with peak latency ranging between 175-215msec as revealed in fig9.

Lang et.al,(1995) warned against using overly large stimulus difference in the clinical application of MMN .When the physical difference between the standard and deviant stimulus is large ,a passive switch of attention can occur (Naatanen 1995) and a positive waveform (P3a) following the MMN wave can be observed . In the present study only two subjects waveforms revealed P3a waveform at lOdB deviance only ,however the remaining subjects did not have any positive waveform following the MMN waveform , indicating that

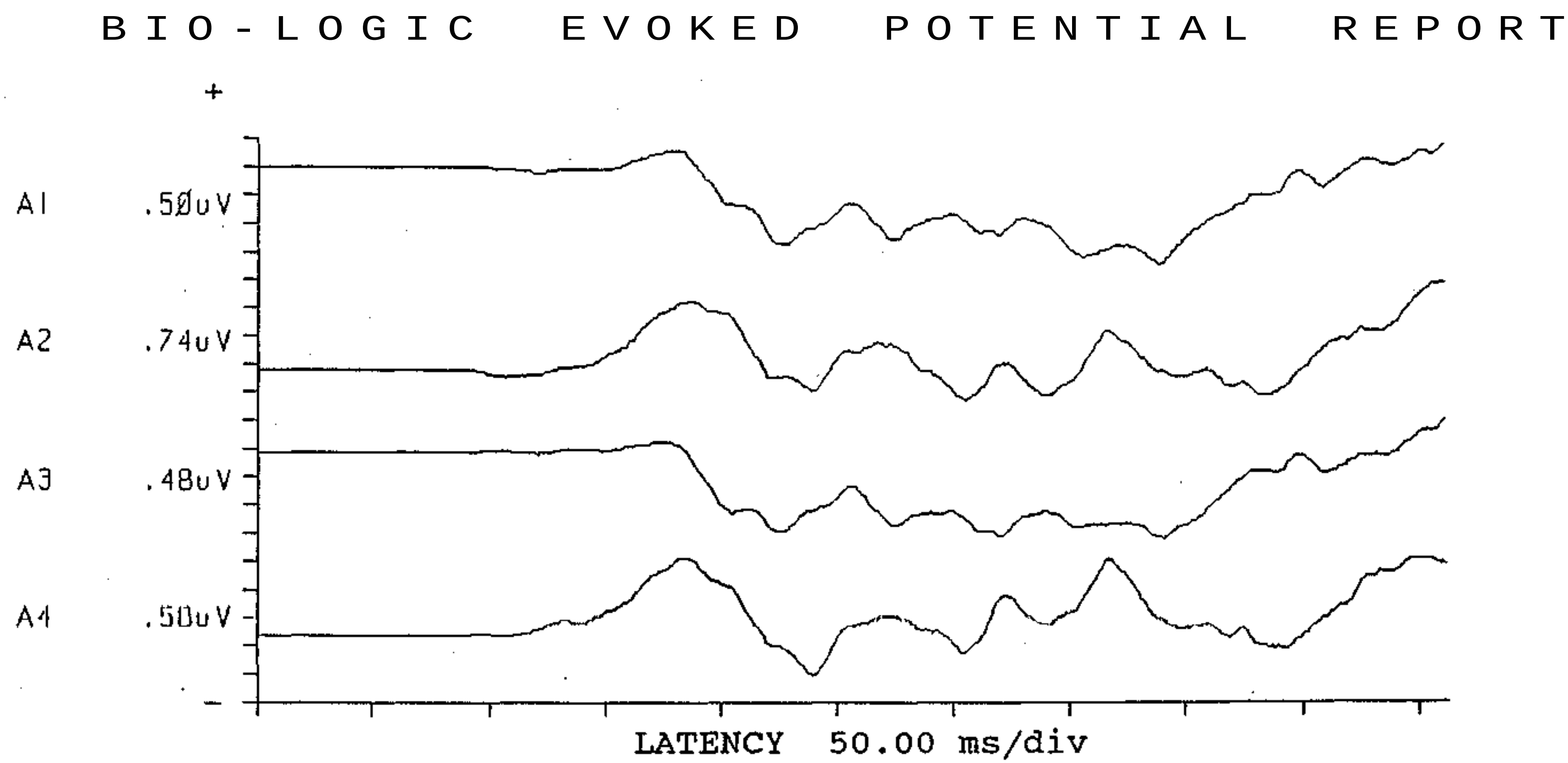



**Fig-4 : Individual representative waveform at 3 dB deviance**

**Al & A2 : CZ Waves** **Al & A3 : Standard stimuli wave**

**A3 & A4: PZ Waves** **A2 & A4 : In frequent stimuli wave**

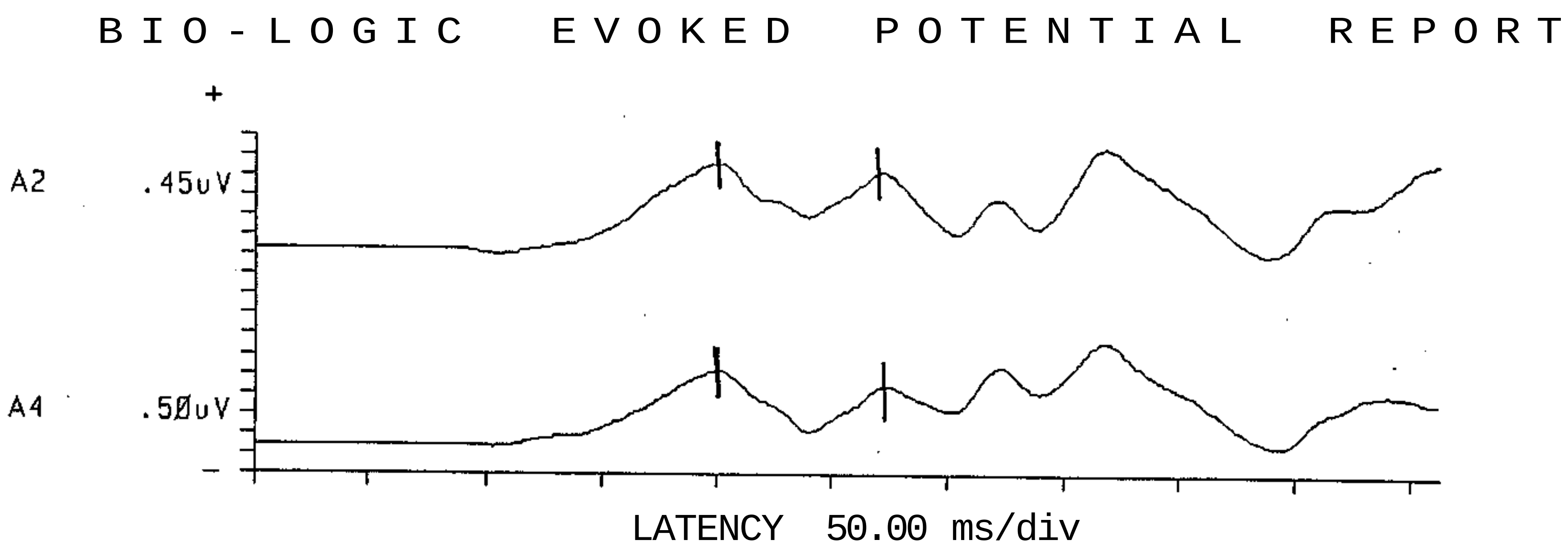



**Fig-5 : Individual representative difference waveform at 3 dB deviance**

**A2 : Standard stimuli wave at CZ - infrequent stimuli wave at CZ**

**A4 : Standard stimuli wave at PZ - infrequent stimuli wave at PZ**

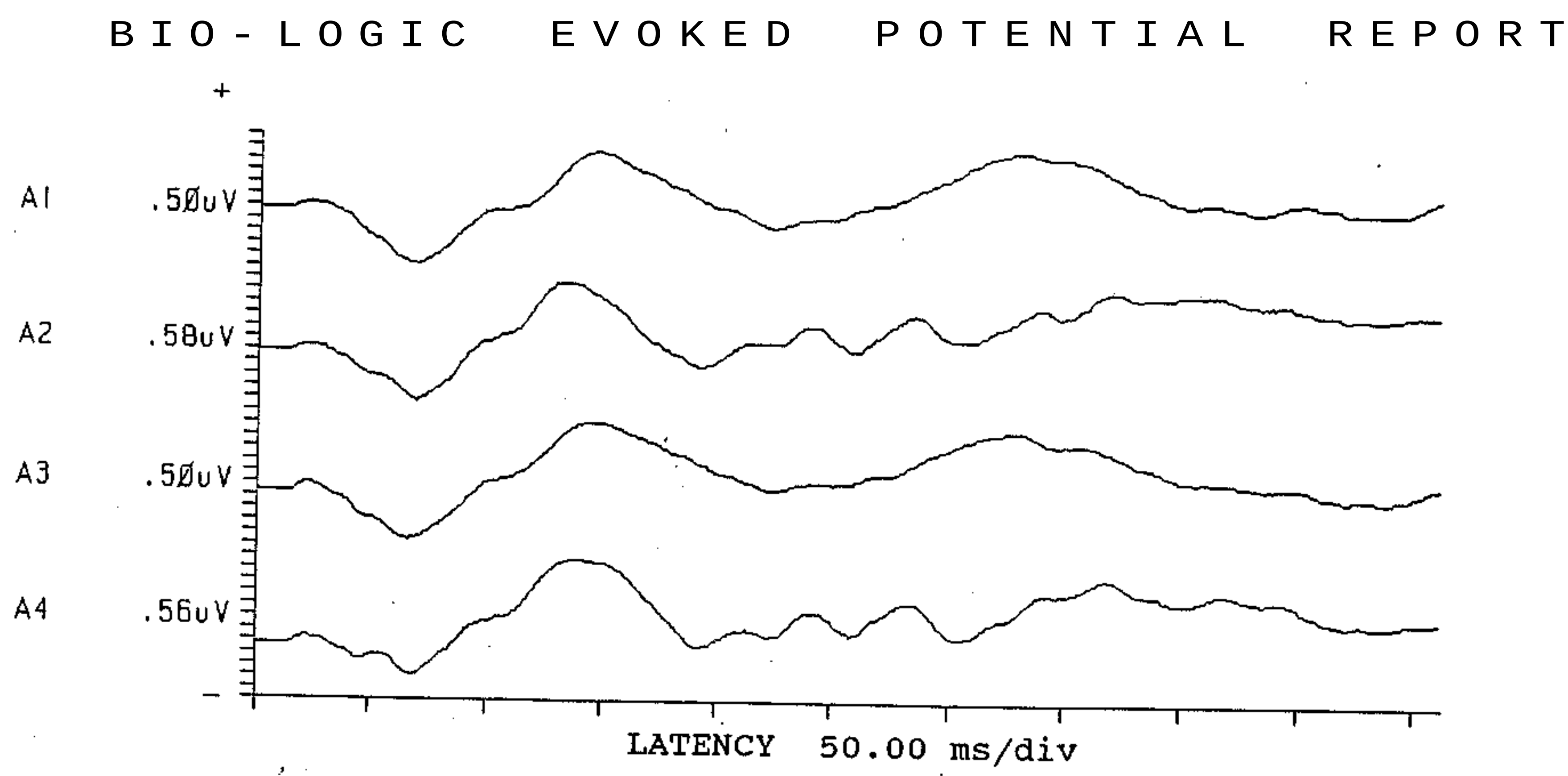



**Fig-6 : Individual representative waveform at 5 dB deviance**

**Al & A2 : CZ Waves** **Al & A3 : Standard stimuli wave**

**A3 & A4 : PZ Waves** **A2 & A4 : In frequent stimuli wave**

# B I O - L O G I C E V O K E D P O T E N T I A L R E P O R T

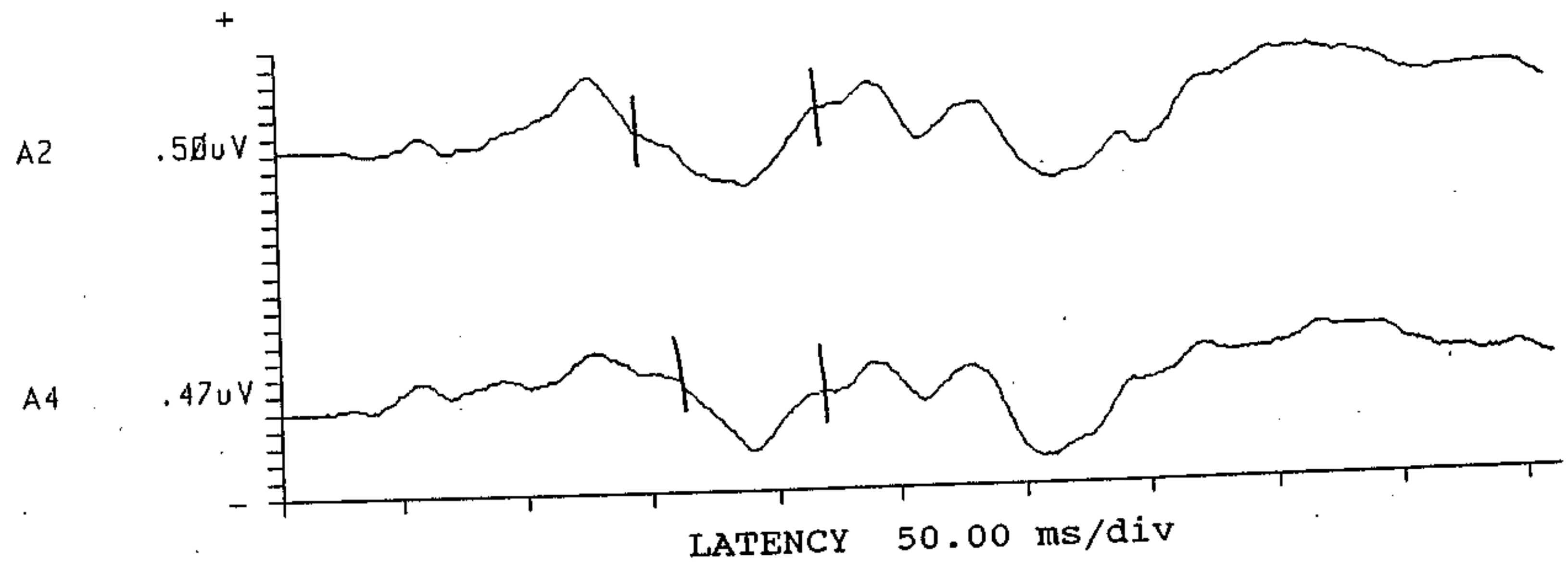



**Fig-7 : Individual representative difference waveform at 5 dB deviance**

**A2 : Standard stimuli wave at CZ - infrequent stimuli wave at CZ**

**A4 : Standard stimuli wave at PZ - infrequent stimuli wave at PZ**

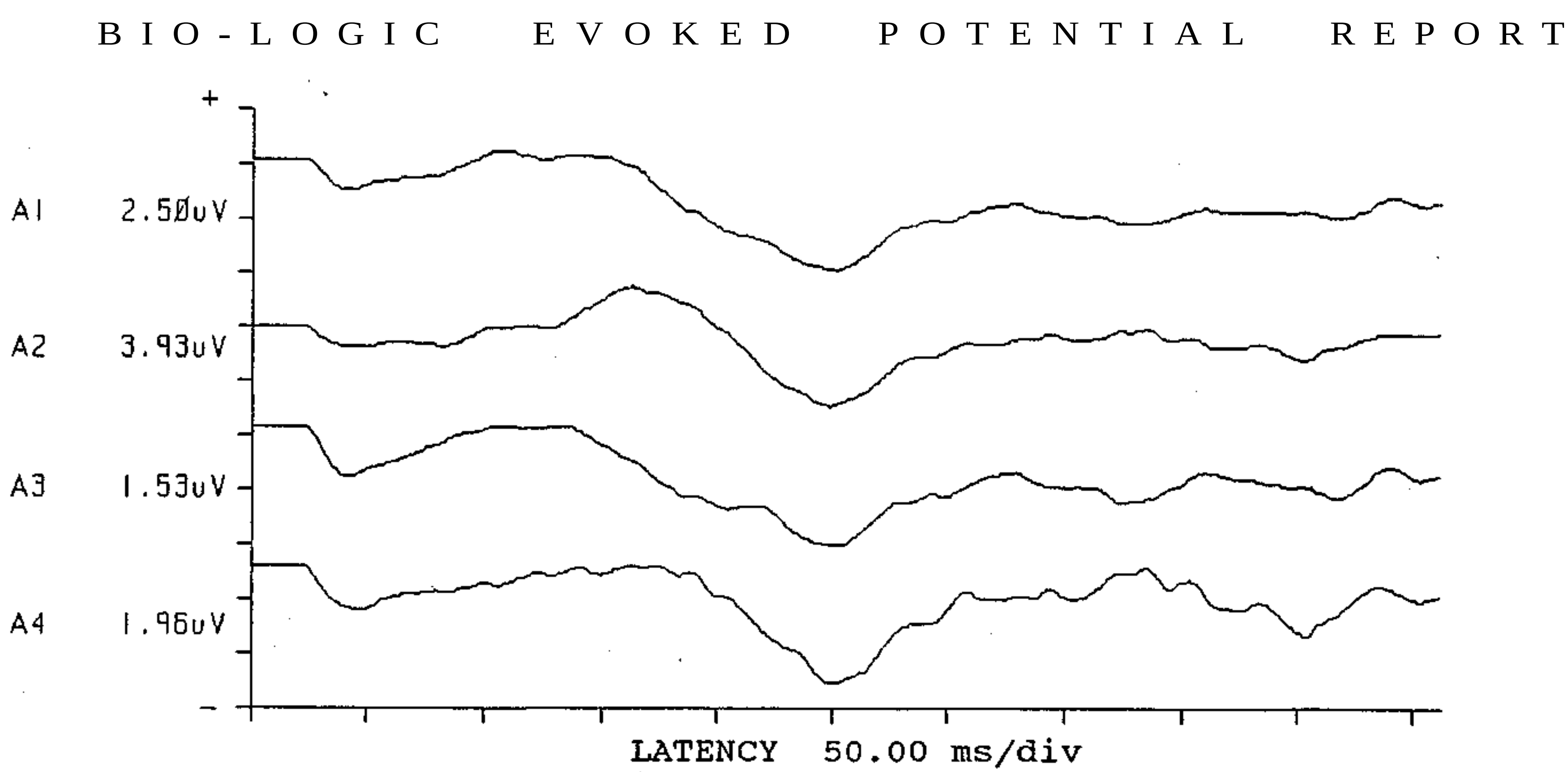



**Fig-8 : Individual representative waveform at 10 dB deviance**

**Al & A2 : CZ Waves Al & A3 : Standard stimuli wave**

**A3 & A4: PZ Waves A2 & A4 : In frequent stimuli wave**

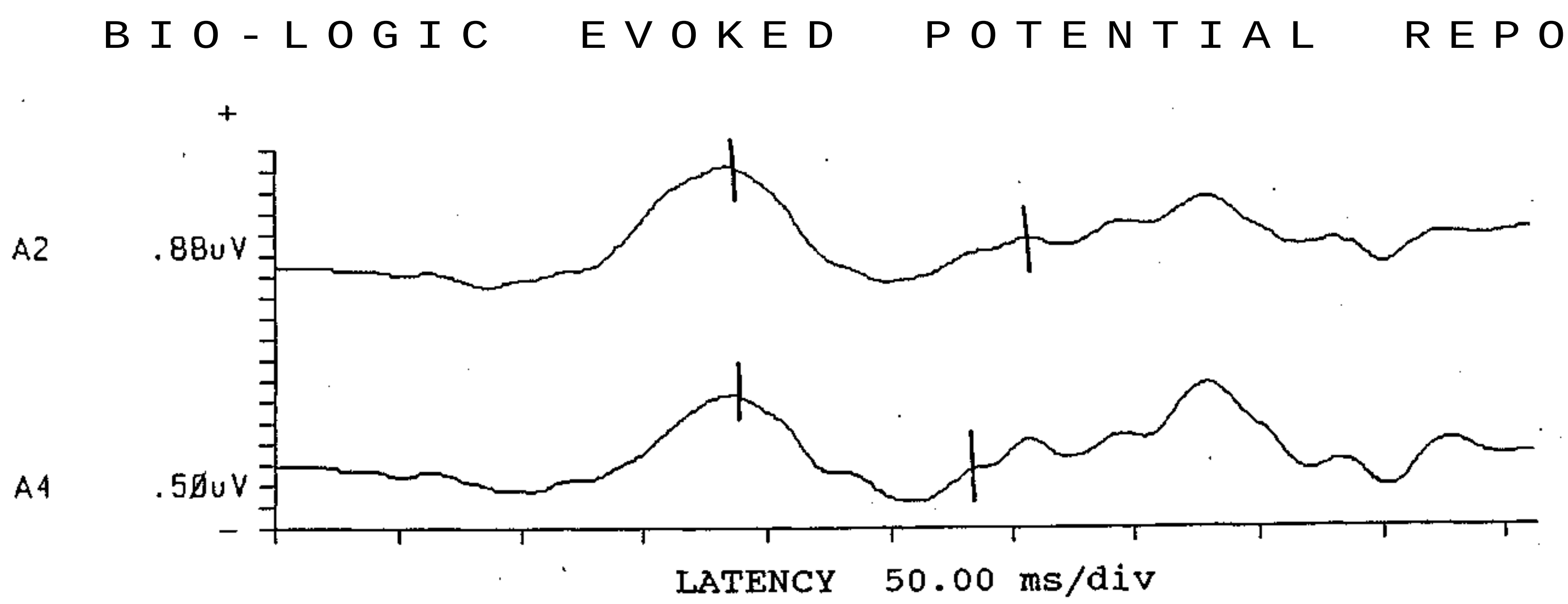



**Fig-9 : Individual representative difference waveform at 10 dB deviance**

**A2 : Standard stimuli wave at CZ - infrequent stimuli wave at CZ**

**A4 : Standard stimuli wave at PZ - infrequent stimuli wave at PZ**

the stimulus deviance selected for the present study was not too large and proved the efficacy of a passive paradigm.

Statistical comparisons were performed using 2-way ANOVA in order to find the effect between / within groups across intensity deviance (conditions) and electrode placement. Duncans Multiple Range Post hoc test with harmonic mean sample size of 60 was used [ there was no statistically significant difference seen between the recording from electrode placements Cz & Pz ] to identify the locus of significant difference between the means. **All** the statistical comparisons were performed on SPSS for windows (SPSS Inc. Chicago. II) implemented on an IBM compatible PC.

**EFFECT OF INTENSITY DEVIANCE**

An attempt was made to study the effect of 3dBnHL, 5dBnHL, l0dBnHL intensity deviance on the following MMN waveform parameters.

| Latency | Amplitude | |
|---|---|---|
| * Onset latency | * Onset Amplitude | * Total Duration |
| * Offset Latency | * Offset Amplitude | * Magnitude |
| * Peak Latency | * Peak Amplitude | |

Table-2 summarizes the Mean, Standard Deviation of the various parameters studied both at Cz and Pz placements for 3dB, 5dB, l0dB deviance.

TABLE 2 : RESULTS OF VARIOUS PARAMETERS STUDIED FOR THE 3 DEVIANT CONDITIONS AT BOTH ELECTRODE PLACEMENTS

| Difference Wave | On Laitcncy (m iiec) | | On Amplitude v) | | Off Latcncy (m gec) | | Off Amplitude (µ v) | | Total (m sec) | | Peak Latency | | Petik Amplitude (µ v) | | Magnitude (m sec). (H v) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mesan | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean I | SD |
| 3dBCz | 26.033 | 9.859 | 1.661 | 0.995 | 26.133 | 12.889 | 2.422 | 2.025 | 60.533 | 28.115 | 225.986 | 68.749 | 1.673 | 1.005 | 114.765 | 9.82 |
| 3dBPz | 29.500 | 12.635 | 1.746 | 1.032 | 27.633 | 11.069 | 2.363 | 1.813 | 63.733 | 25.441 | 240.300 | 42.395 | 1.559 | 0.879 | 106.829 | 9.08 |
| 5 dB Cz without | 33.833 | 19.992 | 2.474 | 1.749 | 31 567 | 18.562 | 2.653 | 1.679 | 71.9 | 36.444 | 217.133 | 60.411 | 2.219 | 1.247 | 175.853 | 1.44 |
| Reading 5 dB Pz without | 29.6 | 12.283 | 2.405 | 1.613 | \| 30 467 | 14.417 | 2.652 | 1.865 | 69.133 | 29.573 | 219.533 | 59.361 | 2.003 | 1.215 | 157.726 | 1.31 |
| Reading lOdBCz | 31.267 | 13.248 | 2.245 | 1.852 | 167 | 16.883 | 3.077 | 2.655 | 80.333 | 34.612 | 175.267 | 49.817 | 2.699 | 2.035 | 256.827 | 2.72. |
| lOdBPz | 30.933 | 12.809 | 2.132 | 1.743 | 43.367 | 24.065 | 3.349 | 2.804 | 80.9 | 31.908 | 169.467 | 63.111 | 2.528 | 1.799 | F230.628 | 2.38 |

**CHANGES IN LATENCY MEASURES**

Table-Al: The results of the MNN onset latency for the three conditions at the two electrode placements Cz & Pz.

| Onset Latency | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 26.033 | 9.859 | 8-43 | 33.833 | 19.992 | 11-92 | 31.267 | 13.248 | 13-70 |
| Pz | 29.500 | 12.635 | 12-50 | 29.6 | 12.283 | 13-59 | 30.933 | 12.809 | 11-55 |

From Table Al it is evident that there was a small change seen in onset latency as the deviance increase. However from Table A2 it is clear that this small change seen in onset latency was not statistically significant across all stimulation conditions (F = 1.750, P = NS ) and electrode placement. (F=0.054,P = NS).

**Table A2**: Results of two way ANOVA : for onset latency
F ratio and P values are depicted for condition and electrode

| Onset Latency | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 1.750 | 0.158 | Not Significant |
| Placement (Cz/Pz) | 0.054 | 0.817 | Not Significant |

OFFSET LATENCY:

Table A3 : Means, SD and Range values of Offset latency at the two electrode placements for the three deviant conditions.

| Offset Latency | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 26.133 | 12.889 | 10-57 | 31.56 | 18.56 | 10-90 | 37.16 | 16.883 | 16-83 |
| Pz | 27.633 | 11.068 | 9-51 | 30.46 | 14.41 | 6-66 | 43.36 | 24.06 | 14-S2 |

Table A4 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size = 60

| Comparison | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| 3dB deviance | 60 | 26.8833 | |
| 5dB deviance | 60 | 31.0167 | |
| l0dB deviance | 60 | | 40.2667 |
| Significance | | 0.147 | 1.000 |

From the group average data given in table A3 it is evident that there was an increase in MMN offset latency with increasing deviance. The same is also depicted in Graphl. This progressive increase in offset latency with increasing deviance was highly significant (F = 7.223, P = 0.00). Results of post hoc analysis (Table A4) indicated that the difference in offset latency for lOdB deviation and that of 3dB & 5dB was statistically significant where as the difference in mean for 3dB and 5dB was not statistically significant.

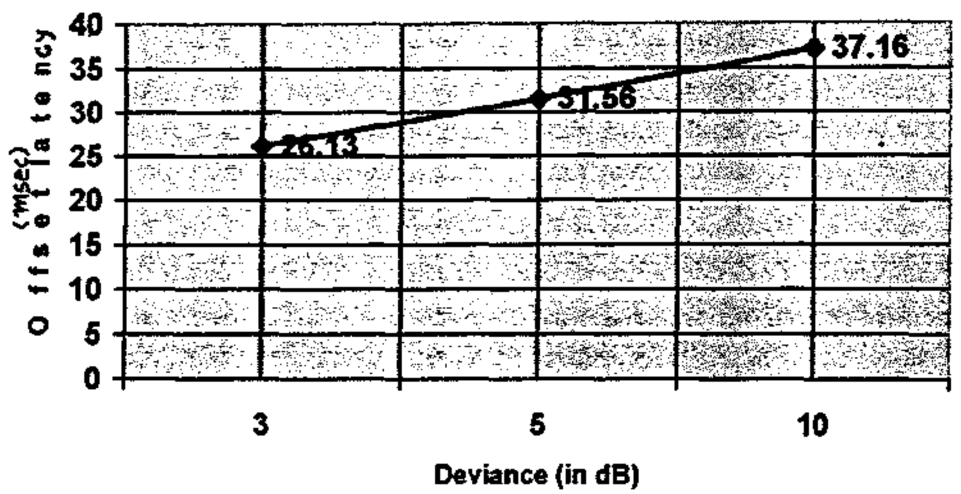
Table A5 : Results of 2 way ANOVA for offset latency

F Ratio, P Values are depicted for both condition and electrode placement.

| **Offset Latency** | F **Ratio** | **P Value** | **Significant / Not Significant** |
|---|---|---|---|
| Intensity Deviance (Condition) | 7.22 | 0.00 | Significant |
| Placement | 0.152 | 0.697 | Not Significant |

From table A5 it can be inferred that there was no significant difference observed between the two electrode placement (Cz&Pz) (F = 0.152, P = NS)

**Graph 1**:
Mean (± SEM) MMN offset latency at Cz as a function of intensity deviance




PEAK LATENCY :

**Table** A6 : Mean, SD, Range values of peak latency at the two electrode placements for the three deviant conditions.

| Peak Latency | 3dB Deviance | | | 5dB Deviance | | | 10dB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 225.9 | 68.7 | 181-328 | 217.13 | 60.41 | 127-337 | 175.26 | 49.81 | 128.295 |
| Pz | 240.3 | 42.39 | 111-323 | 21933 | 59.36 | 127-334 | 169.46 | 63.11 | 126.298 |

Group average data given in Table A6 & Graph 2 reveal that the MMN peak latency values decreased progressively with increasing deviance . This progressive decrease in peak latency was statistically significant (F = 17.565, P = 0.00).

Table A7 : Results of 2 way ANOVA for Peak latency
F Ratio, P Values are depicted for both condition and electrode placement.

| Peak Latency | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 17.565 | 0.00 | Significant |
| Placement (Cz/Pz) | 0.396 | 0.530 | Not Significant |

It can be inferred from table A7 that there was no significant difference seen in electrode placement (F = 0.396, NS) for peak latency.

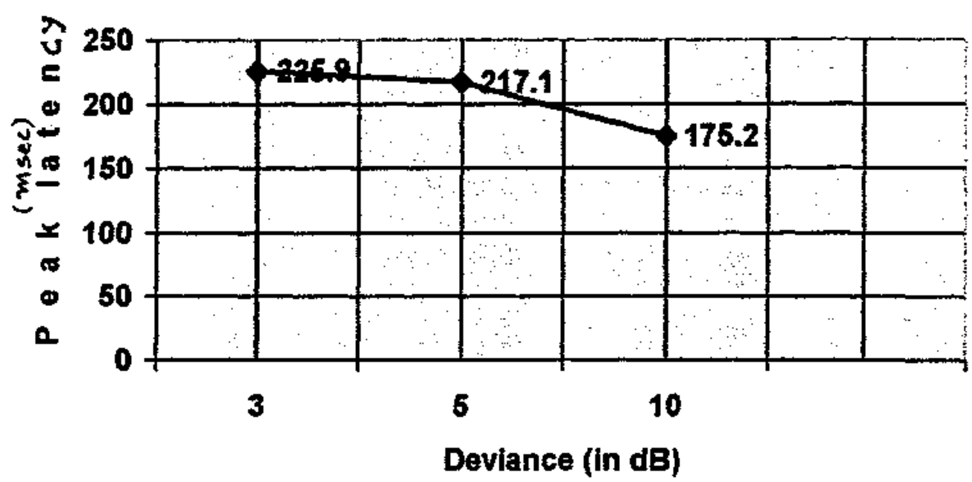
Table A8 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size = 60

| Comparison | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| 3dB deviance | 60 | 172.3667 | 233.1432 |
| 5dB deviance | 60 | 218.3333 | |
| l0dB deviance | 60 | | |
| Significance | | 0.861 | 0.153 |

From table A8 it can be inferred that the means of 3dB deviance and 5dB deviance did not differ significantly. However the mean at lOdB deviance do differ significantly.

**Graph 2** :

Mean ( + SEM) MMN peak latency at Cz as a function of intensity deviance.




The findings regarding the latency measure are in consonance with the few studies reported in literature (Lang et. al., 1995; Naatanen et. al., 1989b; Cs'epe, 1995). In the present study it was evident that the onset latency do not have statistically significant change with increasing deviance. Also the change in latency was not in the same direction.. This is in accordance with Lang et. al. (1995) who reported that onset latency is a more inaccurate ERP latency measure than the peak latency. Further more Cs'epe (1995) opined that the inter individual variations seen in onset latency, is considerably more compared to peak latency . The decrease seen in peak latency with increase in deviance is similar to the results of the other studies. Naatanen et. al. (1989) reported that the peak latency, is inversely related to the degree of deviance.

They further added that infrequent intensity decrements elicited mismatch negativity with shorter latency for softer deviant stimulus, in other words for larger deviance between standard and deviant.

It was also seen from the present study that the offset latency increased with increasing deviance, however not many studies have reported on this parameter and its relation with the degree of deviance.

CHANGES IN AMPLITUDE MEASURES :

Table Bl : Mean, SD and Range values of onset amplitude for the three deviant conditions at both electrode placements.

| Onset Amplitude | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 1.666 | 0.991 | .54-2.45 | 2.274 | 1.749 | .39-8.86 | 2.345 | 1.852 | .55-4.96 |
| Pz | 1.746 | 1.032 | .66-3.33 | 2.405 | 1.613 | .45-5.13 | 2.132 | 1.743 | J24-7.61 |

From table Bl, & Graph 3 it can be inferred that the MMN onset amplitude values increased progressively, with increasing deviance for recording from Cz. Recording from Pz electrode showed an increase in amplitude when the deviance was increased to 5dB. However, the onset amplitude for lOdB deviance was slightly less than that for 5dB deviance.

Table B2 : Results of 2 way ANOVA for onset amplitude

F Ratio, P Values are depicted for both condition and electrode placement.

| Onset Amplitude | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 3.801 | 0.011 | Significant |
| Placement (Cz/Pz) | 0.009 | 0.924 | Not Significant |

It can be inferred from table B2 that there was no significant difference seen between both electrode placements (F = 0.09, P = NS) for onset amplitude.

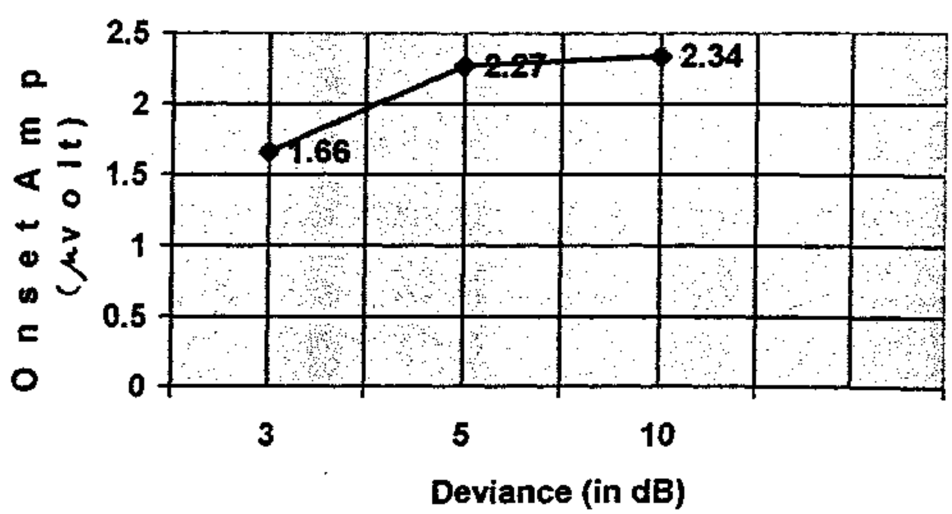
Table B3 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size = 60

| Comparison | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| 3dB deviance | 60 | 1.7035 | |
| 5dB deviance | 60 | | 2.4393 |
| l0dB deviance | 60 | 2.1885 | 2.1885 |
| Significance | | 0.081 | 0.340 |

From table. B3 it can be inferred that the difference in means of 3dB & 5dB was statistically significant where as that for lOdB was not.

**Graph 3 :**

Mean ( ± SEM) MMN onset amplitude at Cz as a function of intensity deviance.



Peak and Offset Amplitude :

Table B4 : Mean, SD and Range values of Peak amplitude for the three deviant conditions at both electrode placements.

| Peak Amplitude | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 1.673 | 1.005 | .22-3.71 | 2.219 | 1.247 | .48-3.49 | 2.699 | 2.035 | .09-8.24 |
| Pz | 1.559 | .879 | .04-3.04 | 2.003 | 1.215 | .22-3.21 | 2.528 | 1.799 | .15-7.73 |

Table B5 : Mean, SD and Range values of Offset amplitude for the three deviant conditions at both electrode placements.

| Offset Amplitude | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 2.422 | 2.025 | .47-7.22 | 2.653 | 1.679 | .23-6.43 | 3.077 | 2.655 | .36-8.83 |
| Pz | 2.633 | 1.813 | .53-6.06 | 2.652 | 1.865 | .03-5.09 | 3.349 | 2.804 | .61-9.04 |

On inspection of data in table B4 and B5 and Graph 4 it can be seen that there was a gradual increase in mean values of both Peak and Offset amplitude with increasing deviance . This progressive increase seen in both the amplitude measures were statistically significant.

(Peak amplitude , F = 9.619, P = 0.004 and offset amplitude, F = 6.225, P = 0.00).

Table B6: Results of 2 way ANOVA for peak amplitude

F Ratio, P Values are depicted for both condition and electrode placement.

| Peak amplitude | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 9.616 | 0.000 | Significant |
| Placement | .826 | .364 | Not Significant |

Table B7 : Results of 2 way ANOVA for Offset amplitude

F Ratio, P Values are depicted for both condition and electrode placement.

| Offset amplitude | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 6.255 | 0.00 | Significant |
| Placement | .17 | .896 | Not Significant |

From table B6 and B7 it can be inferred that there was no significant change seen in peak and offset amplitude at both the electrode placements

Peak amplitude (F = 0.826, NS), Offset amplitude (F = 0.017, NS)

Table B8 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size = 60

| Comparison | N | Subset for alpha = 3.05 | | |
|---|---|---|---|---|
| | | 1 | 2 | 3 |
| 3dB deviance | 60 | 1.6160 | | |
| 5dB deviance | 60 | | 2.113 | |
| lOdB deviance | 60 | | | 2.6133 |
| Significance | | .550 | 1.000 | 1.000 |

Table B9 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size = 60

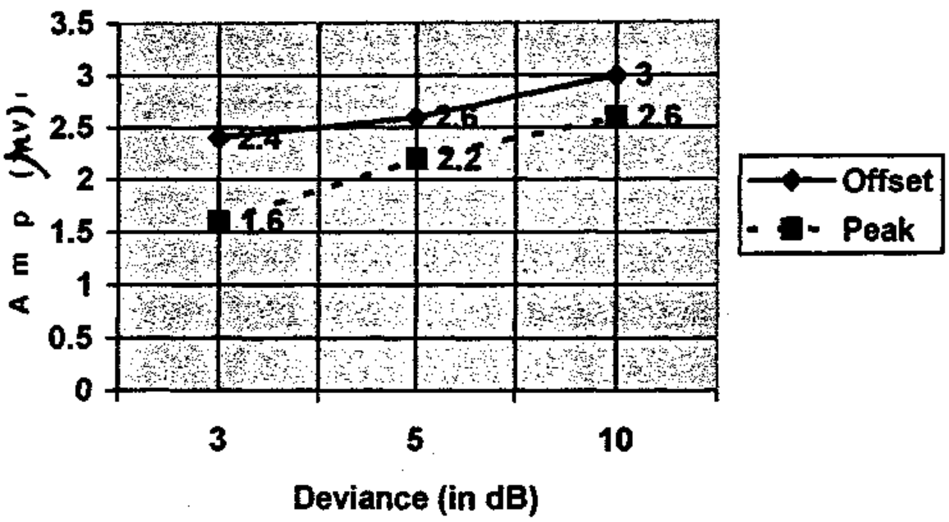
| Comparison | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| 3dB deviance | 60 | 2.3923 | |
| 5dB deviance | 60 | 2.6525 | 2.6525 |
| l0dB deviance | 60 | | 3.2127 |
| Significance | | 0.463 | 0.114 |

From table B8 it can be inferred that the means of 3dB , 5dB and lOdB differ significantly from each other.

From Table-B9 it can be inferred that the mean 3dB, differed significantly from that of lOdB where as the mean for 5dB did not differ significantly from 3dB or lOdB.

**Graph 4**:

Mean (± SEM) MMN peak amplitude and offset amplitude at Cz as a function of intensity deviance.




The findings in the present study regarding the amplitude measures reveal that the amplitude measures increased with increasing deviance and these findings are in concurrence with the few studies reported earlier in literature (Cs'epe, 1995 ; Naatanen et. al., 1989a). Cs'epe (1995) reported that the MMN amplitude measures depend on the stimulation parameters and the degree of deviance. In addition Naatanen et. al., (1989a) also reported that the amplitude of MMN increases proportionally to the magnitude of the stimulus deviation upto a plateau at 10% deviation. They further opined that infrequent decrements in stimulus intensity elicited MMN with larger amplitude for softer deviance stimulus, in other words for larger deviance between the standard and deviant.

**TOTAL DURATION :**

**Table Cl** : Mean, SD Range values of total MMN duration for the three deviant conditions at both electrode placements.

| Total duration | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 60.53 | 20.11 | 31-124 | 71.9 | 36.44 | 27-178 | 80.333 | 34.61 | 31-167 |
| Pz | 63.73 | 25.44 | -27-125 | 69.13 | 29.57 | 26-140 | 80.9 | 31.90 | 34-161 |

From table Cl, & Graph 5 it is evident that the grand average values for MMN total duration increased with increasing deviance. This increase seen in total duration with increasing deviance was statistically significant (F = 3.528, P = 0.001).

**Table C2** : Results of 2 way ANOVA for total duration
F Ratio, P Values are depicted for both condition and electrode placement.

| Total duration | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 3.528 | 0.001 | Significant |
| Placement (Cz/Pz) | 0.055 | 0.814 | Not Significant |

It can be inferred from table C2 that there was no significant difference between both electrode placements (F = 0.05, P = NS) for total duration.

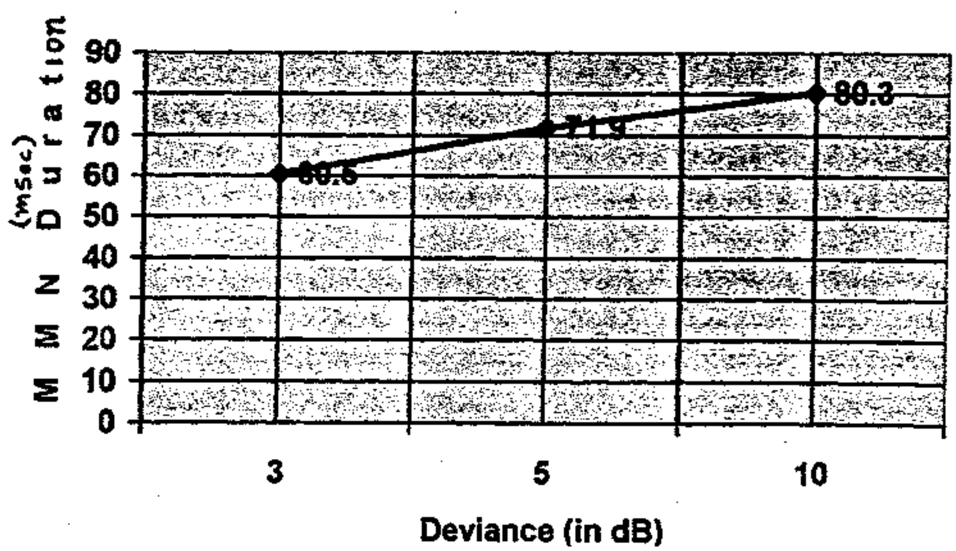
Table C3 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size - 60

| Comparison | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| 3dB deviance | 60 | 62.1333 | |
| 5dB deviance | 60 | 70.5167 | 70.5167 |
| l0dB deviance | 60 | | 80.6167 |
| Significance | | 0.164 | 0.067 |

From table C3 it can be inferred that the means of 3dB, l0dB differed significantly from each other. But the duration of MMN for 5dB deviation was not significantly different from 3dB or lOdB deviation.

**Graph 5 :**

Mean ( ± SEM) MMN Total duration at Cz as a function of intensity deviance.




In the present study the total MMN duration increased with increase in deviance. However these findings are in contradictory with the earlier studies cited in the literature. Naatanen, (1985) reported that MMN duration is inversely related to the degree of deviation. This probable difference in results of the two studies can be attributed to the methodological aspects. The present study employed an intensity deviance between the standard and deviance stimuli. However, Naatanen, (1985) reported his finding with respect to frequency deviance between the standard and deviant stimuli. Thus the difference in parameter employed to elicit MMN between the studies can account for the present contradictory result.

MMN MAGNITUDE :

The MMN magnitude (the area of MMN waveform ) was determined in the difference waveform by multiplying MMN duration and the MMN amplitude.

**Table Dl** : Mean, SD and Range values of MMN magnitude for the three deviant conditions at both electrode placements.

| MMN magnitude | 3dB Deviance | | | 5dB Deviance | | | lOdB Deviance | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) | Mean (msec) | S.D. | Range (msec) |
| Cz | 114.76 | 9.82 | 12.24-347.2 | 175.85 | 1.44 | 27-178 | 256.82 | 2.72 | 31-167 |
| Pz | 106.82 | 9.08 | 20-297.1 | 157.72 | 1.31 | 26-140 | 230.62 | 2.38 | 34-161 |

On inspection of data in table Dl and Graph 6 it can be inferred that the grand average MMN magnitude increased with increasing deviance . This progressive increase in MMN magnitude with increasing deviance was statistically significant ( F = 9.734, P = 0.00)

Table D2 : Results of 2 way ANOVA for MMN magnitude

F Ratio, P Values are depicted for both condition and electrode placement.

| MMN magnitude | F Ratio | P Value | Significant / Not Significant |
|---|---|---|---|
| Intensity Deviance (Condition) | 9.734 | 0.000 | Significant |
| Placement | 0.543 | 0.462 | Not Significant |

From table D2 it can be inferred that there was no significant change seen in MMN magnitude with various electrode placement Cz and Pz (F = 0.543,NS ).

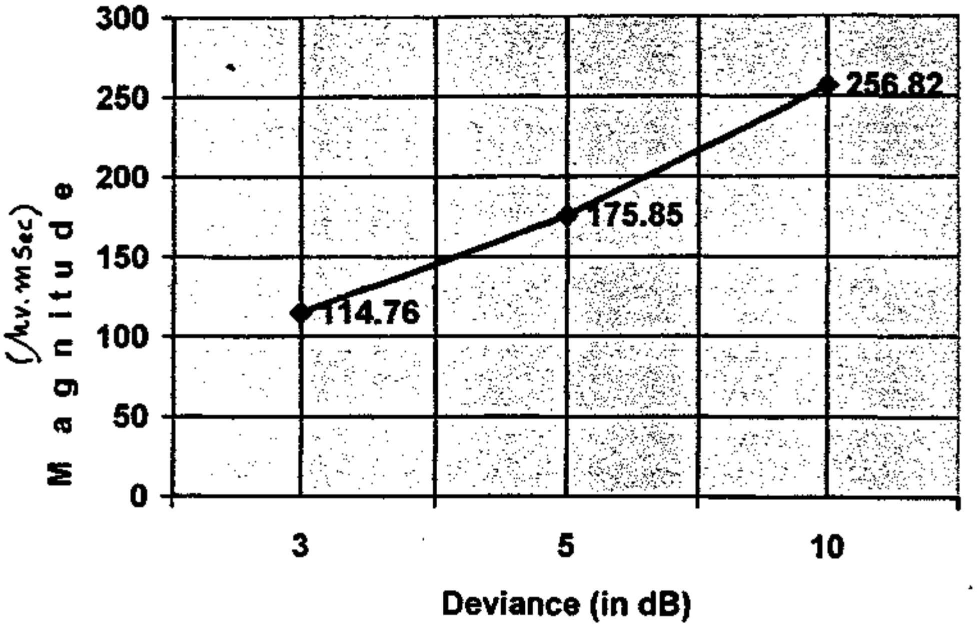
Table D3 : Results of Duncans multiple range post hoc analysis with harmonic mean sample size = 60

| Comparison | N | Subset for alpha = 0.05 | |
|---|---|---|---|
| | | 1 | 2 |
| 3dB deviance | 60 | 110.790 | |
| 5dB deviance | 60 | 166.789 | |
| l0dB deviance | 60 | | 243.727 |
| Significance | | .052 | 1.000 |

From table D3 it can be inferred that the means of 3dB and 5dB do not differ significantly. However the mean of lOdB deviance do differ significantly.

There are not many studies regarding the change in MMN magnitude with intensity deviance. In the present study it was seen that the MMN magnitude increased with increasing intensity deviance this can be attributed to the increase in total duration and amplitude. The small degree of intersubject variations (or small SD) supports the hypothesis that the area (magnitude) of MMN to be a more reliable measure than any of the waveform parameters (Pekkonen et. al., 1993; Mcgee et. al., 1997).

Graph 6:
Mean (± SEM) MMN magnitude and offset amplitude at Cz as a function of intensity deviance.




ii) WHETHER READING CAN CAUSE A SIGNIFICANT CHANGE ON INTENSITY MMN

In order to investigate this Recording was done at 5dB deviance with reading and without reading. Group grand average data given in table El reveal that there was a slight difference in all the parameters studied between reading Vs no reading conditions. However, this difference was statiscally significant only for the few parameters studied. Group grand average data given in table El reveal that there was a slight difference in all the parameters studied between reading Vs no reading conditions. However, this difference seen was statistically significant only for the few parameters studied.

Table El: Mean, Standard deviation values of various MMN parameters studied at both Cz and Pz electrode placement for both conditions (reading Vs No reading)

| Difference Wave | On Latency (m sec) | | On Amplitudc v) | | Off Latency (m sec) | | Off Amplitude ( m sec) | | Total (m sec) | | Peak Latency (m sec) | | Peak Amplitude (µ v) | | Magnitude (m sec). (µ. v) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Mean 1 | SD | Mean ] | SD | Mean | SD | Mean I | SD | Mean | 3D | Mean | SD | Mean | SD | Mean 1 | SD |
| 5 dB Cz with Reading | 27.233 | 13.705 | 1.696 | 1.163 | 33.100 | 15.153 | 1.730 | u.yai | 68.267 | 34.410 | 170.367 | 55.440 | 1.528 | 0.716 | 112.197 | 79.133 |
| 5 dB Pz with Reading | 26.667 | 14.594 | 1.720 | 1.165 | 29.767 | 13.167 | 1.6M | I.UO.J | 71.067 | 28.245 | 178 | 53.392 | 1.423 | 0..802 | 104.427 | 76.127 |
| 5 dB Cz without Reading | 33.833 | 19.992 | 2.474 | 1.749 | [11.567 | 18.562 | 2.653 | 1.6 /y | 71.9 | | | 60.411 | 2.219 | 1.247 | 175.853 | I 144.54 |
| 5 dB Pz without Reading | 29.6 | 12.283 | 2.405 | 1.613 | 30.467 | 14.417 | 2.051 | 1.803 | 69.133 | 29.573 | 219.533 | 59.361 | 2.003 | 1.215 | 157.726 | \| 131.16 |

Table Ela : Range values of various MMN parameters studied at both Cz and Pz electrode placement for both conditions (reading Vs No reading)

| Difference Range f | On Latency J | On Amplitude I | Off Latency | Off Amplitude | Total | Peak Latency | Peak Amplitude | Magnitude |
|---|---|---|---|---|---|---|---|---|
| values<br>5 dB Cz with | 7-57 | 0.22-3.46 | 14-57 | 0.25-3.4 | 26-152 | 87-269 | 0.03-3.13 | .1.63-281.2 |
| Reading<br>5 dB Pz with | 7-59 | 0.21-2.54 | 8-50 | 0.39-4.40 | 22-123 | 94-270 | 0.01-2.83 | .32-33.38 |
| Rending<br>5dB C7. without | 11-92 | 0.39-8.86 | 10-90 | .0.23-6.43 | 27-178 | 127-337 | 0.48-3.49 | 3.48-520.34 |
| Reading<br>5 dB Pz without<br>Reading | 13-59 | 0.45-5.13 | 6-66 | 0.03-5.09 | 26-140 | 127-334 | 0.22-3.21 | 7.48-600.49 |

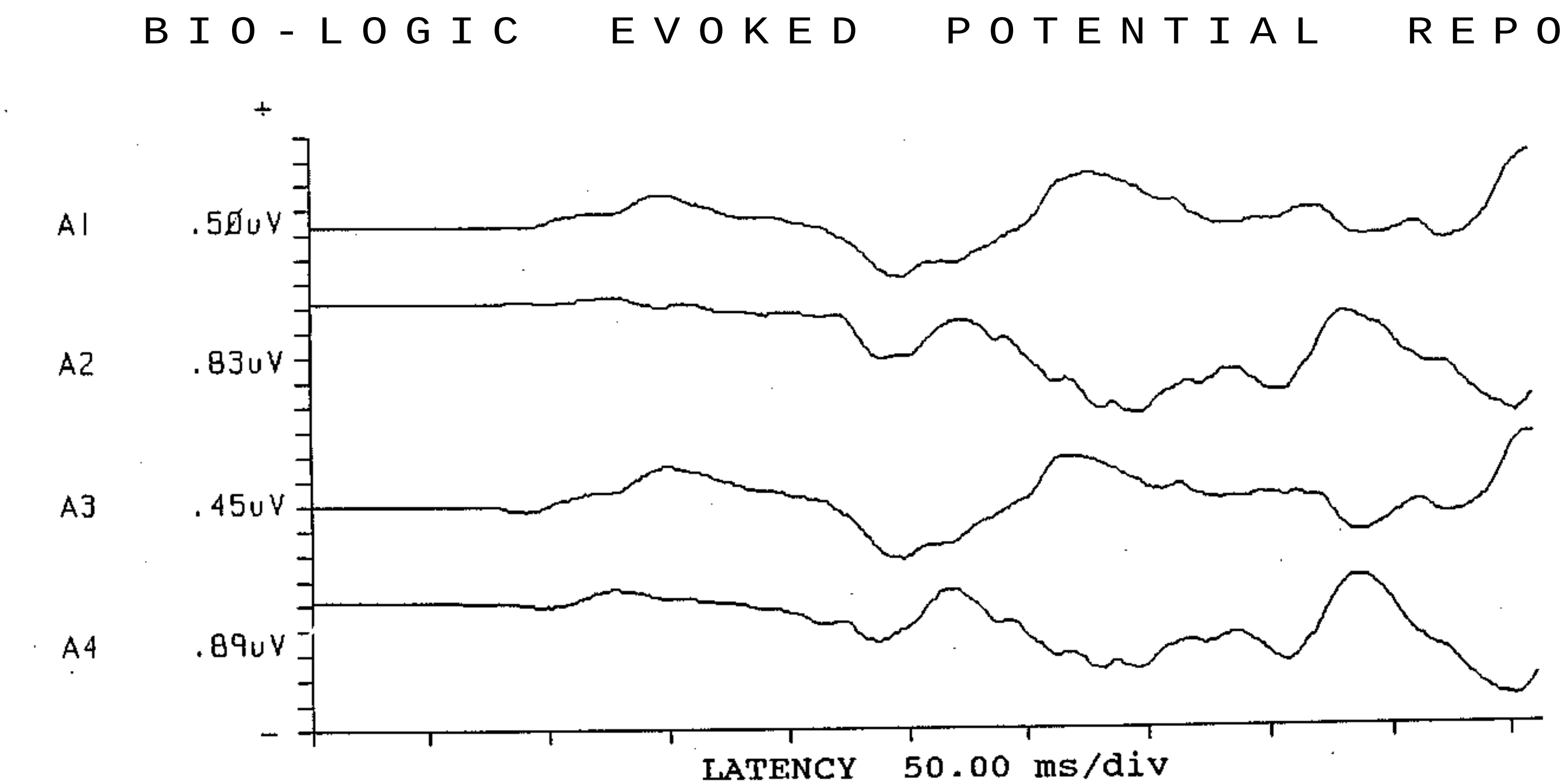



**Fig-10 : Individual representative waveform at 5 dB deviance with reading**

**Al & A2 : CZ Waves** | **Al & A3 : Standard stimuli wave**

**A3 & A4: PZ Waves** | **A2 & A4 : In frequent stimuli wave**

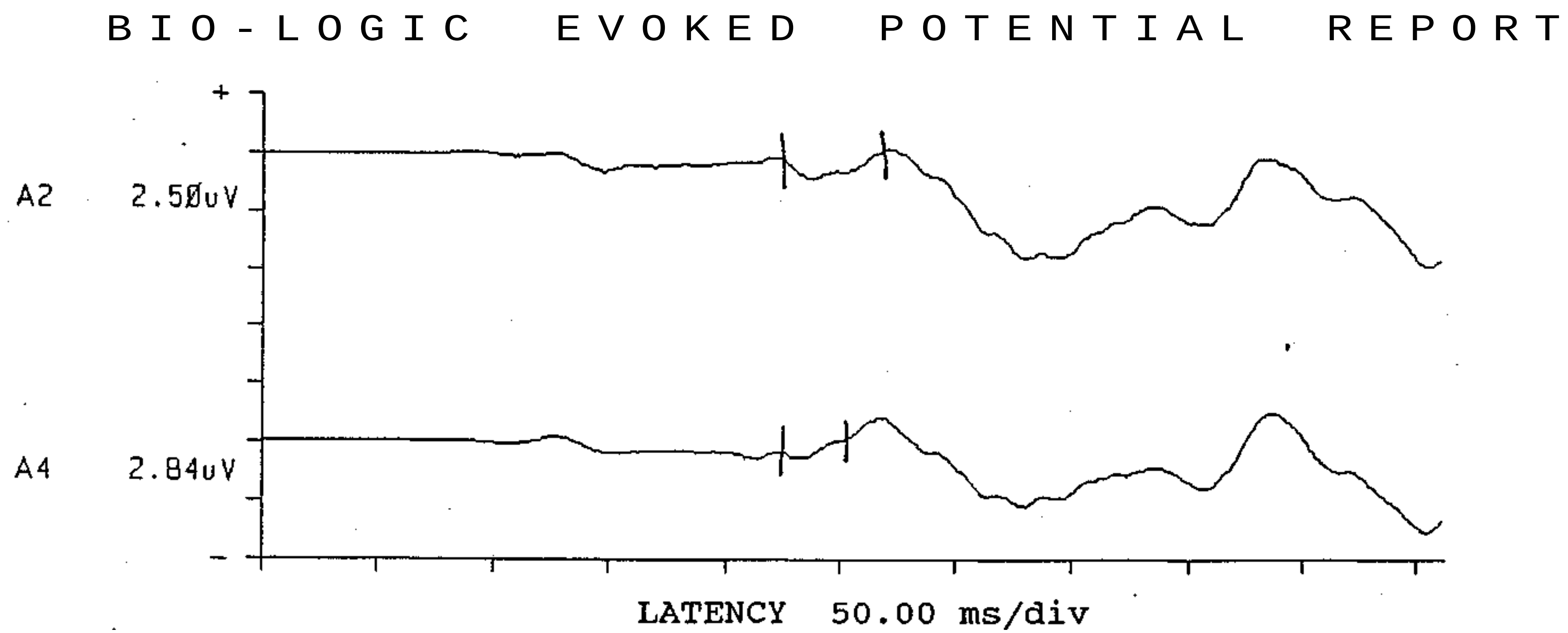



**Fig- 11 : Individual representative difference waveform at 5 dB deviance with reading**

**A2 : Standard stimuli wave at CZ - infrequent stimuli wave at CZ**

**A4 : Standard stimuli wave at PZ - infrequent stimuli wave at PZ**

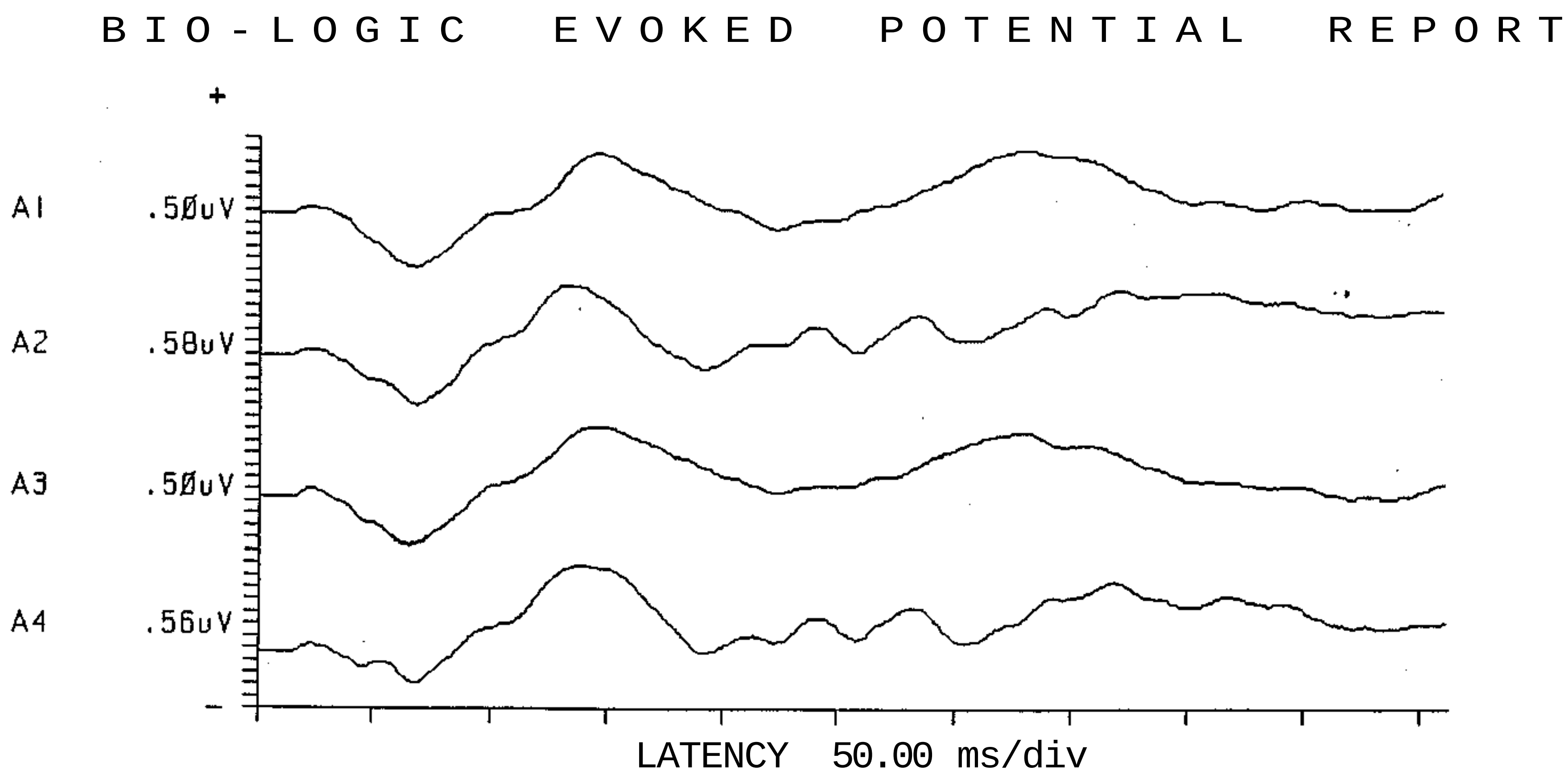



**Fig-12 : Individual representative waveform at 5 dB deviance without reading**

**Al & A2 : CZ Waves** **Al & A3 : Standard stimuli wave**

**A3 & A4 : PZ Waves** **A2 & A4 : In frequent stimuli wave**

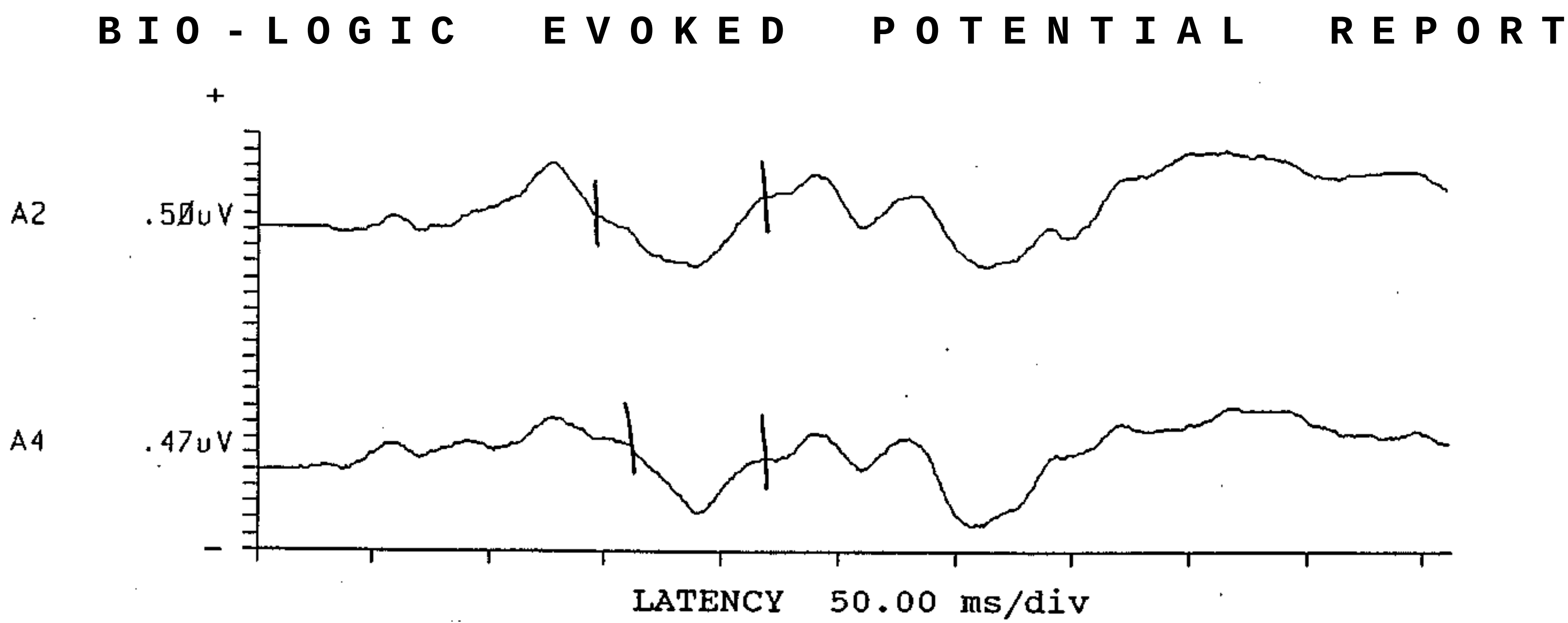



**Fig-13 : Individual representative difference waveform at 5 dB deviance without reading**

**A2 : Standard stimuli wave at CZ - infrequent stimuli wave at CZ**

**A4 : Standard stimuli wave at PZ - infrequent stimuli wave at PZ**

**Wave morphology**:

MMN were judged to be present by visual inspection for all the subjects both in deviant and difference waveform. From Fig-11 it is evident that the general wave morphology was poor with reduced amplitude and area (Magnitude) in reading condition compared to the no reading condition Fig-13. The peak MMN latency in the reading condition fell in the region between 170-225 msec. In case of reading condition the peak latency fell in the region between 217-277 msec, these can be inferred from Fig-11 and 13 respectively.

Latency **measures:**

Table-E2 : Two way ANOVA table for onset latency, offset latency, peak latency, F ratio, P value's are depicted for both condition and' efectrode" placements.

| Latency Measure | | F ratio | P value | Significant/ Not Significant |
|---|---|---|---|---|
| Onset | Reading (Condition) | 0.727 | 0.396 | Not Significant |
| | Electrode placement | 2.866 | 0.93 | Not Significant |
| Offset | Reading (Condition) | 0.22 | 0.883 | Not Significant |
| | Electrode placement | 0.617 | 0.434 | Not Significant |
| Peak | Reading (Condition) | 17.859 | 0.00 | Significant |
| | Electrode placement | 0.231 | 0.632 | Not Significant |

Inspection of Table-E2 reveals that there is no statistically significant difference seen in terms of onset latency (F=0.727, P=NS), Offset latency (F=0.22, P=NS) between the two conditions. However, Statistically significant difference was seen in terms of Peak latency between the two conditions (reading Vs no reading) (F=17.859, P=0.00).

Inspection of Table-El revealed that the mean Peak latency increased in the no reading condition compared to that of the reading condition. In addition it can also be inferred from Table-E2 that there was statistically no significant difference seen in terms of electrode placements for all the latency measures.

**Amplitude Measures**:

Table-E3 : Two way ANOVA table for onset amplitude, offset amplitude, peak amplitude, F ratio, P value's are depicted for both condition and electrode placements.

| Amplitude Measure | | F ratio | P value | Significant/ Not Significant |
|---|---|---|---|---|
| Onset | Reading (Condition) | 7.668 | 0.007 | Significant |
| | Electrode placement | 0.007 | 0.933 | Not Significant |
| Offset | Reading (Condition) | 13.333 | 0.000 | Significant |
| | Electrode placement | 0.024 | 0.878 | Not Significant |
| Peak | Reading (Condition) | 11.569 | 0.001 | Significant |
| | Electrode placement | 0.738 | 0.392 | Not Significant |

Inspection of Table-El reveal that the mean Onset, Offset, Peak Amplitude had greater values in the no reading condition compared to that of the reading condition.

Inspection of Table-E3 reveals that statistically significant difference was seen in all the amplitude measures between the two conditions (reading Vs no reading).

- Onset Amplitude ( F= 7.668, P=0.007)
- Offset Amplitude (F= 13.333, P=0.000)
- Peak Amplitude (F= 11.569, P= 0.001).

**Total Duration:**

Table-E4 : Two way ANOVA table for Total Duration, F ratio, P value's are depicted for both condition and electrode placements.

| Total Duration | F ratio | P value | Significant / Not Significant |
|---|---|---|---|
| Reading (Condition) | 0.021 | 0.886 | Not Significant |
| Electrode placement | 0.000 | 0.998 | Not Significant |

From the Table-E4 it is evident that there was statistically no significant difference seen in terms of total duration between the two conditions(reading Vs no reading ) (F=0.021, P=NS) and electrode placement (F=0.000, P=NS).

**MMN Magnitude**:

Table-E5 Two way ANOVA table for MMN Magnitude, F ratio, P value's are depicted for both condition and electrode placements.

| MMN Magnitude | F ratio | P value | Significant / Not Significant |
|---|---|---|---|
| Reading (Condition) | 8.182 | 0.005 | Significant |
| Electrode placement | 0.401 | 0.528 | Not Significant |

Inspection of Table-El reveal that there is an increase in the mean MMN magnitude value in the no reading condition compared to the reading condition and this increase is statistically significant which can be inferred from table-E5 (F=8.182, P=0.005).

However there was statistically no significant difference seen in terms of electrode placement for MMN magnitude (F=0.401, P=NS).

The present findings are in concurrence with few studies reported in literature (Naatanen et.al., 1993b; Woldroff et. al., 1991).The decrease seen in amplitude, latency measures, total duration and magnitude in an unattended condition like reading in the present study is in accordance with the studies conducted by Natanten et.al.,(1993b) and Woldroff el.al.,(1991).They reported that MMN to intensity deviance is clearly attenuated in the absence of attention suggesting that the intensity MMN to be vulnerable to attention.

The probable neurophysiological explanation for this change seen in an unattended condition such as reading might be due to the attentional effects on the amplifying but not on the computational system of MMN generation. In addition the distinction seen in the present study between reading Vs no reading condition implies that even though the same amount of information is extracted from intensity deviance by the computational mechanism, it resulted in MMN of different sizes because of the differential excitability of the amplifying system. This distinction seen between reading and no reading condition can therefore explain an attentional effect on intensity MMN suggesting that reading can cause significant change on intensity MMN. There are not many studies regarding the effect of attention on the following MMN parameters (viz) Onset latency, offset latency and duration.

In the present study it was found that there was no significant difference in MMN during reading Vs no reading condition for the following parameters (viz) Onset latency, offset latency and total duration. This is in accordance with the results of Sams et. al., (1984), who reported that there was no significant difference seen in total MMN duration between attended (no reading) and unattended conditions (reading)

To summarize, the present study adds to the literature by supporting earlier studies conducted to delineate the effects of degree of deviance between the standard and deviant stimuli on the various MMN waveform parameters. From the present study it can be understood that with increasing deviance then is a significant reduction in peak latency and increase in peak amplitude of MMN. Further more it supports the hypothesis that intensity MMN is vulnerable to attentional changes.

# SUMMARY AND CONCLUSIONS

Mismatch negativity is an auditory evoked potential component elicited in a passive condition. The response is elicited by a deviant stimulus presented within a series of standard stimulus. It reflects process specific to stimulus change. As MMN reflects auditory processing of very fine stimulus difference it provides a useful means for assesing neurophysiological mechanisms involved in the perception of subtle speech contrasts. MMN can be elicited by almost any kind of discriminable stimulus change like a change in frequency, intensity, duration, spatial location and inter stimulus interval (Naatanen, 1992).

Recent years studies have been carried on MMN by measuring and analyzing grand averaged waveforms across healthy subjects with various parameter variations. However, relatively few publications have described the effects of intensity deviance on MMN (Naatanen et. al., 1989). Moreover the effects of intensity deviance on the various MMN measures such as onset latency , offset latency, MMN duration, offset amplitude, onset amplitude, magnitude of MMN were not studied. However a majority of the commercially available electrophysiological units do not have the provision for varying the frequency in smaller steps, but intensity can be varyed in ldB steps. A few reports indicate that the intensity MMN is vulnerable to attentional changes (Naatanen et. al., 1993b; Woldroff et.al., 1991). But further investigations are required to support this. In these context the present study was planned with the aim to investigate the following :

I. The effects of intensity deviance of 3dB, 5dB & l0dB on MMN

An attempt was made to study the effect of intensity deviances on the following waveform parameters

1. Latency (onset, offset, peak)
2. Ampltude (onset, offset, peak)
3. Total duration
4. MMN magnitude

II. To investigate whether reading can cause a significant difference on intensity MMN.

The MMN waves were recorded in thirty normal hearing individuals in the age range of 18-23 years for various intensity deviance in two conditions using Biologic auditory evoked potential system (Navigator). In the first condition recording was done without reading for 3dB,5dB,10dB deviance. In the second condition recording was done with reading for 5dB deviance.

Analysis of results show that there was a significant increase in onset amplitude, offset amplitude, peak amplitude, offset latency, total duration & MMN magnitude with increasing deviance.

The following conclusions were drawn from the study.

1. There was statistically significant increase in onset amplitude with increasing deviance
2. There was statistically significant increase in offset amplitude with increasing deviance
3. There was statistically significant increase in peak amplitude with increasing deviance

4. There was statistically significant increase in offset latency with increasing deviance

5. There was statistically significant decrease in peak latency with increasing deviance

6. There was no statistically significant change in onset latency with increasing deviance

7. There was statistically significant increase in total duration with increasing deviance

8. There was statistically significant increase in MMN magnitude with increasing deviance

9. There was a significant increase in onset amplitude, offset amplitude, peak latency, peak amplitude and magnitude in no reading condition compared to reading.

10. There was no significant difference observed in the onset latency, offset latency, total MMN duration between reading Vs No reading condition.

To conclude, the results of the present study suggest that the degree of intensity deviance has a significant effect on the various MMN measures with greater difference seen at larger intensity deviances. However a reliable MMN can be obtained at intensity deviance as low as 3dB. In addition there was no difference in the waveform recorded at the various electrode placements. Hence for clinical practice especially in cases where an immediate diagnosis cannot be made and maximum information is desirable, efficient MMN recording can be done for l0dB deviance either with Cz / Pz electrode placement. Further more in most intensely focussed conditions such as reading, the MMN to intensity change was attenuated but not fully abolished, suggesting a passive attentional requirement while recording MMN for intensity deviation.

Limitations :

1. Only 5 electrodes were used
2. No EoG (Electro Occulographic) recordings were done
3. Only 3dB, 5dB, and l0dB deviance were studied
4. Reading was used as a method to deviate attention. Watching a video film would have caused lesser occular movements.

REFERENCES

Aaltonen, O., Eerola, 0., Hellstrom, A, Uusipaikka, E., & Lang, AH. (1995). Perceptual magnet effect in the light of behavioural and Psychophysiological data. In : C. Barber, T. Blum (EDS), Evoked potentials III. The third international Evoked potentials symposium.

Aaltonen, O., Eerola, 0., Lang, A.H., Uusipaikka, E., Tuomainen, J. (1994). Automatic discrimination of phonetically relevant vowel parameters as reflected by mismatch negativity. Journal of the Acoustical Society of America, 1996.

Aaltonen, 0., Niemi, P., Nyrke, T., & Tubkanen, M. (1987). Event-related brain potentials and the perception of a phonetic continuum. Biological Psychology, 24,197-207.

Aaltonen, O., Tuomainen, I, Laine, M., & Neimi, P. (1993). Cortical differences in tonal frequency versus vowel processing as revealed by an ERP component called the mismatch negativity (MMN). Brain and language, 44, 139-152.

Alho, K. (1995). Cerebral generators of mismatch negativity (MMN) and its magnetic counterpart (MMNm) elicited by sound changes Ear and Hearing, 16,38-50.

Alho, K., Huotilainen, M, Tiitinen, H., Hmoniemi, R.J., Knuutila, J., & Naatanen, R (1993). Memory-related processing of complex sound patterns in human auditory cortex: An MEG study. NeuroReport, 4, 391-394.

Alho, K., Woods, D.L., Algazi, A, Knight, R T., & Naatanen, R (1994 b). Lesions of frontal cortex diminish the auditory mismatch negativity. Electroencephalography and Clinical Neurophysiology, 91, 353-362.

Aulanko, R, Hari, R, Lounasmaa, 0. V., Naatanen, R, & Sams, M. (1993). Phonetic invariance in the human auditory cortex. NeuroReport, 4,1356-1358.

Aulanko, R, II ononiemi, R.J., & Sams, M. (1995). Detecton of phonetc changes in natural speech. Electroencephalography and clinical neurophysiology.

Bertrand, O., Perrin, F., & Peraier, J. (1991). Evidence for a tonotopic organization of the auditory cortex observed with auditory evoked potentials. Acta Otolaryngology Suppl., 491,116-123.

Bottcher-Gandor, C, & Ullsperger, P. (1992). Mismatch negatvity in event related potentials to auditory stimuli as a function of varying inter stimulus interval. Psychophysiology, 29, 546-550.

Butler, R. A (1968). Effects of changes in stimulus frequency and intensity an habituation of the human vertex potential. Journal of Acoustical society of America, 44, 945-950

Campbell, K., Bell, I., & Bastian, C. (1991). Evoked potentials measures of information processing during natural sleep. In : R Broughton & R Ogilvce (Eds.), Sleep, around, and performance (pp. 88-116). Cambridge, MA : Birkhauser.

Cowan, N. (1984). On short and long auditory stores. Psychological Bulletn, 1996, 341-370.

Cowan, N., Winkler, I., Teder, W., & Naatanen, R (1993). Memory prerequisites of mismatch negativity in the auditory event-related potential (ERP). Journal of Experimental Psychology : Learning. Memory, and Cognition, 19, 909-921.

Cse'pe, V. (1995). On the origin and development of mismatch negativity. Ear and Hearing, 1995,1,91-104.

Cse'pe, V., Karmos, G., & Molnar, M. (1987). Evoked potential correlates of stimulus deviance during wakefulness and sleep in cat : Animal model of mismatch negativity. Electroencephalography and Clinical Neurophysiology, 66, 571-578.

Cse'pe, V., Karmos, G, & Molnar, M. (1989). Subcortical evoked potential correlates of early information processing : Mismatch negativity in cats. In E. Basar & T.H. Bullock (Eds.), Dynamics of Sensory and Cognitive Processing by the Brain (pp. 279-289). Berlin: Springer-Verlag.

Cse'pe, V., Molnar, M (1997). Towards the possible clinical Application of the Mismatch Negativity component of Event Related potentials. Audiology and Neuro-Otology. 2, 354-369.

Cse'pe, V., Pantev, C, Hoke, M., Hampson, S., & Ross, B. (1992). Evoked magnetic responses to minor pitch changes: localization of the mismatch field. Electroencephalography and Clinical Neurophysiology, 84, 538-548.

Elberling, C., Bak, C., Kofoed. B,., Lebech, J., & Saermark, K. (1982}. Auditory magnetic fields. Source location and 'tonotopic organization' in the right hemisphere of the human brain. Scandinavian Audiology, 11,61-65.

Fant, G. (1960). Acoustic theory of speech production. Haque. Mouton &, Co..

Ford, J.M., & Hillyard, S.A. (1981). Event related potentials (ERP's) to interruptions of steady rhythm. Psychophysiology, 18, 322-330.

Giard, M. R, Perrin, F., Pernier, J., & Bouchet, P. (1990). Brain generators implicated in the processing of auditory stimulus deviance : A topographic ERP study, Psychophysiology, 27, 627-640.

Grillon, C, Sinha, R, O'Malley, S.S. (1995). Effects of ethanol on the processing of low probability stimuli : An ERP study. Psychopharmacology. 4, 455-465.

Groenen, P., Snik, A., & Broek, P.V.D. (1996). On the clinical relevance of mismatch negativity : result from subjects wth normal hearing cochlear implant users. Audiology & Neurootology; 1,112-124.

Gunter, T. C, Jackson, J.L., Mulder, G. (1996). : Focussing on aging : An electrophysiological exploration of spatial and attentional processing during reading. Biological Psychiatry, 1996, 2,103-145.

Hari, R, Hamalainen, M., Ilmoniemi, R, Kaukoranta, E., Reinikainen, K., Salminen, J., Alho, K., Naatanen, R, & Sams, M. (1984). Responses of the primary auditory cortex to pitch changes in a sequence of tone pips : Neuromagnetic recordings in man. Neuroscience Letters, 50,127-132.

Hari, R, Rif, J., Tiihonen, J., & Sams, M. (1992). Neuromagnetic mismatch fields to single and paired tones. Electroencephalography and Clinical Neurophysiology, 82,152-154.

Hillyard, S.A., Mangun, G.R., Woldorff, M.G., & Luck, S.J. (1973). Neural systems mediating selective attention. In : Naatanen, R (1995), the mismatch negativity: a powerful tod for cognitive neuroscience. Ear and Hearing, 16, 6-18.

Huotilainen, M, Ilmoniemi, R. J., Lavikainen, J., Tiitinen, H., Alho, K., Sinkkonen, J., Knuutila, J., & Naatanen, R (1993). Interaction between representations of different features of auditory sensory memory. NeuroReport, 4,1279-1281.

Imada, T., Hari, R., Loveless, N., McEvoy, L, & Sams, M. (1993). Determnants of the audtory msmatch response. Electroencephalography and clinical Neurophysiology, (1987), 144-153.

Jaaskelainen, I. P., Lentokoski, A., Alho, K., Kujala, T., Pekkonen, E., Sinclair, J. D., Naatanen, R, Sillanaukee, P.(1995). Low dose of ethanol suppresses mismatch negativity of auditory event related potentials. Alcoholism elin Exp. Res, 3, 607-610.

Jaaskelainen, I. P., Pekkonen, E., Alho, K., Sinclair, J. D., Sillanaukee, P., Naatanen, R.(1995). Dose related effect of alcohol on mismatch negativity and reaction time performance. Alcohol. 6,491-495.

Jaaskelainen, I. P., Pekkonen, E., Hiravonen, J., Sillanaukee, P., Naatanen, R (1996). Mismatch negativity subcomponents and ethyl alcohol. Biol. Psychiatry, 1,13-25.

Javitt, D. C, Doneshka, P., Grochowski, S., Kitter, W.(1995). : Impaired mismatch negativity generation reflects widespread dysfunction of working memory in schizophrenia. Arch Gen Psychiatry, 7, 550-558.

Javitt, D. C, Grochowki, G., Shelley, A M., Ritter, W. (1998). Impaired MMN generation in Schizophrenia as a function of stimulus deviance, Probability, and inter stimulus / interdeviant interval. Electroencephalography and Clinical Neurophysiology, 108,143-153.

Javitt, D. C, Schroeder, C. E., Stienschneider, M., Arezzo, J.C., Ritter, W., Vaughan, H. G. (1994). Detection of stimulus deviance within primate primary auditory cortex : intracortical mechanism of mismatch negativity (MMN) generation. Brach Research, 667,192-200.

Javitt, D. C, Schroeder, C. E., Steinschneider, M., Arezzo, J. C, & Vaughan, H.G., Jr. (1992). Demonstration of mismatch negativity in the monkey. Electroencephalography and Clinical Neurophysiology, 83, 87-90.

Jennet, B., Plum, F., Persistent vegetative state after brain damage.(1972). Lancet, 734-737.

Kane, N.M., Curry, S.H., Butler, S.R., & Cummins, B.H. (1993). Electrophysiological indicator of awakening from coma. Lancet, 341,688.

Kane, N. M., Curry, S. H., Rowlands, C. A., Manara, A. R., Lewis, T., Moss, T., Cummins, B. R, & Butler, S. H (1996). Event-related potentials-neurophysiological tools for predicting emergence and early outcome for traumatic coma. Intensive Care Medicine, 22,39-46.

Karayanidis, F., Andrews, S., Ward, P. B., Midice, P. T.(1995). : ERP indices of auditory selective attention in aging and Parkenson's disease. Psychophysiology, 4, 335-350.

Karmos, G., Winkler, I., Molnar, M., & Csepe, V. (1993). Animal model of middle latency auditory evoked responses-intra-cortical generators of mismatch negativity. In: H. J. Heinze, T.F. Mnte, & G.R. Mangum (Eds), New Developments in Event-related potentials (pp. 95-102). Boston: Birkhauser.

Kaukoranta, E., Sams, M., Har, R., Hamalainen, M., & Naatanen, R. (1989). Reactions of human auditory cortex to a change in tone duration. Hearing Research, 41,15-21.

Kemner, C, Verbaten, M. N., Cuperus, J.M., Camffennan, G., Van Engeland, H. (1995). Auditory event-related brain potentials in autistic children and three different control groups. Biol. Psychiatry, 3,150-165.

Kemner, C, Verbaten, M. N., Koelega, H. S., Buitelaan, J. K., Vander Gaag, R. J., Camffennan, G., Van Engeland, H.(1996). Event-related brain potentials in children with attention deficit and hyperactivity disorders : Effects of stimulus deviance and task relevance in the visual and auditory modality. Biol. Psychiatry, 6, 522-534.

Kiedal, W., Kallert, S., Kerth, M., & Homes, I. (1993). Cited by F.E. Musiek & J.A. Baran, Tutorial: Neuroanatomy, Neurophysiology and central auditory assessment, part-I: Brainstem. Ear and hearing, 7(4), 214-1986.

Kirino, E., Shinomiya, M.(1996). ERP study of information processing disturbance on Schizophrenia - from aspects of automatic processing and controlled processing. Seishin shinkeigaku Zasshi Psychol neurolJpn, 10,807-821.

Klatt, D. (1980). Software for a cascade / parallel fonnant synthesizer. Journal of the Acoustical Society of America, 67, 971-995.

Korpilahti, P., & Lang, H. (1994). Auditory ERP components and mismatch negativity in dysphasic children. Electroencephalography and Clinical Neurophysiology, 91,256-264.

Kraus, N., & McGee, T. (1994). Mismatch negativity in the assessment of central auditory function. American Journal of Audiology, 3,139-151.

Kraus, N., McGee, T., Carrell, T., King, C, Littman, T., & Nicol, T. (1994a). Discrimination of speech-like contrasts in the auditory thalamus and cortex. Journal of the Acoustical Society of America, 96,2758-2768.

Kraus, N., McGee, T., Carrell, T., Sharma, A., Koch, D., King, C., Tremblay, K., & Nichol, T. (1995 b). Neurophysiologic bases of speech discrimination. Ear and Hearing, 16,19-37.

Kraus, N., McGee, T. J., Carrell, T. D., Zecker, S. G., Nichol, T. G, & Koch, D. B. (1996). Auditory neurophysiologic responses and discrimination deficits in children with learning problems. Science, 273, 971-973.

Kraus, N., McGee, T., Ferre, J., Hoeppner, J. A., Carrell, T., Sharma, A, Nicol, T.(1993). Mismatch negativity in the neurophysiologic / behavioural evaluation of auditory processing deficits : A case study . Ear and Hearing, 4, 223-234.

Kraus, N., McGee, T., Littman, T., Nichol, T., & King, C. (1994b). Non-primary auditory thalamic representation of acoustic change. Journal of Neurophysiology, 72,1270-1277.

Kraus, N., McGee, T., Micco, A, Sharma, A., Carrell, T. & Nichol, T. (1993). Mismatch negativity in school-age children to speech stimuli that are just perceptibly different. Electroencephalography and Clinical Neurophysiology, 88,123-130.

Kraus, N., Micco, A, Koch, D., McGee, T., Carrell, T., Wiet, R., Weingasten, C, Sharma, A(1993). The mismatch negativity cortical evoked potential elicited by speech in cochlear implant users. Hearing Research, 65,118-124.

Kropotov, J. D., Ponomarev, V. A (1991). Subcortical neuronal correlates of component $P_{300}$ in man. Electroencephalography and Clinical Neurophysiology, 78,40-49.

Kurtzberg, D., Vaughan, H. G Jr., Kreuzer, J. A., & Fliegler, K. Z. (1995). Developmental studies and Clinical application of mismatch negativity : Problems and prospects. Ear and Hearing, 16,104-116.

Lang, H., Eerola, O., & Aaltonen, O. (1995a). Intra individual variation of the mismatch negativity. In : Lang, HL, Eerola, O., Korpilathi, P., Holopainen, I., Salo, S., Uusipaikka, S., & Aaltonen, O. (1995), Practical ssues in the clinical application of mismatch negativity. Ear and hearing, 16,118-129.

Lang, H., Eerola, O., Korpilahti, P., Holopainen, I., Salo, S., Uusipaikka, E., & Aaltonen, O. (1995). Practical issues in the clinical applications of the mismatch negativity. Ear and Hearing, 16,118-129.

Lang, H., Mikola, H. (1995b). Slight variations of vigilance affect the mismatch negativity. In : Lang, H., Eerola, O., Korpilahti, P., Holopainen, I, Salo, S., Uusipaikka, E., & Aaltonen, 0. (1995), Practical issues in the clinical application of mismatch negativity. Ear and hearing, 16, 118-129.

Lang, H., Nyrke, T., Ek, M., Aaltonen, O., Raimo, I., & Naatahen, R. (1990). Pitch discrimination performance and auditory event related potentials. In : C.H.M. Brunia, AW.K. Gaillard, A. kok, G., Mulder, & M.N. Verbaten (Eds), psychophysiological Brain research, vol.1 (pp. 294-298). Tilburg : Tilburg University press.

Lang, H., Portin, R., & Rinne, J. (1995c). Inter individual variation of the mismatch negativity. In : Lang, H., Eerola, O., Korpilahti, P., Holopainen, I., Salo, S., Uusipaikka, E., & Aaltonen, 0. (1995), Practical issues in the clinical application of mismatch negativity. Ear and hearing, 16,118-129.

Levdnen, S., Ahonen, A, Hari, R., McEvoy, L., & Sams, M. (1996). Deviant auditory stimuli activate human left and right auditory cortex differently. Cerebral Cortex, 6,288-296.

Levdnen, S., Hari, R., McEvoy, L., & Sams, M. (1993). Responses of the human auditory cortex to changes in one versus two stimulus features. Experimental Brain Research, 97,177-183.

Loewy, D.H., Campbell, K.B., Bastein, C.(1996). The mismatch negativity to frequency deviant stimuli during natural sleep. Electroencephalography and Clinical Neurophysiology, 6,493-501.

Lounasmaa, O. V., Hari, R, Joutsiniemi, S. L., & Hamalainen, M. (1989). Multi SQUID recordings of human cerebral magnetic fields may give information about memory processes in the human brain. Europhysics Letters, 9, 603-608.

Lyytinen, H., Blomberg, A. P., Naatanen, R. (1992). Event-related potentials and automatic responses to a change in un-attended auditory stimuli. Psychophysiology, 29, 523-534.

Makeig (1995). Effects of attention and stimulus probablity on the auditory complex event-related potentiial. Society for Neuro sciences Abstracts.

Makela, J., Salmelin, R., Kotila, M., & Hari, R. (1994). Neuro magnetic correlates of memory disturbance caused by infarction in interior thalamus. Society for Neuroscience Abstracts, 20, 810.

Mantysalo, S. & Naatanen, R. (1987). The duration of a neuronal trace of an auditory stimulus as indicated by event-related potentials. Biological Psychology, 24, 183-195.

McGee, T., Kraus, N., & Nicol, T. (1997) . Is it really mismatch negativity ? An assessment of methods for determining response validity in individual subjects. Electroencephalography and clinical Neurophysiology, 104,359-368.

Molnar, M., Stinner, J. E., Csepe, V., Winkler, I., Karmos, G. (1995). Correlation dimension changes accompanying the occurance of the mismatch negativity and the $P_3$ event-related potential component. Electroencephalography & Clinical Neurophysiology, 95,118-126.

Naatanen, R (1975). Selective attention and evoked potentials in humans - A critical review. Biological Psychology, 2,237-307.

Naatanen, R (1979). Orienting and evoked potentials. In H.D. Kimmel, E.H. Van 01st, & J.F. Orlebeke (Eds.), the Orienting reflex in humans (pp 61-75). Hillsdale, NJ: Erlbaum.

Naatanen, R (1985). Selective attention and stimulus processing : reflections in event-related potentials, magnetoencephalogram and regional cerebral blood flow. In : M.l. Posner & O.S.M. Marin (Eds), Attention and performance XI (PP. 355-373). Hillsdde, N.J.: Erlbaum.

Naatanen, R (1986). The Orienting response Theory : A integration of informational and energetical aspects of brain functiion. fin R Hockey, A.W.K. Gaillard & M.Coles (Eds.),Energetics and human iinformaton processing (pp 91-111). Dordrecht: Martinus Nijhoff.

Naatanen, R (1990). The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. Behavioral and Brain Sciences, 13,201-233.

Naatanen, R (1992). Attention and Brain function. Hillsdale, N. J.: Erlbaum.

Naatanen, R. (1995). The mismatch negativity : A powerful tool for cognitive neuroscience. Ear and Hearing, 16, 6-18.

Naatanen, R, & Alho, K. (1995). Mismatch negativity - a unique measure of sensory processing in audition. International Journal of Neuroscience, 80, 317-337.

Naatanen, R., & Gaillard, A.W.K. (1983). The orienting reflex and the $N_2$ deflection of the ERP. In : A.W.K. Gaillard & W. Ritter (Eds), Tutorials in event-related potential research : Endogenous components (pp. 119-141). Amsterdam: North-Holland.

Naatanen. R., Gaillard, A. W. K., & Mantysalo, S. (1978). Early selective-attention effect on evoked potential reinterpreted. Acta Psychologicsa, 42, 313-329.

Naatanen, R., Gaillard, A.W.K. & Mantysalo, S. (1980). Brain-potential correlates of voluntary and involuntary and involuntary attention. In : H.H. Kornhuber and L. Deecke (Eds), Motivation, Motor and Sensory processes of the brain : Electrical potentials, behavior and clinical use. Progress in Brain Research, Vol.54, Elsevier, Amsterdam, 343-348.

Naatanen, R, Jiang, D., Lavikainen, J., Reinikainen, K., & Paavilainen, P. (1993b). Event-related potentials reveal a memory trace for temporal features. NeuroReport, 5,310-312.

Naatanen, R, & Michie, P. T. (1979). Early selective attention effects on the evoked potential. A critical review and reinterpretation. Biological Psychology, 8, 81-136.

Naatanen, R., Paavilainen, P., Alho, K., Reinikainen, K., & Sams, K. (1987). Inter-stimulus interval and mismatch negativity. In : C. Barber & T. Blum, (Eds), Evoked Potentials III (392-397). London : Butterworths.

Naatanen, R., Paavilainen, P., Alho, K, Reinikainen, K., & Sams, M. (1989a). Do event-related potentials reveal the mechanism of the auditory sensory memory in the human brain? Neuroscience Letters, 98,217-221.

Naatanen, R., Paavilainen, P., Reinikainen, K. (1989b). Do event-related potentials to infrequent decrements in duration of auditory stimuli demonstrate a memory trace in man? Neuroscience Letters, 107,347-352.

Naatanen, R, & Picton, T. W. (1987). The Nl wave of the human electric and magnetic response to sound : A review and an analysis of the component structure. Psychophysiology, 24,375-425.

Naatanen, R, Sams, M, Alho, K., (1986). The mismatch negativity : The ERP sign of a cerebral mismatch process. In : C.W. McCallum, R Zappoli, F. Denoth (Eds), cerebral psychophysiology. Electroencephalography and clinical Neurophysiology, 38,172-178.

Naatanen, R, Sams, M., Alho, K., Paavilainen, P., Reinikainen, K., & Sokolov, E.N. (1988). Frequency and location specificity of the human vertex Nl wave. Electroencephalography and clinical Neurophysiology, 69, 528-531.

Naatanen, R, Schroger, E., Karakas, S., Tervaniemi, M., & Paavilainen, P. (1993c). Dvelopment of a memory trace for complex sound patterns in the human brain. Neuro Report, 4, 503-506.

Naatanen, R., Simpson, M., Loveless, N. E. (1982). Stimulus deviance and evoked potentials. Biological Psychology, 14,53-98.

Nordby, H., Hammerborg, D., Roth, W. T., & Hugdahl, K. (1991). ERPs to infrequent omissions and inclusions of stimulus elements. Psychophysiology Suppl., 28, S42.

Nordby, H., Roth, W. T., & Pfefferbaum, A. (1988). Event-related potentials to time deviant and pitch deviant tones. Psychophysiology, 25,249-261.

Novak, G. P., Ritter, W., & Vaughan, H. C, Jr. (1992). The chronometry of attention-modulated processing and automatic mismatch detection. Psychophysiology, 29,412-430.

Oodes, R.D. (1991). Bases for irrelevant information processing in Schizophrenia : Room for manoeuvre. Behavioral and Brain Sciences, 14, 38-39.

Oades. R. D., Dittmann-Balcar, A., Schepker, R., Eggers, C, Zerbin, D. (1996). Auditory event-related potentials (ERPs) and mismatch negativity (MMN) in healthy children and those with attention deficit or Tourelte / tic symptoms. Biol. Psychiatry, 2, 163-185.

Oades, R. D., Zerbin, D., Dittmann-Balcar, A. : Eggers, C.(1996). Auditory event related potential (ERP) and difference wave topography in schizophrenic patients with / without active hallucinations and delusions : A comparison with young obsessive-compulsive disorder (OCD) and healthy subjects. Int. J. Psychophysiology, 3, 185-214.

O'Tonnell, B. F., Hokama, H., McCarley, RW., Smith, R.S., Salisbury, D. F., Mondrow, E., Nostor, P. G., Shenton, M.E.(1994). : Auditory ERPs to non-target stimuli in schizophrenia : Relationship to probability, task, demands & target ERPs. Int. J. Psychophysiology, 3,219-231.

Paavilainen, P., Alho, K., Reinikainen, K., Sams, M., & Naatanen, R (1991). Right-hemisphere dominance of different mismatch negativities. Electroencephalography and Clinical Neurophysiology, 78,464-479.

Paavilainen, P., Cammann, R, Alho, K., Reinikainen, K., Sams, M, & Naatanen, R (1987). Event-related potentials to pitch changes in auditory stimulus sequence during sleep. In : R Johnson, J.W. Rohrbaugh & R Parasuraman (Eds). Current trends in event-related brain potential research. Electroencephalography and Clinical Neurophysiology supplement, 40, 246-255.

Paavilainen, P., Jiang, D., Lavikainen, J., Naatanen, R. (1993). Stimulus duration and the sensory memory trace : An event-related potential study. Biological psychology, 35,139-152.

Paavilainen, P., Karlsson, M. L., Reinikainen, K., & Naatanen, R (1989). Mismatch negativity to change in spatial location of an auditory stimulus. Electroencephalography and Clinical Neurophysiology, 73,129-141.

Paavilainen, P., Tiitinen, H., Alho, K., & Naatanen, R. (1993). Mismatch negativity to slight pitch changes outside strong attentional focus. Biological psychology, 37,23-41.

Pantev, C, Hoke, M., Lehnertz, K., Ltkenhvner, B., Anogianakis, G., & Wittkowski. W. (1988). Tonotopic organization of the human auditory cortex revealed by transient auditory evoked magnetic fields. Electroencephalography and Clinical Neurophysiology, 69, 160-170.

Pekkonen, E., Jousmaki, V., Kononen, M., Reinikainen, K., & Partanen, J. (1994). Auditory sensory memory impairment in Alzheimeri disease : An event-related potential study. NeuroReport, 18, 2537-2540.

Pekkonen, E., Jousmdki, V., Partanen, J., & Karhu, J. (1993). Mismatch negativity area and age-related auditory memory. Electroencephalography and Clinical Neurophysiology, 87,321-325.

Pekkonen, E., Jousmdki, V., Reinikainen, K, & Partanen, J., (1995). Automatic auditory discrimination is impaired in Parkinson's disease. Electroencephalography and Clinical Neurophysiology, 95,47-52.

Pekkonen, E., Rinne, T., Naatanen, R.(1995): Variability and replicability of the mismatch negativity. Electroencephalography and Clinical Neurophysiology, 6, 546-554.

Pekkonen, E., Rinne, T., Reinikainen, K., Kujala, T., Alho, K., Naatanen, R.(1996). Aging effects on auditory processing : An event related potential study. Exp. Aging Res., 2,171-184.

Picton, T.W. (1995). The Neurophysiological evaluation o£. Auditory Discrimination. Ear and Hearing, 16,1-5.

Picton, T, Rodrignez, R. T., Linden, R. D., Maiste, A C. (1985). The neurophysiology of human hearing. Human Communication Canada, 9, 127-136.

Ponton, C. W., & Don, M. (1995). The mismatch negativity in cochlear implant users. Ear and Hearing, 16,130-146.

Renault, B., Lesevre, N. (1979) .A trial -by -trial study of the visual omission response in reaction time situations . In : D .Lehmann & E . callaway (Eds). .Human Evoked potentials .Plenum Press, New York ,317-330.

Ritter, W., Deacon, D., Gomes, H., Javitt, D. C, & Vaughan, H.G. Jr. (1995). The mismatch negativity of event-related potentials as a probe of transient auditory memory: A review. Ear and Hearing, 16, 51-66.

Ritter ,W., Pavilainen ,P ., Lavikainen ,J., Reinikainen, k., Alho, K ., Sams , M . , & Naatanen , R . (1992). Event related potentials to repetition and change of auditory stimuli .Electroencephalography and clinical Neurophysiology ,83 ,306 -321.

Robinson, D.W., Dadson, RS. (1956). A redetennination of the equal loudness relations for puretone. British Journal Applied Physics, 7,166-181.

Sallinen, M, Kaartinen, J., & Lyytinen, H. (1994). Is the appearance of mismatch negativity during state and sleep related to the elicitation of K-Complex ? Electroencephalography and clinical Neurophysiology ,91, 140 -148..

Sams, M, Alho, K & Naatanen, R (1983). Sequential effects in the ERP in discriminating two stimuli. Biological Psychology, 17,41-58.

Sams, M., Alho, K & Naatanen, R. (1984). Short-term habitation and dishabituation of mismatch negativity of the ERP. Psychophysiology, 21, 434-441.

Sams, M., Aulanko, R., Aaltonen, O., & Naatanen, R (1990). Event-related potentials to infrequent changes in synthesized phonetic stimuli. Journal of Cognitive Neuroscience, 2, 344-357.

Sams, M, Hamalainen, M., Antervo, A, Kaukoranta, E., Reinekainen, K., Hari, R (1985a). Cerebral neuromagnetic responses evoked by short auditory stimuli. Electroencephalography and Clinical Neurophysiology, 61,254-266.

Sams, M., Har, R., Rif, J., & Knuutila, J. (1993). The human auditory sensory memory trace persists about 10 s : Neuromagnetic evidence. Journal of Cognitive Neuroscience, 5, 363-370.

Sams, M, Kaukoranta, E., Hamalainen, M, & Naatanen, R (1991). Cortical activity elicited by changes in auditory stimuli : Different sources for the magnetic N100m and mismatch responses. Psychophysiology, 28,21-29.

Sams, M., Naatanen, R. (1991). Neuromagnetic responses of the human auditory cortex to short frequency glides. Neuroscience Letters, 121,43-46.

Sams, M., Paavilainen, P., Alho, K., & Naatanen, R. (1985). Auditory frequency discrimination and event-related potentials. Electroencephalography and Clinical Neurophysiology, 62,437-448.

Scharf and Houstma, A.J. (1986). Audition II. Loudness, pitch, localization, aural distortion , pathology. In : K.R. Boff, L. Kaufman & J.P. Thomas (Eds), Handbook of perception and human performance, Vol.1, sensory processes and perception. New York, Wiley. 15-2-15-60.

Scherg, M., Vajsar, 1, & Picton, T. (1989). A source analysis of the human auditory evoked potentials. Journal of Cognitive Neuroscience, 1,336-355.

Schrodt, A., Cohen, R., Berg, P., & Hopmann, G. (1992). Automatic (MMN) Vs. controlled (P300) processing deficits the ERP's of Schizophrenic patients. Abstracts of the 10th international conference on Event-Related-Potentials of the Brain (EPIC X), Eger, Hungary, May 31 - June 5,141.

Schroger, E. (1994). An Event-Related-Potential study of sensory representation of unfamiliar tonal patterns. Psychophysiology, 31,175-181.

Schroger, E. (1994b). Attentional capture and mismatch negativity. Psychophysiology, 31, 88-89.

Schroger, E. (1995). Processing of auditory deviants with changes in one Vs. two stimulus dimentions. Psychophysiology, 32, 55-65.

Schroger, E., Naatanen, R., & Paavilainen, P. (1992). Event-related potentials reveal how non-attended complex sound patterns are represented by the human brain. Neuroscience Letters, 146,183-186.

Sharma, A., Kraus, N., McGee, T., & Nicol, T. (1993). Acoustic versus phonetic representation of speech as reflected by the mismatch negativity event-related potential. Electroencephalography and Clinical Neurophysiology, 88, 64-71.

Shelley, AM., Ward, P.B., Catts, S.V., Michie, P.T., Andrews, S., & McConaghy, N. (1991). Mismatch negativity : An index of pre attentive processing deficit in Schizophrenia. Biological Psychiatry, 30,1059-1062.

Sokolov, E. N. (1975). The neuronal mechanisms of the orienting reflex. In E.N. Sokolov and O.S. Vinogradova (Eds.). Neuronal mechanisms of the orienting reflex (pp. 217-235). Hillsdale, N. J.: Erlbaum.

Squires, N. K., Squires, K. C, Hillyard, S. A (1975). Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. Electroencephalography and Clinical Neurophysiology, 38, 387-401.

Synder & Hillyard, S.A (1976). In : Paavilainen, P., Jiang, D., Lavikainon, I, Naatanen, R. (1993). Stimulus duration and sensory memory trace : An Event-Related-Potential study. Biological Psychology, 35,139-152.

Tiitinen, H., Alho, K., Huotilainen, M, Hmoniemi, R. J., Simola, J., & Naatanen, R. (1993). Tonotopic auditory cortex and the magnetoencephalographic (MEG) equivalent of the mismatch negativity. Psychophysiology, 30, 537-540.

Tiitinen, H., May, P., Reinikainen, K., Naatanen, R. (1994). Attentive novelty detection in humans is governed by pre attentive sensory memory. Nature, 372, 90-92.

Towey, J. P., Tenke, C. E., Bruder, G. E., Leite, P., Friedman, D., Liebowitz, M., Hollander, E. : Brain event-related potential correlates of over focused attention in obssessive compulsive disorder. Psychophysiology, 1994, 6, 535-543.

Vieregge, P., Verlegner, R., Wascher, E., Stuven, F., Kompp, D.(1994). Auditory selective attention is impaired in Parkinsons disease. Event-related evidence from EEG potentials. Cognitive Brain Research, 1994,2,117-129.

Vinogradova, 0. S. (1975). The hippocampus and the orienting reflex. In E.N. Sokolov and O.S. Vinogradova (Eds.), Neuronal mechanisms of the orienting reflex (pp. 128-154). Hillsdale, N. J.: Erlbaum.

Winkler, I. (1996) : Necessary and sufficient conditions for the elicitation of the mismatch negativity : in Ogura, C, Koga, Y., Shimokoch, M. (Eds.) ;Reeent Advances in Event-related Brain Potentials Research. Amsterdam, Elsevier, 1996, pp. 36-44.

Winkler, I., & Naatanen, R. (1992). Event-related potentials in auditory backward recognition masking : A new way to study the neurophysiological basis of sensory memory in humans. Neuroscience Letters, 140,239-242.

Winkler, I., & Naatanen, R. (1993). Event-Related Brain potentials reflect traces of echoic memory in humans. Perception and Psychophysics, 53, 443-449.

Winkler, I. & Schroger, E. (1995). Neural representation for the temporal structure of sound patterns. Neuro Report, 6,690-694.

Woldorff, M., Hackley, S. A., & Hillyard, S. A. (1991). The effects of channel-selective attention on the mismatch negativity wave elicited by deviant tones. Psychophysiology, 28, 30-42.

Woods, D. L. (1992). Auditory selective attention in middle-aged and elderly subjects : An event-related potential study. Electroencephalography and Clinical Neurophysiology, 84, 456-468.

Woods, D. L., Alho, K., & Algazi, A. (1993). Intermodal selective attention : Evidence for processing in tonotopic auditory fields. Psychophysiology, 30, 287-295.

Woods, D.L., Knight, R.T., Scabini, D.(1993b). Anatomical Substrates of auditory selective attentioa Behavioural and electrophysiological effects of posterior association cortex lesions. Cognative Brain research, 1,227-240.

Yokoyama, Y., Nakashima, K, Shimoyama, R., Urakami, K., Takashashi, K(1995). Distribution of event -related potentials in patients with dementia. Electronyography and clinical Neurophysiology, 7,431-437.

# Appendix-I

(a) Standards for calibration of pure tone audiometer.

The following standards were used for the calibration of audiometer.

Air Conduction (Earphones) - ANSI S3 - 6 1989.

Bone Conduction (BC vibrator) - ANSI S3-26 1981.

(b) Standards for calibration for Immittance

The immittance audiometer used for the study was calibrated using the following standards

ANSI S3 - 7 1973

ANSI S3 - 39 1987

ANSI S3-6 1969

JEC 645 1979

IEC 126 1973

# APPENDIX-II

## Calibration of nHL

Normal hearing level (nHL) refers to normal threshold for click or brief tone stimuli. 0 dB nHL varies depending on test environment and stimuli used.

A group often normal hearing subjects (5 male, 5 females) were taken. The behavioral threshold for clicks was estimated. The behavioral threshold estimation was done using the same instrument and in the same test environment as the actual ABR testing. Threshold was defined as the lowest level at which 50% of the responses were observed. Their average behavioral threshold was taken as 0 dB nHL for that stimulus. The nHL value obtained for the test room was 30 dB SPL.