DEVELOPMENTAL CHANGES IN MISMATCH NEGATIVITY (MMN)

Register No.M9809

Independent Project submitted as part fulfilment for the
First Year M.Sc, (Speech and Hearing), submitted to
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ALL INDIA INSTITUTE OF SPEECH AND HEARING: MYSORE 570006

MAY 1999

CERTIFICATE

This is to certify that this Independent Project entitled : **DEVELOPMENTAL CHANGES IN MISMATCH NEGATIVITY (MMN)** is the bonafide work in part fulfilment for the degree of Master of science (Speech and Hearing) of the student with Register No.M9809.

Mysore
May, 1999

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CERTIFICATE

This is to certify that this Independent Project entitled : **DEVELOPMENTAL CHANGES IN MISMATCH NEGATIVITY** (MMN) has been prepared under my supervision and guidance.

Mysore
May, 1999

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DECLARATION

This Independent Project entitled : **DEVELOPMENTAL CHANGES IN MISMATCH NEGATIVITY (MMN)** is the result of my own stum under the guidance of Ms.Vanaja C.S. Lecturer in Audiology, All India Institute of Speech and Hearing, Mysore and has not been submitted earlier at any University for any other diploma or degree.

Mysore
May, 1999

Reg. No M9809

DEDICATED TO

PAATI & TAATA

AMMA & APPA

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INTRODUCTION

Electrophysiological measures are one of the objective tests of the auditory function. They complement the information provided by the behavioural measures (Naatanen and Alho, 1997). For over 30 years, audiologists have used the Auditory Evoked Potential as an objective test of hearing. The basic application of evoked potentials has been to assess hearing thresholds, and in site of lesion testing.

An evoked potential (EP) refers to a series of electrical changes occurring in the peripheral and central nervous system, usually related to the sensory pathways. When these electrical changes are caused by sensory stimulation of the end organs (eg) the auditory system, they are called SENSORY EVOKED POTENTIALS (SEPs). Depending on the sensory system that is being stimulated, they are named as AUDITORY EVOKED POTENTIAL (AEP); VISUAL EVOKED POTENTIAL (VEP); or SOMATOSENSORY EVOKED POTENTIAL (SSEP). There have been several approaches to classifying and naming AEPs, but none has been completely standardised yet. These classification systems are based upon aspects such as the time domain within which the response occurs after stimulus onset, known as "latency epoch" [(ie.) short/early, middle, late/long] (Ruth and Lambert, 1991); "anatomic origin" (eg. Brainstem, cortical); "stimulus response relationship" (Eg. transient vs. sustained, endogenous vs. exogenous) or "electrode placement" (i..e. near vs. far) (Jacobson and Hyde, 1985).

The exogenous potentials are primarily elicited by some external event related dimensions of the stimulus. The endogenous potentials are responses which are due to internal events such as cognition or perception. The event related potentials are endogenous potentials. In recent years, research studies have considered the possibility of studying auditory discrimination with the "event related potentials" or ERPs. This is a general term used to describe the many different electrical changes associated with something that happens at a particular time. When this something is a sensory stimulus, the ERP is an evoked potential (Picton, 1995). "Event related potentials are virtually the only means that the current technology provides to evaluate the physiologic events of the normal brain, as it performs spectacular feats of information processing" (Hillyard and Picton, 1979). While clinical interest in the long latency potentials particularly the exogenous potentials, preceded the interest in short latency potentials, the acceptance of their utility has vacillated over time (Squires and Hecox, 1983). One of the reasons for their waning popularity is undoubtedly that they are most affected by change in the patient state than are the earlier auditory potentials. In contrast, the endogenous (Event-Related) potentials occur in proximity to the stimuli, but are relatively invarient to changes in the physical parameters of the eliciting stimulus (Desmedt and Debicker, 1979; Donchin et al. 1978). The various endogenous (event related) potentials are P300, Mismatch Negativity (MMN), Contingent Negative Variation (CNV), N400, Processing negativity.

P300 originally described by Sutton et al. (1965), depends on the attention and discrimination of stimulus difference. It is elicited

by an "odd ball paradigm" in which an unexpected stimulus occurs in a series of expected stimuli. The unexpected stimuli can even be the omission of an expected stimulus. The P300 can be elicited by visual, auditory and somatosensory stimuli. As the name suggests it is a positive deflection usually seen at a latency between 250-350 msecs. It has been suggested that P300 may be a neural correlate of sequential information processing short-term memory, and/or decision making (Squires, et al. 1976, 1977; Ford et al. 1980; Donchin, 1981; Harrison, et al. 1986).

Contingent Negative Variation (CNV) is a slow, negative potential following the late auditory potentials and it usually depends upon the association between two stimulus. Stimulus conditions that produce CNV are similar to Pavlovian conditioning. This response has gained widespread acceptance by psychologists (Kraus and McGee, 1994).

N400 is an endogenous potential that appears to reflect semantic processing of language. N400 is also not modality specific, and can be elicited by auditory, visual and sign language stimuli (McCallum et al. 1984; Herning et al. 1987; Kutas et al. 1987). Because it appears to assess language function, N400 could be a valuable part of an auditory processing battery. This potential involves the perception of semantic incongruity. The more complex or unexpected the stimulus, the larger the N400 response (Kraus and McGee, 1994).

"Processing Negativity" (Nd) is a broad, negative, attention related response which also occurs within and extends after, the N1 time frame, increasing the amplitude of N1 component (Hink, et al. 1978; Donald and Little, 1981;Okita, 1981, Hillyard and Kutas, 1983). The Nd appears to be related to memory and cognition (Kraus and McGee, 1994).

The Mismatch Negativity is a negative component of the event related potential (ERP) elicited by any discriminable change in auditory stimulation (Naatanen and Alho, 1997). It reflects central processing of very fine acoustic differences in acoustic stimuli. It can occur when the difference between the standard and deviant stimuli is as small as 8 Hz or 5 Hz, or even when stimulus differences are near psychophysical threshold (Naatanen, 1992; Sams, et al. 1985; Kraus et al. 1993; Sharma et al. 1993). It appears that MMN reflects a neuronal representation of the discrimination of numerous auditory stimulus attributes. If this response reflects the ability to discriminate between the acoustic stimuli, then it may not only be of research interest but may have value clinically because speech perception, by its very nature, depends on a neuronal response to stimulus change (Kraus and McGee, 1994).

MMN is usually obtained by presenting a train of repetitive homogeneous tones (termed standards) at a rate of around one tone per second, occasionally interspersed with a tone that differs physically (termed a deviant) (Ritter et al. 1995). Close examination of the response to the test stimuli when the stimuli are close together in frequency shows a clear waveform difference that is not detected by

simple N1-P2 measurements : a small negative deflection is superimposed on the waveform in the latency range of the P2 wave (Picton, 1995), So far, all acoustic features that are discriminable elicit the MMN, such as changes in intensity, frequency, duration, rise time and perceived location (Naatanen 1992). Sams, Paavilainen, Alho and Naatanen (1985) showed that the MMN was present when the deviant stimuli were just discriminable from the standard stimuli but not when the difference was not perceptible. The MMN is therefore a prime candidate for an objective neurophsyiological test of auditory discrimination. It occurs when the subject discriminates between stimuli at intensities similar to those used in normal speech, it can be recorded when the difference between the deviant and standard stimuli are close to discrimination limen (or just noticeable difference) and it occurs whether or not the subject is attending to the stimuli.

According to the current experimental evidence, the MMN provides a feature specific measure of the ongoing sensory analysis and auditory discrimination of various auditory stimuli. These characteristics make MMN a promising tool for testing individual perceptual abilities, maturation of acoustic discrimination or auditory dysfunctions of various origin. The MMN might be a very important measuring technique in assessment of intact and impaired processing in children as an early and objective diagnosis of central hearing-impairment would be of great significance (Csepe, 1995).

Csepe and Molnar (1997) state that two characteristics of MMN, namely its attention insensitivity and its recordability in a broad range of consciousness makes it a unique candidate for clinical application. Of these factors, the relative attention independence is one of the most important in applications and or application oriented research. MMN has been used in a variety of areas. They are

a) MMN as a measure of consciousness (Kane et al. 1996; Rockstroh et al. 1995).
b) MMN as a measure of memory trace efficiency (Pekkonen et al. 1993; Woods, 1992; Pekkonen et al. 1994).
c) MMN as a measure of lack of perceptual processing (Pekkonen et al. 1994; Karayanidis et al. 1995; Vieregge et al. 1994).
d) MMN as a measure of processing accuncy (Kraus et al. 1993; Ponton et al. 1995).

However, before MMN can be used as a clinical tool, it is necessary to establish normative data on it. As with other evoked potentials, a lot of variables that affect the MMN need to be considered while obtaining norms. Age is one such important variable which should be considered while recording and innerpreting the MMN.

Developmental Change in AEPs

It is well known that the infant AEP differ substantially from those obtained from adults. In general, age related changes tend to reflect the maturational development of the cochlear and/or neural generators of the AEP being recorded. This development, in

turn, proceeds in a peripheral to central direction. Thus, the electrocochleographic components of the early response may be mature at or shortly after birth, whereas developmental related changes in the late latency response can occur after several years.

The Auditory Brainstem Response (ABR) matures at an age of around 18-24 months of age. The morphologic and temporal characteristic of ABR change dramatically with age.

Numerous studies have demonstrated the Middle Latency Response (MLR) is obtained inconsistently in children (Skinner and Glattke, 1977; Hirabayashi, 1979; Suzuki et al. 1983a, 1983b; Kileny, 1984; Kraus et al. 1985; Stapells et al. 1988; Collett et al. 1988) and it has been suggested that this inconsistency is age related. From birth to adolescence, the detectability of wave Pa increases monotonically from 20% at birth to 90% at 12 years of age (Kraus et al. 1985). The response follows a systematic developmental course and the trend of increased detectability with age exists regardless of whether the child is normally developing or has a wide range of neurologic, cognitive or speech and hearing disorders.

In the late latency potentials, the developmental changes do not involve changes in a single parameter, like a gradual latency or amplitude shift, as a function of age (Courchesne, 1990). Rather it appears that various passively elicited event related potentials develop at different rates. Development of P_1, N_1, P_2 & P_3 b waves appears to continue beyond the first 10 years of life. On the other hand, the MMN and the P_3a-like response are evident early in life

(Kurtzberg et al. 1986; Courshesne, 1990; Kraus et al. 1992, 1993, Csepe, et al. 1992). The P300 potential as reported by Kurtzberg, et al. (1986) was present in response to speech stimuli at birth. The component similar to P_3a does not change in latency from childhood to adulthood. Latency of P3b decreases systematically throughout childhood, reaching asymptote beyond puberty (Goodin et al. 1978; Martin et al. 1988; Polich et al. 1985; Courshesne 1990; Finley et al. 1985; Johnson, 1989).

The MMN as said earlier matures quite early in life. Most of the studies done on the maturation report of a stable MMN response by the school going age (Kraus et al. 1993; Csepe, Dieckmann, Hoke and Ros, 1992). A majority of these studies have been carried out using speech stimuli. The investigations done using puretones have used frequency deviation and there are relatively few studies on MMN to deviations in intensity. Naatanen et al. (1989) studied changes in MMN to the amplitude deviations. The results indicated that large MMN was obtained with greater reduction in intensities of the softer stimuli. Naatanen and Picton (1987) also reported of similar findings in another study where in the intensity was increased compared to the standards. Thus it appears that MMN responds to the magnitude of intensity difference rather than the increment/decrement in intensity. These investigations have not studied the developmental changes in MMN to intensity variations in puretones. Moreover a majority of the instruments commercially available for electrophysiological measurements do not have the facility of varying the frequency in small steps (i.e.) 10 Hz, 15 Hz or 19 Hz, etc. The frequency can be varied only in octaves or mid octaves whereas intensity can be varied

in small steps of 1 dB or 2 dB. Literature too suggests of having as small a deviation as possible to elicit a good MMN. Most of the investigations done to study the developmental changes in MMN have either used speech stimuli or puretones with frequency deviations and as already mentioned, relatively few studies have used intensity deviations to study the developmental changes.

Thus the aim of this study was to :

(i) Study the developmental changes and maturation of the MMN to intensity deviation in terms of
   a) Absolute latency
   b) Amplitude
   c) Duration and
   d) Magnitude

(ii) To compare the latency, amplitude, duration and magnitude in reading and no reading conditions.

(iii) To compare the latency, amplitude, duration and magnitude for Cz and Pz recordings.

REVIEW OF LITERATURE

In the 1970's the most intensively studied "cognitive component" of the event related potentials (ERP) was the P300 (P300 or the late vertex positive complex). It usually was, and is characterized as being elicited by infrequent target events. This suggested that the two central factors underlying the P_3 were stimulus deviation from the frequent events and the significance of this deviation. But 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 Naatanen et al. (1978) in their study used dichotic stimulus presentation and the subjects task was to detect occasional deviant stimuli in the stimulus sequence presented to the designated ear, while ignoring the concurrent stimuli presented to the opposite ear. The tones were either of a slightly higher frequency or tones of a slightly greater intensity than the standard tones. It was found that the deviant stimuli in both the attended and unattended stimulus sequence elicited a negativity in the latency range of 100 to 200 msec, which could not be seen in the response to standard stimuli. They called this wave/response, the Mismatch Negativity (MMN). On the basis of the relatively large MMN amplitudes above the temporal areas, they further suggested that "the mismatch negativity reflects specific auditory stimulus discrimination processes taking place in the auditory primary and secondary areas.

Naatanen et al. (1982) demonstrated that the MMN could be elicited when a single odd ball sequence was presented to a passive

subject. They also reported that if the difference between the standard and deviant stimuli is large, the peak latency of the MMN becomes short and the MMN overlaps and adds to the N_1 wave. When the difference is small, the latency becomes longer and there is little, if any change in the N_1 wave. Picton et al. (1985) described a technique, that would be to record the response to a stimulus occurring in a homogenous train of standard stimuli and to compare the response to the same stimulus when it occurs as the improbable deviant stimulus in a train containing both standard and deviant stimuli. Another way of eliciting MMN is to present a subject with rapidly recurring standard and target stimuli in one ear and a similar series of different stimuli in the other ear and ask the subject to attend to only one ear in order to detect the targets in that ear. This leads to a significant difference in the ERPs between the target and standard stimuli in both ears. The effect is easily seen by subtracting the response to the standard stimulus from the response to the target stimulus. The resultant waveform (i.e.) difference waveform shows a clear negative deflection beginning during the N_1 wave but peaking later (Picton, 1995). Ritter et al. (1995) reported that themost common way in which the MMN is obtained is by presenting a train of repetitive, homogenous tones (termed standards) at a rate of around one tone per second, occasionally interspersed with a tone that differs physically (termed deviants).

Sams et al. (1985) showed that the MMN was present when the deviant stimuli were just discriminable from the standard stimuli, but not when the difference was not perceptible. Thus the MMN is a prime candidate for an objective neurophysiological test of auditory

discrimination because it occurs when the subject discriminates between stimuli at intensities similar to those used in normal speech and can be recorded When the differences between the deviant and the standard stimuli are close to the discrimination limen (or just noticeable difference) and occurs whether or not the subject is attending to the stimuli (Picton, 1995). In spite of it not being affected by the presence or absence of attention, the MMN is affected by the stimulus parameters which are used to elicit it, which will be discussed later.

NEUROANATOMICAL AND PHYSIOLOGICAL ORIGIN/S OF MMN

As already known, infrequent "deviant" stimuli occurring in a sequence of repetitive, "standard" sounds elicit a mismatch negativity (MMN). A majority of the investigators opine that the MMN is generated by a neuronal mismatch between the deviant sensory input and a sensory memory trace representing the standard stimuli (Cown, Winkler, Teder and Naatanen (1993); Naatanen et al. 1989; Naatanen et al. 1989; Ritter et al. 1995; Winkler et al. 1993). 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 et al. 1990;Lyytinen et al. 1992; Naatanen, 1979, 1990 and 1992). Naatanen (1990) suggests that there seems to be two alternative interpretation for the elicitation of the MMN by the deviant stimuli:

a) ***The refractoriness (sensory adaptation or fatigue) explanation:***

The MMN is composed of contributions from neurons sensitive to the frequency of the deviant stimulus but not that of the standard stimulus. In course of the experiment, these neurons remain responsive owing to long intervals between consecutive deviant stimuli. Neurons responsive to the standard stimulus frequency, however, as well as those responsive to both frequencies, become strongly refractory because of fast rate of the effective stimuli.

b) ***The memory-trace explanation***

Rather than the generation of MMN by the activation of "fresh" afferents, Naatanen (1990) suggests that it is generated by a process which registers the stimulus difference or change. Thus, on this hypothesis, the MMN is generated by a separate mechanism, responding only to a difference between consecutive stimuli, not to the stimulus perse. A response to the difference can be characterized as a second order response because the mechanism must actually relate two consecutive responses, one for each stimulus. This implies that at the moment of the occurrence of the deviant stimulus a memory trace or representation of the standard should have existed.

Thus, localizing cerebral generators of MMN might help identify brain mechanisms of auditory sensory memory and involuntary attention. Using a dipole modeling method, Scherg et al. (1989) demonstrated that the scalp distribution of MMN elicited by

an occasional frequency change in an unattended standard tone presentation monoaurally may be modelled with vertically oriented generators (dipoles) in the left and right supratemporal auditory cortices. They observed that MMN to a small frequency change could be modelled with one dipole source in the supratemporal auditory cortex of each hemisphere, whereas two dipoles in each hemisphere were needed to explain the negativity elicited by a large frequency change.

MMN generators in the left and right auditory cortices were also implicated by the scalp-current density (SCD) maps of Giard et al. (1990). They recorded MMNs to frequency changes in unattended tones presented to one ear during attention to tones delivered to the other ear. The SCD analysis suggested that the activity of the auditory cortex contralateral to the stimulated ear contributed more strongly to the MMN than did the ipsilateral auditory cortex activity.

An other study by Giard et al. (in Alho 1995) suggested that MMNs to frequency, intensity and duration changes may be generated by different supratemporal neuronal populations. The dipoles for the three MMN were located along the supratemporal auditory cortex, but differed in orientation, and/or location.

However, there are evidences to state that MMN may also have generators in the auditory cortical areas outside the supratemporal cortex. Paavilainen et al. (1991) reported of MMN to frequency, intensity and duration changes recorded with electrodes at the midline and at lateral lines crossing left and right auditory cortices. The MMNs

consisted of two subcomponents one at 150-200 msecs, inverted in polarity at sites below the auditory cortex and this is consistent with the supratemporal origin. The second component did not invert in polarity at 200-300 ms and they might have been generated by radially oriented dipole on the lateral aspect of the temporal lobe.

Alho (1995) also reported the major source of MMN is situated in the auditory cortex. However the exact location of this generator appears to depend on which feature of a sound is changed (ie. frequency, intensity or duration), as well as on the complexity of the sound (ie. a simple tone versus complex sound). He also adds on that there is some evidence for contribution of frontal lobe activity to the MMN which might be related to the involuntary switching of attention to a stimulus change occurring outside the focus of attention. In addition, intracranial MMN recordings in animals suggest that at least in some species, MMN subcomponents also may be generated in the thalamus and hippocampus.

Apart from localizing generators recorded from scalp, magnetoencephalography (MEG) has also been used to localize the MMN generators. Hari et al. (1984) were the first to record the magnetic counterpart of MMN, the MMNm. It was elicited for 1030 Hz deviant and 1000 Hz standard, tones presented to a subject concentrating on reading. The equivalent current dipole for MMNm was located near the vicinity of a supratemporal N_1 (N_1m) generator that is located in or near the primary auditory cortex. Moreover, a number of studies subsequent to this have indicated that the equivalent current dipole for an MMNm to a frequency change is located, on

average, 1 cm anterior to the N_1m dipole (Csepe et al 1992; Hari et al. 1992; Sams, et al. 1991; Naatanen, 1993). MMNm dipoles for changes in other features of simple tones, including intensity, duration, and interstimulus interval, also have been localised to supratemporal auditory cortex (Hari et al. 1989; Levanen et al. 1993; Lounasmaa et al. 1989; Kaukoranta et al. 1989; Sams et al, 1991). Levanen et al. (1993) and Sams et al. (1991), reported that the MMNm dipoles are located anteriorly to the N_1m dipole. Results of another investigation by Levanen et al. (in Alho, 1995) suggested that MMNm dipoles for changes in tone frequency, duration, and interstimulus interval are located in different areas of supratemporal auditory cortex, suggesting that different neuronal populations are involved in representing these features. Moreover, they observed that MMNm responses to changes in frequency, intensity and interstimulus interval, peaked on an average, 9-34 msec, earlier over the left hemisphere irrespective of the ear of stimulus delivery.

Intracranial recordings ofMMN have been carried out on animal and human subjects to determine MMN generators including localization of these generators. Csepe, Karmos and Molnar (1987) recorded ERPs in the cat to standard (4000 Hz) and deviant (3000 Hz) tones of very short duration (1 msec). The electrodes were located over the auditory cortex areas AI (middle ectosylvian gyrus) and AII (Ventral region of the ectosylvian gyrus) as well as over the association cortex and at the vertex. The MMNs recorded over the association cortex and at the vertex began at the latency of 30-40 msec, while the MMN at AI and AII commenced 20-30 msec, later. Thus, the authors suggest that the early MMNs observed over the association cortex

and vertex might have been caused by far field components originating from subcortical structures. In a further study, Csepe et al. (1989) used additional electrodes placed in the medial geniculate body (MGB) of the thalamus and in the dorsal hippocampus. The MMNs recorded over the auditory and association cortices and at the vertex resembled those observed in the previous study, but in the MGB an MMN-like response to deviants began at 20 msecs. and was followed by a positivity. On the hippocampus, an even earlier MMN-like negativity, one beginning at about 10 msec, was recorded. These authors interpreted that an MMN subcomponent is generated already at the thalamic level and that the hippocampus participates in the comparison of different stimuli.

Csepe, Karmos and Molnar (1987a, 1987b and 1993) recorded MMN from the subcortical areas i.e. Medial Geniculate Body (MGB) and inferior colliculus (IC) representing the sensory specific system. They found that the peak latency of the AI and AII responses is about 20 msec, later than that of MGB and IC responses which is a big difference if only primary responses are taken into account. These data seem to strengthen the hypothesis that deviating acoustic stimuli are compared at different levels of the auditory pathway and involves both primary and secondary pathways. Ritter et al. (1995) have suggested that inhibitory cortical mechanisms may have an important role in sensory-memory mechanisms involved in MMN generation. These studies have used frequency deviations to elicit MMN. The study done by Javitt et al. (1992) has used intensity deviation. Epidural auditory ERPs were recorded from 3 cynomolgous monkeys in response to deviant clicks (65 dB SPL) occurring among standard

clicks of 85 dB SPL. The oddball loud or soft stimuli elicited a long duration fromto central negativity peaking at approximately 85 msec, which is intermediate in latency between the cat and human MMNs and this is consistent with the size and complexity of the monkey brain relative to those of cat and human. This suggests that the monkeys might serve as a heuristically valuable system to study the neurochemical and neuroanatomical substrates of early context dependent ERP generation.

Kropotov et al. (1991) recorded MMNs directly MMNs from the temporal cortex (Broadmann's area 21 and 42) in two patients with intracranial electrodes implanted for diagnosis and therapy. These MMNs peaked at 200 msec, from stimulus onset by deviant tones (1100 Hz) and standard tones (1000 Hz). These were obtained both when the patients were reading a book and ignoring the tones and when they attended to tones in order to respond to deviant tones. No MMN to deviant tones of ignored auditory input was observed in this study nor in investigations wherein other structures including hippocapus, the amygdala and the basal ganglia have been have been studied. In these studies, a P_3 positivity, sometimes preceded by an N_2 negativity was observed in response to deviant tones when they were target stimuli requiring active attention (Kropotov et al. 1991; Wood et al. 1980; Velasco et al. 1991).

As reviewed above, a major contribution of the supratemporal cortical activity to MMN elicited by different kinds of stimulus changes is indicated by source localization of scalp recorded ERPs and magnetoencephalographic fields recorded outside the head.

More direct evidence for the contribution of auditory cortex activity to MMN has been provided by intracranial MMN recordings. Thus, since MMNs can be elicited even in the absence of attention, it provides an objective method to investigate these mechanisms and their dysfunctions and also to study more general principles of representing sensory information in the human brain.

CLINICAL APPLICATIONS OF MMN

Among the various event-related potential components (ERPs), the MMN is one which provides feature specific information about the central processing of discriminable changes in auditory stimulation. Importantly, various applications that the MMN provides, yield feature specific information about the sound representation and this develops rather early in comparison to other ERP waves (Csepe and Molnar, 1997). The MMN has been used for clinical application in various fields as discussed below:

a) **As a Measure of Conciousness**

Although MMN can be elicited in a relative broad range of levels of conciseness and vigilance, it is not clear what quality and quantity of stimulus deviations are sufficient for its elicitation. There are however very promising clinical trials for using MMN for clinical predictions of disturbed states of consciousness.

In an extensive study by Kane et al. (1996), a large number (54) of coma patients were investigated using pitch-deviation-elicited

MMN. They correlated the MMN results with the chances of 90 day outcome in order to predict the liability of MMN for predicting the outcome of a come after traumatic brain injury (TBI). The presence of MMN was highly related to the emergence from the coma. They, therefore suggested that using MMNs all or none character was an early neurophysiological indicator of recovery from coma caused by TBI. They also reported of high sensitivity and specificity. In spite of its high sensitivity and specificity, one has to be careful when using it as a diagnostic tool because though the presence of MMN helped to manage TBI patients and counsel their relative, absence did not mean impending death in all cases.

A similar study was done by Rockstroh et al. (1995) on patients with apallic syndrome, also described as "persistent vegetative state" that follows severe head trauma. In this study the presence of MMN significantly correlated with the level of dysfunction as assessed by the Disability Rating Scale (Rappaport et al. 1982). They concluded that the comparison processes reflected by the MMN need a "functional efficiency of the cortex" that failed in most of the patients investigated.

b) As a Measure of Memory Trace Efficiency

Most of the clinically oriented MMN research is based on the memory trace concept that the MMN is a product of a comparison of the incoming signal against the neuronal trace built up by the frequently repeated stimuli (standard). The magnitude and strength

of memory trace gave a big impetus to those studies in which patients whose sensory memory was impaired.

The aims were however slightly different A set of them aimed at describing those generator areas with intact functioning, and which were assumed to be crucial in the comparison process. The others focused on the problem whether a faster memory decay or lack of automatic, perceptual processing was relevant to the disorder investigated.

Pekkonen et al. (1993) measured pitch and duration MMN at different (Interstimulus Intervsl (ISIs). They found that when repetition rate of 2/3 is used, age had no affects on the auditory attributes (pitch and duration). But a significant increase in the ISI, however led to a significant attenuation of the MMN in older subjects. The authors concluded that while the automatic stimulus comparison processes was not affected by aging, the functional limitations of the trace were influenced.

On the contrary Gunter et al. (1996) reported that there was an enhancement in the sensitivity of processing of the auditory attributes in the aged subjects. This discrepancy may be due to the experimental parameters differentiating sensitivity and aging. By measuring MMN in the same paradigm as that described in his earlier study in (1993). Pekkonen et al. (1994) found a decrease in the MMN amplitude as a function of ISI. They used 1/s and 3/sec ISI in older control subjects and subjects with Alzheimer's disease. They concluded that memory trace decays faster in patients with

Alzheimer's disease than the age matched controls. There was no trace preservation specific to Alzheimer's patients but the degree of MMN attenuation was more expressed than in older subjects. In another study by Yokoyama et al. (1995) on patients with dementa of the Alzheimers disease reported of no significant amplitude change of the MMN. They reported of longer latency but this was not found in different patients suffering from vascular dementia They suggested using this for differential diagnosis, but they are not clear as to why this difference in latency is seen.

c) As **a Measure of Lack of Perceptual Processing**

(i) Parkinson's Disease

While the use of MMN in different types of dementia was based on the assumption that it was the trace perserveration which played the main role in MMN abnormalities, in Parkinson's disease an impaired change detection was supposed in general. In the study of Pekkonen et al. (1995), the pitch MMN in non-demented patients with Parkinson's disease was observed to be smaller than in the age matched controls. The area was measured and the MMN attenuation was interpreted as a consequence of dopamine deficiency in these patients.

Contrary to the above findings Virregge et al. (1994) reported that there were no assumed differences between controls and patients with ideopathic Parkinson's disease when duration MMN was recorded. Their results provide evidence for a distinctive impairment of the controlled processing i.e. a disturbed auditory

selective attention as revealed by a significantly smaller processing negativity (PN) and unchanged P300.

(ii) Schizophrenia

To contribute to the understanding of the neurophysiological deficits in Schizophrenia, MMN was used. By using MMN, the research on Schizophrenia primarily focused on whether the information processing is impaired on the level where controlling is required or at a lower level i.e. automatic change detection level. Javitt et al. (1995) compared 20 medicated and 11 non-medicated patients and an age matched control. MMN and P3 were measured in both active and passive conditions for pitch deviations. The MMN was significantly impaired in Schizophrenics both in medicated and non-medicated group and its peak to peak amplitude was also reduced. The reduced MMN was similar in the 2 groups, but this decrease was significant in the medicated group whereas tendentious in the unmedicated group when compared to the normals. Furthermore, the amplitude reduction of MMN showed significant correlation with P300.

d) As a Measure of Processing Differences

(i) Obsessive Compulsive Disorder (OCD)

While attention deficit appears to be a nuclear disorder in Scbizophrnia, in obsessive compulsive disorder an over focussed attention is assumed. In the study by Towey et al. (1994), no differences were found between MMNs of patients and controls. But

they reported of lack of N_2b abnormalities in patients which draws attention to the comparatively different race of the frontal lobe in processing underlying attentional shift (MMN) or contributing to different types of attention control (N2b vs. PN). But Oades et al. (1996) have shown distinctive differences between MMN and PN. The OCD group showed a right side predominance of the MMN and an extreme regional allocation of the PN. It is however still not known to what extent of region in the frontal lobe is affected in an obsessive compulsive disorder.

(ii) Effect of Alcohol and the Frontal Lobe

The experimental evidence of a frontal source in MMN generated was assumed and was shown by the effect of alcohol (Jaaskelainen et al. 1995; Grillon et al. 1995).

Jaaskalainen et al. (1995) used low dose of ethanol and reported of dramatic amplitude reduction and significant latency delay of the MMN. However the same dose of ethanol left PN and P_3 unaffected. But Grillon et al. (1995) reported opposite to this and reported that ethanol does not affect the MMN, but changes the P_3. Although no MMN change was found, reduction of the novelty P_3, having a strong frontal component, implies impact of alcohol on the frontal processing of task-irrelevant stimuli. In a recent study by Jaaskelainen et al. (1996), effect of different dose of alcohol of MMN at different ISI's have been reported. The lower dose did not effect the ERP at 0.8s ISI but at longer ISI (2.4s) even the low dose

suppressed the MMN, whereas a higher dose attenuated MMN at both the ISIs used. Based on these findings and on the changed scalp distribution of MMN a strong impact of alcohol on the frontal generator was suggested.

In spite of all the contributing results, one cannot draw a general conclusion about the most important site of alcohol effect related to automatic information processing based on the duration MMN.

(iii) Aphasia and Assumption of Different Generators in Tone and Speech Processing

Event related potentials were recorded from 4 aphasics, 2 with lesions in the posterior part of the left frontal lobe and 2 with lesions in the posterior part of the left temporal lobe by Aaltonen et al. (1993). The patients with the lesions in the frontal lobe had intact MMN to pure tone and vowel deviations, whereas those with lesions in the temporal lobe lacked MMN to vowel contrast, but had normal MMN to tone deviation. Thus the presence of MMN to tone deviation in all 4 patients indicates that MMN does not show an across the board effect. Studies conducted by Csepe et al. (1995) reported of MMNs to both 'tone deviations of pure tones and also to vowel deviations. The main difference between the two groups could be observed in the MMN to stop consonants. The Broca's aphasic show normal MMN to deviating (place of articulation) consonants over the intact hemisphere, while the Wemicke's aphasia shows only a late sustained negativity rather than a real component. These findings

are in agreement with the behavioural scores on the phoneme discrimination tasks. These MMN data are in agreement with neurolinguistic investigations.

e) **As a Measure of Processing Accuracy**

One of the most exciting applications is the use of MMN in patients with cochlear implants. The study by Kraus et al. (1993) recorded MMN to speech stimuli of dissimilar spectral components. They reported of MMN in all good CI users and that it was very similar to that recorded in normal listeners. Thus the speech perception abilities of the CI users depend on the central auditory processing reflected by MMN. In another study by Ponton et al. (1995) MMN to changes in stimulus train duration and pitch were recorded. The MMN recorded in CI users resembled that of the normal hearing individuals. Thus the MMNs all or none nature and the strong correlation between the goodness of Cochlear Implant (CI) use and behaviouraldiscrimination is an important application in the measure of processing accuracy.

In general we can conclude that the MMN is a good candidate for clinically oriented research, in some cases even for clinical application. But, there is, however an urgent need for systematic studies on the normative range of the different MMN types and on their confidence interval and inter and intra-individual variabilities.

FACTOR AFFECTING MISMATCH NEGATIVITY

There are two types of parameters which affect the MMN. They are EXOGENOUS FACTORS AND ENDOGENOUS FACTORS. Exogenous factors are related to the stimuli used for testing and the recording parameters, whereas the endogenous factors are subject related factors. These factors viz. exogenous and endogenous can be further divided as below :

I EXOGENOUS FACTORS

a) Stimulus related factors

1) Type of stimulus i.e. deviant and frequent
2) Intensity of stimuli i.e. deviant and frequent
3) Frequency of stimulus i.e. deviant and frequent
4) Rate of stimulus presentation
5) Number of stimulus presentation
6) Probability of the deviant stimulus
7) Interaction of different stimulus parameters.

b) Recording parameters

1) Place of electrode
2) Filter characteristics
3) Recording condition and duration of the session

II ENDOGENOUS FACTORS

1) Attention
2) Task
3) Sex
4) Age

I EXOGENOUS FACTORS

a) Stimulus related factors

1) *Type of stimulus*

There are different types of stimuli which can be used to elicit MMN. The MMN is elicited by an discriminate change of a repetitive sound and can be elicited by stimulus differences that approximate behavioural discrimination threshold (Naatanen, 1995). Different investigators have made use of different stimuli depending on the need of their study, but the most commonly used are the simple stimuli i.e. the puretones and complex stimuli (speech). The initial studies of MMN were carried out using pure tones (Naatanen et al. 1978; Naatanen et al. 1982; Picton, Rodriguez, Liden and Maeste, 1985). Later the studies used more of speech stimuli because of the hypothesis put-forth that if MMN reflects the processing of fine differences in simple stimuli, it could also be elicited by just perceptibly different acoustic contrasts that are important for speech perception (Kraus et al. 1995). There have been many studies conducted using just perceptibly different speech stimuli. Kraus et al (1995) used different variants of the phoneme /da/ to obtain behavioural discrimination functions. They also used a more easily discriminable contrast i.e. /da/ - /ga/. Eliott and Hammer, 1998; Elliott, Hammer and Scholl (1989) in their studies used speech sounds differing in spectral change where stimuli differed similarly in the onset frequency of second and third formant transitions /ba/ - /da/ - /ga/. Nonetheless, available clinical cases and research results indicate that a variety of stimuli can be used to elicit a MMN.

2) *Intensity of stimuli*

As it is already known that to elicit MMN, an odd ball paradigm is used which includes the presence of a stimulus termed "deviant" when compared to the standards. This deviant stimuli could be either different from the standards in terms of frequency, intensity, ISI, etc.

The intensity of the stimuli has been reported to have an effect on the late potentials. It has been reported by Roth et al. (1930) in a series of 3 papers that the amplitude of the P300 depends on the intensity of the evoked stimulus. Although these studies did not use the "oddball" paradigm, the results raise serious doubts regarding the P300 amplitude variance in general.

Butcher (1983) however reported of a significant effect of intensity on the latency of P300. He reported that when the stimulus intensity was increased from 10 dB SL to 50 dB SL, there was an average reduction in P300 latency of about 29.3 ms. In line with the above findings Papanicolaou et al. (1985) reported that there was no effect of intensity on the amplitude of P300, but a statistically significant increase in the latency contingent on reduction of stimulus intensity was noted.

Most of the studies done on the MMN component highlight more about the deviance of the intensity of the stimuli from each other rather than the effect of the intensity of the stimulus per se. There have been a few studies which report of the effect on the intensity deviations on the MMN.

Naatanen et al (1989) reported of a study wherein standard stimuli of 80 dB SPL were delivered with a probability of 90% whereas the deviant stimuli were similar to the standards but of a lower intensity (57, 70 or 77 dB SPL) which had a probability of occurrence of 10% with the 77 dB stimulus, there were two consecutive negative waves seen,. Of which the earlier was the Ni whereas the latter was the MMN. They reported that with further reductions in intensity, the MMN component became larger and earlier, overlapping with the Ni component.

A similar study was conducted by Naatanen and Picton (1987) wherein they used intensity increments instead of decrements. They too reported of similar results (i.e.) shortening of latency and an increase in the amplitude of the MMN component with decrease in intensity.

Thus it can be seen that with either an increase or decrease in the intensity of the deviant stimuli, there is a shortening of latency along with an increase in the MMN amplitude. Thus these studies shed light on the size of deviation of the deviant stimuli from the standard one.

3) Frequency of the stimulus

Of the various stimulus related factors, the effect of frequency deviation i.e. the difference between the standard and the deviant stimuli has been vastly researched. The effect of the frequency of the stimuli used to elicit an MMN has not be researched much.

But Butcher (1983) has reported about the effect of stimulus frequency on P300. He reported that there is no significant effect of stimulus frequency on the P300 response. Contradicting this, Polich (1989) reported that both the latency and amplitude of the response are significantly affected by changes in frequency of the stimulus and also that P300 is affected by an interaction of stimulus intensity and duration.

There have been various reports of the effect of stimulus frequency deviance on MMN, Lang et al. (1995) report that when the difference between the standard and the deviant stimuli is small, it is easier for the subject to ignore the test stimuli, but with a smaller difference, however, the MMN amplitude is low and the signal to noise ratio is poor. They also report that with a large difference in the frequency of the standard and deviant stimulus, neurons in the primary auditory cortex activated by the deviants are different from those activated by the standards. In addition, if there is a longer ISI between the deviants, the N_1 generator activation caused by the deviants may be significantly larger than that caused by the standards leading to an enhancement of the N_1 omponent which gets superimposed on the MMN.

Lang et al. (1990) have reported that if a puretone of 1 kHz is used as a standard, deviance of about 50-100 Hz or more is usually obstrusive currently it is unknown what the safe upper limits are for the deviance of frequency, intensity and duration of puretone stimuli as well as for complex stimuli.

4) No. of Stimuli Used

The MMN response is buried in the physiological EEG-background activity. The background activity will not be cancelled in the averaging. Hence, more than 10,000 deviant responses should be averaged for resolving the hypothetical 0.3 μV MMN response. 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 to 2700 standard responses (Lang et al. 1995).

5) Rate of stimulus presentation

If simple stimuli are used, the MMN amplitude increases when the ISI (interstimulus interval) is shortened, provided the intervals between the deviants are of the same duration (Naatanen et al. 1987). This is in contrast to the fast decrement of the amplitude of the N_1 and P_3b component (Mantysalo et al. 1987; Sams et al. 1993). In addition to the selective increase of the MMN, a higher stimulation frequency shortens the recording session leading to an improved recording quality. In practice however an ISI of about 300 msec has shown to be appropriate for MMN applications when using simple or vowel stimuli. When speech stimuli are used, the MMN may sometimes deteriorate with too short an ISI (Lang et al. 1995).

6) Probability of the deviant stimulus

The MMN amplitude also is affected by the probability of deviants in the stimulus sequence. When the probability is lower,

the MMN amplitude increases. However, the total time of recording increases which again reduces the quality of the response. Till now, it has not been determined systematically which probability of the deviant yields optimal MMN responses. Rather good results have been obtained if every 5th to 10th stimulus is a deviant, in a "pseudorandom stimulus sequence" (Lang et al. 1995). It is imperative that the stimulation program does not generate two or more deviants, one immediately after the other; because then those deviants function as new standards and the MMN response in the difference waveform is attenuated (Sams et al. 1983).

7) **Interaction of different stimulus parameters**

The selection of the stimulation parameters is primarily determined by the experimental question. One has to bear in mind that the MMN response is generated by any psychophysical difference between the standard and deviant stimuli. Thus although the stimulation parameters are physically independent of each other, a psychophysical interaction may exist between them. The physical properties of the stimuli are normally fixed in the stimulus generation phase and they should not be affected by the presentation device (Lang et al. 1995).

b) Recording parameters

1) Place of electrode

Naatanen (1992) recommends use of the nose as reference instead or ear or mastoid because the phase shift in parasagittal and

temporal deviations makes it easier to identify the MMN topographically and to distinguish it from the N_2b waveform, which has a different scalp distribution. In clinical practice, however, the placement of an electrode on the nose is difficult and there are numerous artifacts particularly in children. In most psychophysiological MMN studies, three midline electrodes (Fz, Cz and Pz) referred to the ear or mastoid electrodes, plus two EOG electrodes have been used. This facilitates the identification of the waveform in ambiguous cases as MMN scalp distribution is frontoparietal. To achieve more complete scalp distribution for "brain mapping", which also improves the identification of ambiguous MMN response, all 21 electrodes of the 10 to 20 system are needed (Lang et al. 1995).

2) Filter characteristics

A frequency band of 0.1 to 30 Hz is sufficient for the MMN recording. 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. Sampling rates of higher than 100 Hz and analogue to digital conversion of at least 10 to 12 bits are recommended for data acquisition (Lang et al. 1995).

3) Recording condition and duration of the session

MMN recording should be performed in a room with sufficient protection against noise and disturbance. Complete noise

isolation is not required because the stimuli are usually delivered via earphones. If free field stimulation is used, the standard and deviant stimuli might attenuate differently, thus generating an extra unintentional deviance.

Lang et al. (1995) report that it typically takes about 8 to 10 minutes to record the necessary number of responses. But along with the preparation and electrode placement, to record five to six blocks (including 200 deviant and 1000 standard stimuli at a rate of 3 Hz) in a 1 hour session is the maximum duration of a session for the elderly and school aged children. For younger children, the test session must be even shorter. Even in young adults, the MMN amplitude begins to attenuate after 1 to 2 hour on average (Lang et al. 1995).

II ENDOGENOUS FACTORS

1) Attention

Evidence for the MMN independence of attention was produced by Naatanen et als. (1978,1980) selective listening studies with dichotic stimuli, The negative difference waves obtained by subtracting the temporal ERP for standard stimuli from those for deviant stimuli were very similar for attended and ignored input) The interstimulus interval (ISI) used was, however, rather long (800 msec) and constant and this does not force the subject to develop a sharp attentional focus to be able to perform the task. (Alho et al (1989) also reported of similar findings and added that even a considerable variation in the task difficulty, which should affect the strength of

attentional focus does not affect MMN. However, using a short, random ISIs between 200-500 msecs, Naatanen(1990) obtained some tentative evidence for an attentional modulation of the MMN amplitude. Moreover Woldorff et al. (1991) and Woldorff and Hillyard (1990) using occasional intensity decrements as deviant stimuli found that the deviance related difference was considerably larger within the attended than within the ignored input and hence they suggested that the MMN can be affected by verystrongly focussed attention) Naatanen et al. (1993) in their study reported that the MMN to frequency deviation was resilient to attention at least in the sense that it cannot be eliminated by even presumably complete withdrawal of attention, whereas the intensity MMN appears to be vulnerable to attention as previously suggested by Woldorff et al. (1991) They also report that when attention is very strongly focussed on the input delivered to the opposite ear (dichotic paradigm), minor decrements in stimulus intensity seem to elicit no or only a very small MMN, whereas MMNs are elicited when attention focused elsewhere is less intense (reading). Moreover Lang et al. (1995) report that MMN strongly varies with alertness even if the subject is not allowed to fall asleep. On the various states of vigilance, the MMN amplitude and latency behaved in different ways. In the beginning when the subject felt drowsy, both the MMN latency and amplitude increased. When the S1, sleep episodes with slow eye movements started to occur, the amplitude began to decrease while the latency continued to increase. The MMN amplitude also decreased significantly without preceding sleep deprivation when a monotonous recording session lasted for about 1 to 1.5 hour, although individual variation are great.

Thus the results show that it is of importance to maintain the subject's attention during MMN recording, to avoid monotonous experiment procedure and never to use tired test subjects.

2) Task

Usually during eliciting MMN, a passive condition is preferable to avoid mixed waveforms caused by N2P3 waves typical of active conditions (Naatanen, 1995). Ignoring can be achieved by focussing the subject's attention away from the test stimuli. Watching a video movie, instead of reading has proven useful with children and aphasic patients. In watching a TV screen, the eye movements (with related electroculographic artifacts) are smaller than when the subject is reading a book (Lang et al. 1995). On the other hand, reading provides an objective measure of the efficiency of ignoring.

Further, it is possible to use a dichotic paradigm to direct attention away from the MMN stimuli. In the dichotic paradigm, the subject is presented with rapidly recurring standard and target stimuli in one ear and a similar series of different stimuli in the other ear and asked to attend to only one ear in order to detect targets in that attended ear (Picton, 1995). A task requiring active attention of one ear does not interfere with the passive tasks performed by the other ear. The dichotic paradigm has recently been successfully applied for simultaneous recording of MMN and P_3. In this method, neither the MMN nor P3 parameters change significantly as compared with the conventional approach. Attention is controlled, and total recording

time is shortened (Lang and Mikola, 1994). The continuity watching a video movie or some other visual task is necessary not only to direct the subject's attention away from the test stimuli and to maintain the subject's 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 response (Lang et al. 1995).

c)Sex

There have not been many reports on the differences between MMN in males and females. In a study by Aaltonen et al. (1994), it was observed that gender influenced the latency of MMN. They report of significantly longer latency of MMN in females than in males for complex stimuli.

d) Age

Although various event-related potentials (ERP) hold some promise for the assessment of higher cortical processes, including discrimination, learning and memory, it is unfortunately true that ERP components associated with active cognitive processes are variable and are sensitive to fluctuations in attention. Because MMN is an automatic response that is not significantly influenced by attention, it would appear an ideal probe of auditory sensory memory and discrimination in infants and young children and in the clinical assessment of auditory processing disorders in the paediatric population. However, before it can be utilized as a clinical tool, it is

necessary to establish that the MMN can be reliably elicited in normal individuals under the same stimulating conditions that is to be used with the clinical populations. Therefore a number of studies have investigated the changes in MMN due to age.

Alho et al. (1990) reported of event related potentials (ERPs) of eight sleeping human newborns to occasional pitch changes in a repetitive sequence of tone pips. They reported that the ERP to the 1200 Hz deviant tone appearing among the 1000 Hz standard tones tended to be negatively displaced in relation to the standard tone ERP. This negative deflection was seen at a mean latency of 296 msec, largest at the Fz and Cz and was seen in six out of eight newborns studied. They also report of a negativity beginning at around 100 msec, to the infrequent 1200 Hz tones presented with no intervening standards, but this negativity tended to have a shorter duration that the negativity to the same deviants presented among standard tone.

Cheour et al. (1998) compared MMN in the pre-term infants, full-term new borns and full-term three month old infants. The stimuli used were Klatt synthesized Finnish vowels /y/ and /i/. The results revealed that the infant MMN amplitude seems to resemble that of adults. They also report of no significant differences in MMN amplitude between the three groups. The MMN latency, however, decreased significantly with age. In another study on infants by Pang et al. (1998) MMN was measured in 15 normal awake eight month old infants and these were compared to the MMNs elicited in ten adults. The stimuli used were consonant /ta/ and /da/. With /da/ as the standard with 80% probability and the /ta/ as deviant with a

probability of 20% and the ISI was 600 msec. ERPs were analysed at eleven electrode sites. An MMN was observed in both infants and adults, but a clear difference in scalp distribution was noted. A clear infant MMN was observed only at C_3 and T_3 electrodes, whereas in adults the sites were Fz, Cz, C_3, C_4 and P4. The MMN in adults was largest at Cz and C_3 -whereas in infants it was at T_3. These data indicate a possible maturational change in the MMN.

Kurtzberg et al. (1995) investigated the infant's capacity to discriminate speech sound. They employed the consonant vowel (C V) syllables /da/, /ba/ and /ta/ as stimuli. They found that any of the three CV syllables elicited an enhanced negativity in the latency range of 700-800 msec, followed by a more variable positive wave. They named it as the cortical discriminative response (CDR) and considered it different from MMN due to its longer latency and it being present only in infants who were awake.

All the above reported studies have used speech stimuli. Using puretones Alho et al. (1990) recorded cortical ERPs in fourteen infants (seven normal full term and seven pre-term), at seven months of age. Recordings were taken in the waking state. They used 1000 Hz standard stimuli with 90% probability, whereas the deviants with 1200 Hz had 10% of probability of occurrence. The ISI was 610 msec. The responses to the deviant stimulus consisted of a positivity that peaked at 250-300 msec, with the pre-term group exhibiting a significantly larger deflection compared to full term infants. They, however, as reported in the earlier studies, did not find a negative potential in either group of infants.

Contradictory to the above study, Kurtzberg et al. (1995) report that in the twentyfive healthy waking infants they studied, 75% of them had an indication of negativity in the ERPs. They defined MMN as any negative deflection in the latency range of 150-400 msec. 1000 Hz standard tones with intervening 1200 Hz deviant tones with 15% probability were used as stimuli. The interstimulus duration used were 750 msec, and 1000 msec.

Studies have also been carried out on older children (particularly school-age) to investigate the age related changes in MMN. Kurtzberg et al. (1995) recorded MMN in 4-10 years old children using a 750 msec. ISI. The standard stimulus was 1000 Hz and the deviant was 1200 Hz. They reported mat approximately 2/3rd of the subjects showed a clear MMN in the grand mean responses. In the l/3rd of the children, a clear MMN was not present, despite a robust obligatory response to both the standard and deviant stimuli. They therefore concluded that intersubject and intrasubject variability could lead to a substantial incidence of false negative records.

Kraus et al. (1995) conducted a study on normal school-age children (7-12 years) using stimuli which were just-perceptibly different varients of the phoneme /da/ which differed in the formant transition onset frequency. They reported that both the adults and children show a robust MMN despite the developmental differences in the preceding P_1-N_1 waves. Statistical comparison however, revealed no significant difference in the peak latency, duration or onset to peak amplitude of the MMNs recorded. But children showed a larger MMN, with the difference being apparent in a significantly

larger peak to offset amplitude and a larger overall area compared to adults. Similar findings have also been reported by Csepe (1995), Kraus et al. (1992) and Kraus et al. (1993).

Neurodevelopmental trends of the MMN has been reported by Lyytinen et al. (1992). They used auditory stimuli which differed either in pitch or in rise time in schoolage group 8-12 years. They reported of larger amplitude for the standard stimuli and significantly longer latencies than adults. Then MMN reflected by the difference wave, however, did not differentiate significantly the children and adults Csepe et al. (1995) compared the amplitude, latency and scalp distribution changes of MMN to speech and non-speech deviations in schoolage children (8-10 years of age). They found that high amplitude MMN was elicited by all stimulus deviations. The scalp distribution of the MMN to speech and nonspeech stimuli was different. The MMN elicited by puretones and vowel deviations appeared with the usual fronto central maximum and showed a slight right hemipshere preponderance as in adults as reported by Paavilainen et al. (1991). The MMN in this age group showed an exquisite sensitivity to speech stimuli. The highest amplitude MMN was elicited by a stop consonant if the contrasting feature was place of articulation. Csepe et al., earlier in 1992 had compared the maturation of the component structure of AEPs to repetitive unchanging stimuli and that of the MMN to frequency deviations. They reported that the AEPs recorded in children under 13 years do not show a stable waveform to different frequencies. Under 10 years of age, a relatively late (about 200 msecs) negativity appeared to be the most prominent

wave of the AEPs. The response did not show systematic changes to different frequencies and intensities as did the adult N_1. The MMN to frequency deviations appeared to be rather stable in the children resembling the adult response and these data are in agreement with the results of other studies. However, the latency to frequency deviations did not differ between adults and children. While its amplitude was larger in all age groups of children. Kurtzberg et al. (1995) report of the presence of MMN in relation to the other components N_1 and P_1 in their study on 8 year old children. They recorded MMN from 10 children (4 boys and 6 girls) using standards of lOOOHz and deviants of 1200 Hz with a probability of 15%. The ISI was 750 msec and intensity was 85 dB SPL. They used 31 electrodes according to the international 10-20 electrode system. They considered the responses at Fz for amplitude and latency measurement MMN was defined as the most negative deflection between 160 ms-254 msecs. They found the presence of MMN in 60% of runs when P_1 and N_1 were present; whereas MMN was present only in 50% of the runs, MMN was present but, N_1 and P_1 were absent. When both N_1 and P_1 were present, however, in 24-29% of runs, MMN was absent. Thus the authors suggest a tenous relationship between the obligatory components and the apparent presence of MMN. In a recent study by Amenedo et al. (1998), MMN and N_2b were elicited during a selective dichotic listening task in 16 young aged, 16 middle aged and 19 elderly subjects. They found that the peak latencies, amplitude and mean amplitude of MMN were quite stable regardless of age whereas the N_2b latency was longer in middle aged and elderly subjects than the young subjects. But the results of a study done by

Joutsiniemi et al. (1998) is contradictory to the above study. They report of no significant difference in peak latencies (measured from stimulus offset) for 40 subjects ranging from 9-84 years of age, but they reported of diminishing amplitude as a function increasing age.

Thus a review of literature suggest of some developmental trend and the maturation of MMN. Most of the studies report of a presence of MMN at a very early age; it resembles adult MMN in terms of morphology but the latency and amplitude undergo changes throught the childhood years and mature quite early when compared to the other cognitive potentials. Thus Kurtzberg et al. (1995) suggest that considering only the developmental changes in ERP waveform and refractory properties, it is dangerous to presume that ERPs such as the MMN will exhibit the same properties in infants and children as in adults in the absence of experimental evidence. These studies have used either speech stimuli of non-speech stimuli with frequency deviations to study the developmental changes in MMN. Intensity deviations have not be used to study the development of the MMN. Thus art an effort to study the developmental changes in MMN for intensity deviation, the present study was taken-up.

METHODOLOGY

The present study aimed at studying the age related changes in the MMN potential. An attempt was made to study

a) Absolute latency of MMN

b) Duration of MMN

c) Amplitude of MMN.

d) Magnitude of MMN for children and adults.

The above stated measure were compared in reading and no reading condition and also for the Cz and Pz electrode sites.

SUBJECTS

A total of 60 subjects were taken for the study. They were divided into 2 groups based on their ages. The following table indicates the no.of subjects in different age groups.

No.of subjects	Age Range	Male/Female
GROUP I	30 children	7-10 years
10 children	7-8 years	5 M and 5 F
10 children	8-9 years	5 M and 5 F
10 children	9-10 years	5 M and 5 F
GROUPII		
30 adults	18-30 years	15 M and 15 F

SELECTION CRITERIA

1) All the subjects had volunteered for the study.
2) The subjects had no past/present history of otological/ neurological/psychological problems.
3) They had normal auditory thresholds i.e. < 25 dB HL (ANSI 1989) over the frequency range of 250 Hz - 8000 Hz.
4) They had good general health at the time of testing.
5) They were as able to relax and sit without much extraneous movements for the duration of testing.

INSTRUMENTATION

1) A calibrated audiometer Beltone Model 112 with TDH-50P earphones lodged in MX-41/AR ear cushions was used for the pure tone audiometry.
2) The Middle ear Analyser GSI33, Version 1 was used to rule out middle ear pathology if present.
3) The Electrophysiological test Unit: Biologic Auditory Evoked Potentials (Navigator) Systems with software EP 317 was used for recording MMN.

TEST PROCEDURE

a) Procedure for Pure tone Testing

Auditory pure tone thresholds for air-conduction was assessed across frequencies between 250 Hz - 8000 Hz in octaves. Modified Hughson-Westlake procedure was applied for estimation

of thresholds. Pure tone average was calculated for threshold values at 500 Hz, 1000 Hz and 2000 Hz.

b) **Immittance Testing**

Subjects with thresholds less than 25 dB HL were screened for middle ear function. Tympanogram and reflexes in both ears were recorded using an immittance meter.

c) **MM**N **Recording**

1. ***Patient Set-Up***

The subjects were seated in a comfortable position with head supported to ensure a relaxed posture and minimum rejection rate.

2. ***Instructions to the Subjects***

Subjects were instructed to be relaxed throughout the recording.

The testing was carried out in two conditions. In the first condition, the subjects were only informed to pay no attention to the auditory stimuli. In the 2nd condition they were instructed to read a book to distract the attention from auditory stimuli.

3. Electrode Placement

The electrode site for the two channel mapping recordings were selected with Cz and Pz as positive, Fpz as common and A_1 and A_2 as negative.

Site	Headbox connection
Forehead (Fpz)	Common
Vertex (Cz)	Channel 1, input 1
Left Ear (A1)	Channel 1, input 2
Parietal (Pz)	Channel *2*, input 1
Right ear (A2)	Channel *2*, input 2

Silver chloride disc electrodes were fixed at the above said sites after a thorough skin surface cleaning with surgical spirit and a skin preparing solution and later fixed with standard EEG paste (conducting paste) suitably secured in place with surgical tape.

4. Measuring Impedance

The impedance of the electrodes with reference to the common electrode for both the channels were measured. The impedance values were less than 5 kOhms and the interelectrode impedance difference was less than 3 kOhms. If the impedance was more than 5 kOhms, the electrode sites were cleaned again and the electrodes were secured again. The negative electrodes A_1 and A_2 were linked together by means of a jumper.

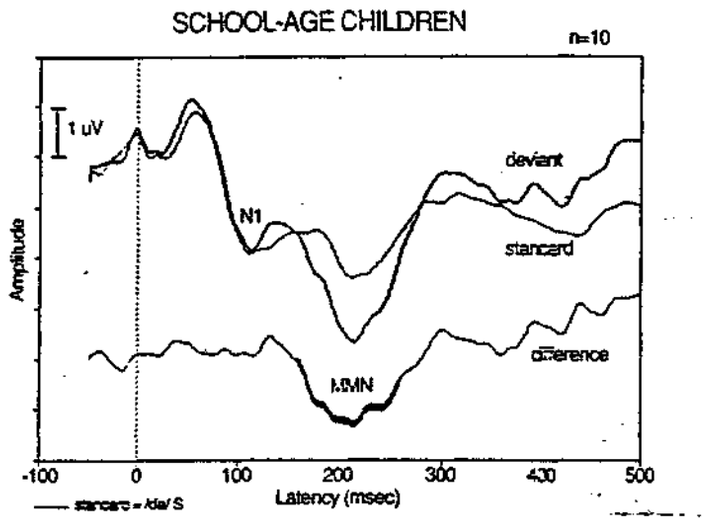
5. Procedure for Recording

The earphones were placed on the subjects ear being careful not to dislodge any electrode. The blue earphone was placed on the left ear and the red on the right. MMN was then recorded using the following test protocol:

(i) Stimulus type - Alternating tone burst
(ii) Frequency-Frequent -1000 Hz Infrequent - 1000 Hz
(iii) Intensity - Frequent - 60 dB nHL Infrequent - 65 dB nHL
(iv) Repetition rate - 1.1/sec
(v) Rise time - 10 msec
(vi) Fall time -10 msec
(vii) Plateau - 30 msec
(viii) Gain - 50,000
(ix) Maximum stimuli - 500
(x) Band pass filter - 0.1 Hz - 300 Hz
(xi) Notch filter - off
(xii) Ratio of Frequent: Infrequent = 5:1
(xiii) Transducer - Headphones

ANALYSIS

The MMN was obtained from subtraction of the frequent stimuli waveform from the wave of the infrequent stimuli (i.e.) the difference wave was obtained.



MMN WAVEFORM.

Latency of the waveform was measured at the peak of the wave.

Duration of MMN was measured from the onset of the negativity to the peak of the negativity called the ON TIME/ONSET TIME and from the peak to the end of the response called the OFF TIME.

Amplitude was measured from trough to peak or peak to trough of the wave.

Magnitude of wave was calculated by multiplying the duration and amplitude

All these were performed for reading and no reading condition and also for Cz and Pz recordings

RESULTS AND DISCUSSIONS

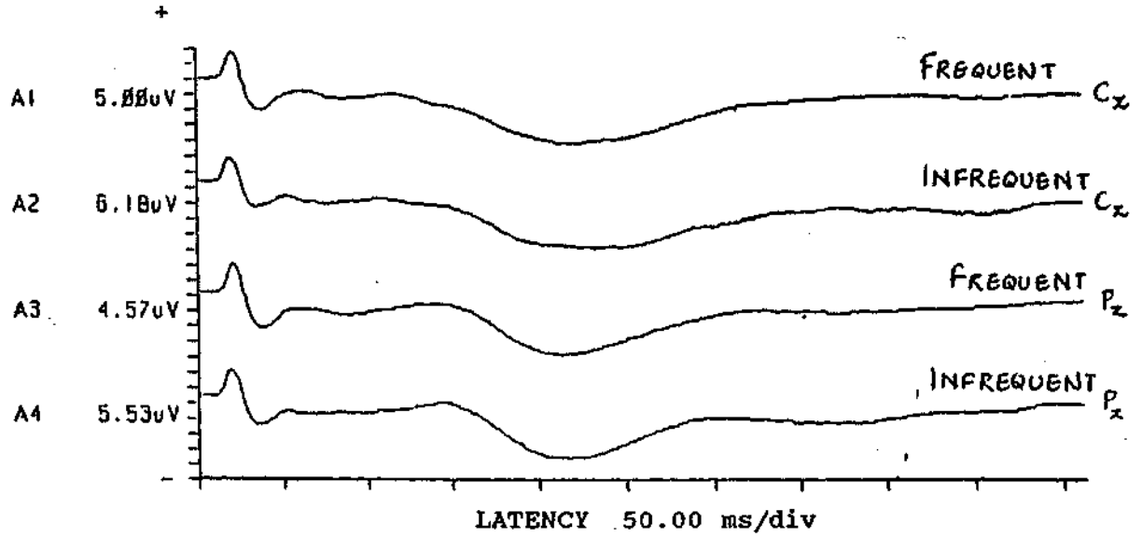
The aim of the study was to see if there was any trend in the development of MMN for intensity deviation in terms of latency, amplitude, duration and magnitude and also to compare the same for reading and no reading condition in Cz and Pz recording sites. A total of sixty subject i.e. 30 adults (18-30 years) and 30 children (7-10 years) sub-grouped as 10 children in each of the following age groups: 7-8 years; 8-9 years and 9-10 years, were included in the study.

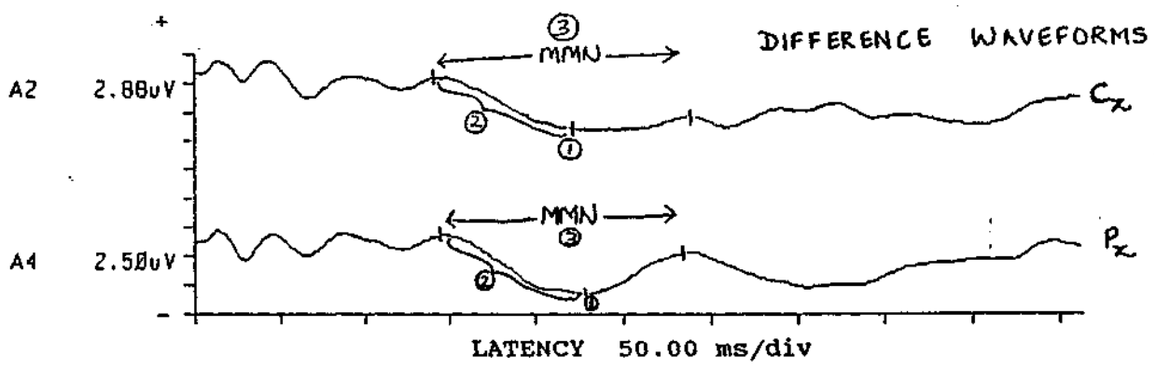
MMN could be recorded for all the thirty adults. In children, MMN waveform was obtained for all but one child in the 8-9 years age group. The MMN waveforms were analyzed for latency, duration, amplitude and magnitude. All of these were subjected to statistical analysis using NCSS software.

Developmental Trend for MMN

Statistical analysis included calculation of mean, SD and range for latency, amplitude, duration and magnitude for adults and children. Separate analysis was carried for children group as a whole and for subgroups of children. Two sample 'T' test was carried out to check if the means obtained for adults and children were statistically significant. Mann-Whitney 'U' test was used to compare the difference in mean obtained for adults and each subgroup of children. The difference in mean obtained for subgroups of children were also compared using Mann-Whitney 'U' test.

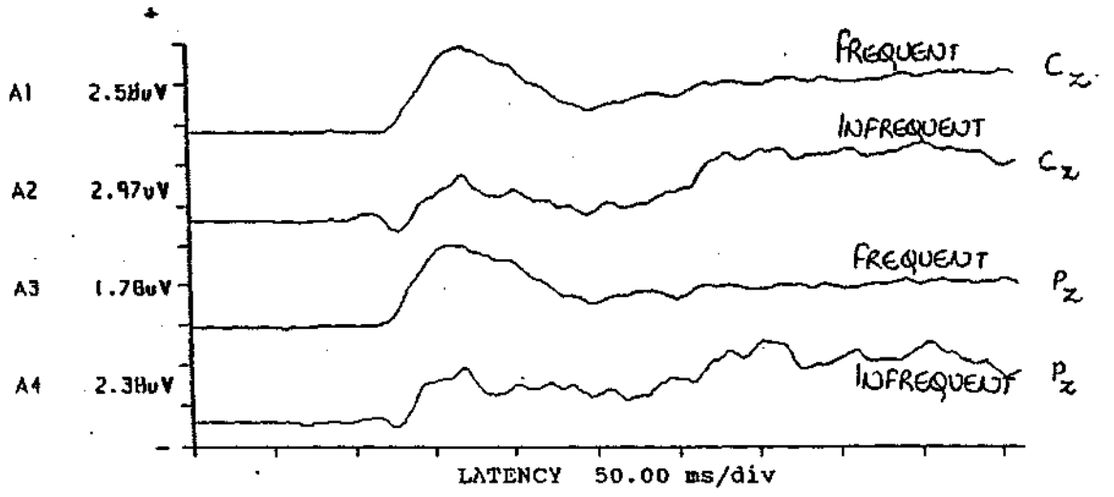
FIG. 2 REPRESENTATIVE MMN WAVEFORM FOR 7-8 YRS.

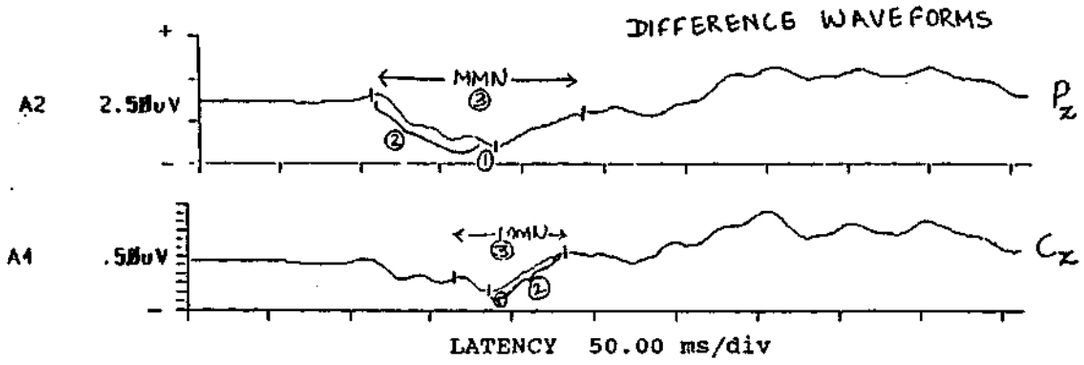




	Cz RECORDING	Pz RECORDING
1. LATENCY (msec)	255	240
2. AMPLITUDE (μV)	2.16	3.16
3. DURATION (msec)	82	113
4. MAGNITUDE (μV·msec)	177.12	357.08

FIG. 3 REPRESENTATIVE MMN WAVEFORM FOR 8-9 YRS.

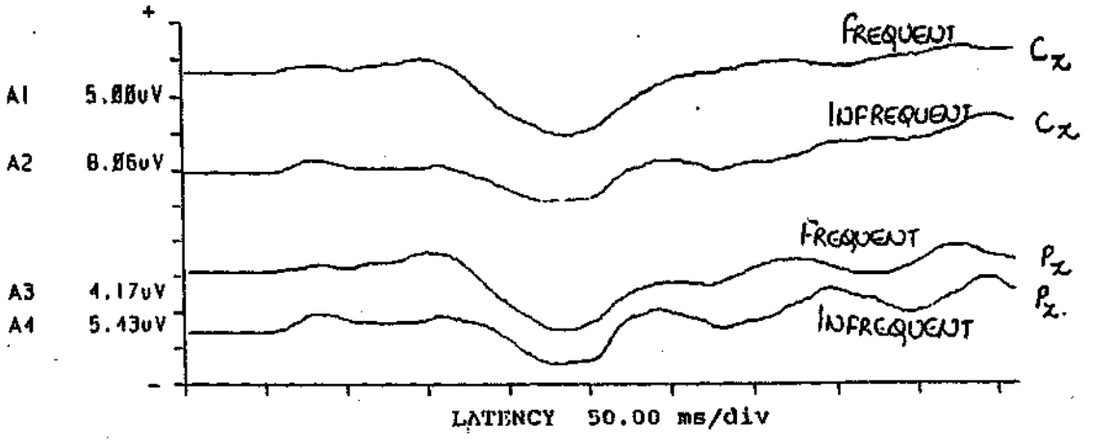




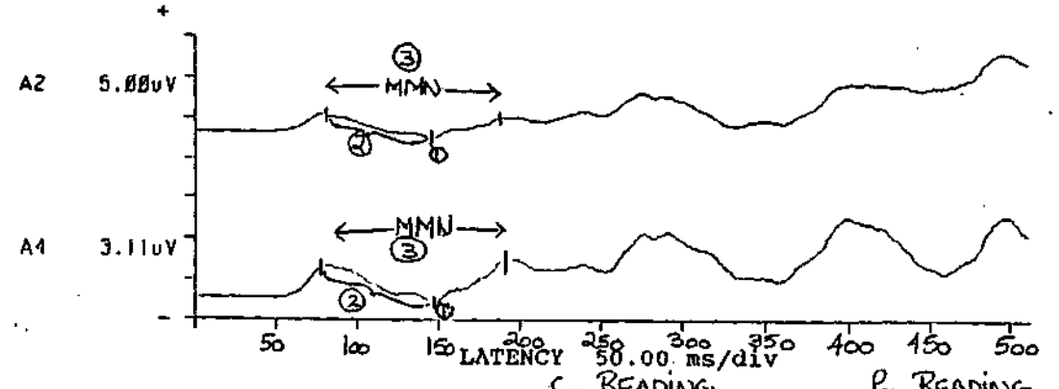
	C_z RECORDING	P_z RECORDING
① LATENCY (msec)	164	177
② AMPLITUDE (μV)	1.60	3.06
③ DURATION (msec)	66	100
④ MAGNITUDE ($\mu V \cdot msec$)	105.60	306

4.1(c)

FIG 4. REPRESENTATIVE MMN WAVEFORM FOR 9-10 YRS.

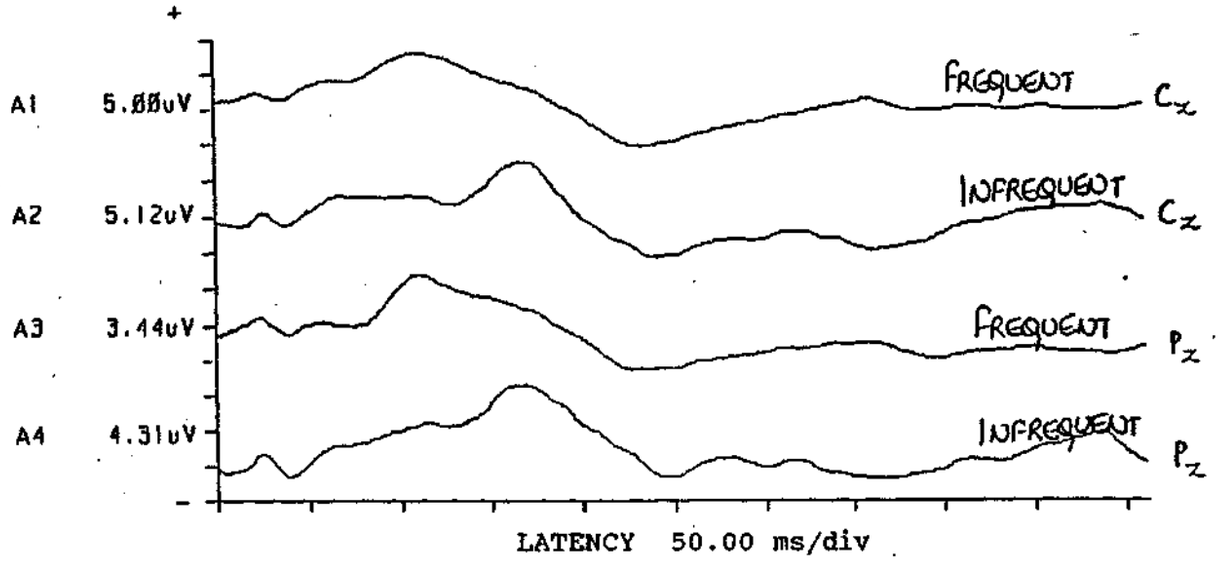


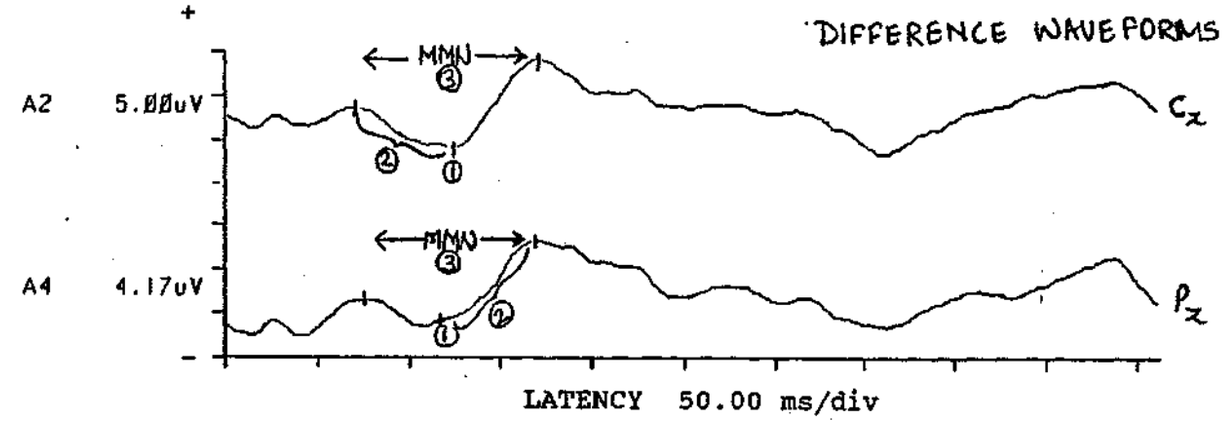
DIFFERENCE WAVEFORMS



	C_z READING	P_z READING
① LATENCY (msec)	144	147
② AMPLITUDE (μV)	2.64	3.16
③ DURATION (msec)	113	117
(1) MAGNITUDE (msec.μV)	308.86	351.08

FIG·5 REPRESENTATIVE MMN WAVEFORM FOR ADULTS (18-30 YRS)





	C_z RECORDING	P_z RECORDING
1. LATENCY (msec)	124	120
2. AMPLITUDE (μV)	2.21	2.13
3. DURATION (msec)	62	60
5. MAGNITUDE (μV.msec).	137.02	145.8

a) Latency

Table-1 : Latency of MMN in msec.

No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult	Cz	30				
	18-30	WR		184.90	29.09	140	294
		WOR		181.86	25.28	121	226
		Pz	30				
		WR		186.73	31.70	139	294
		WOR		183.60	27.59	118	231
2.	Children	*Cz*	29				
	7-10	WR		205.31	68.61	140	522
		WOR		194.66	33.87	123	258*
		Pz	29				
		WR		197.45	32.01	143	250
		WOR		194.76	33.62	122	258
3.	Children	Cz	10				
	7-8	WR		212.50	37.88	160	258
		WOR		212.10	40.27	154	258
		Pz	10				
		WR		213.50	34.33	164	250
		WOR		211.40	38.13	159	258
4.	Children	Cz	9				
	8-9	WR		194.89	28.61	150	266
		WOR		184.56	24.82	123	213
		Pz	9				
		WR		196.89	27.67	150	224
		WOR		184.78	31.54	122	216
5.	Children	Cz	10				
	9-10	WR		180.80	27.95	140	216
		WOR		184.90	25.00	147	219
		Pz	10				
		WR		184.30	25.26	144	213
		WOR		187.10	26.57	144	223

PS: WR = With Reading; WOR — Without Reading

The table above depicts the latency values of MMN in both the groups. As can be seen, there is a clear developmental trend in

the latency of MMN, with the adult group showing the least latency. The children in the age group of 7-8 years had the longest latency in Cz and Pz recordings, whereas the latency values in the 9-10 years old children were nearly the same as that of adults. When compared to the adult group, the children group showed more variability in terms of latency. In children the S.D. for Cz= 68.15 and S.D. for Pz = 32.01 and for adults S.D. for Cz= 29.09 and Pz = 31.70. This indicated that in children there is more variability than adults.

Table 2 : Comparison between the adult and children group (2 sample *T* Test)

Sl.. No.	Variable	No.	Mean	S.D.	F-Ratio	Probability level
1.	Cz Latency					
	Adult	30	184.90	29.09		
					5.564	0.000
	Children	29	205.31	68.61		
2.	Pz Latency					
	Adult	30	186.73	37.10		
					1.020	0.957
	Children	29	197.45	32.01		

Table 2 shows that there was a significant difference between the latency for adult group and children group in the Cz recording (P value = 0.000), whereas such a significant difference was not seen in the Pz recording (P value = 0.9574).

Table 3: Comparison between adult group and each children sub-group (Mann-Whitney U Test)

Sl.. No.	Variable	No.	Mean (msec)	Z-value	Probability level
1.	Cz Latency				
	Adult	30	184.90		
				-1.89	0.059
	Children (7-8 years)	10	212.50		
	Pz Latency				
	Adult	30	186.73		
				-2.108	0.035
	Children (7-8 years)	10	213.50		
2.	Cz Latency				
	Adult	30	184.90		
				-1.25	0.211
	Children (8-9 years)	9	194.89		
	Pz Latency				
	Adult	30	186.73		
				-1.25	0.211
	Children (8-9 years)	9	197.89		
3.	Cz Latency				
	Adult	30	184.90		
				0.19	0.851
	Children (9-10 years)	10	180.80		
	Pz Latency				
	Adult	30	186.73		
				-0.328	0.7429
	Children (9-10 years)	10	186.30		

4.5

The results of Table 3 can be summarized as follows:

i) There was a significant difference in the latency between the adult group and the 7-8 years group at 0.05 level for both Cz and Pz recordings.

ii) The difference in latency between the adult group and children groups (i.e.) 9-10 years and 8-9 years was not statistically significant.

Table 4 : Comparison of latencies within the children group(Mann-Whitney U test)

No.	Variable	No.	Mean (msec)	Z-value	Probability level
1.	Cz Latency				
	Children (7-8Years)	10	212.50	0.816	0.414
	Children (8-9 years)	9	194.89		
	Pz Latency				
	Children (7-8 years)	10	213.5	-1.225	0.221
	Children (8-9 years)	9	196.88		
2.	Cz Latency				
	Children (7-8 years)	10	212.50	1.66	0.096
	Children (9-10 years)	10	180-80		
	Pz Latency				
	Children (7-8 years)	10	213.50	1.776	0.076
	Children (9-10 years)	10	187.10		
3.	Cz Latency				
	Children (8-9 years)	9	194.89	1.224	0.221
	Children (9-10 years)	10	180.80		
	Pz Latency				
	Children (8-9 years)	9	196.88	1.266	0.206
	Children (9-10 years)	10	187.10		

Results as seen in the table 4 revealed that there was no significant different between the sub-group of children for latency measures.

These results clearly indicate that the latency of MMN is the longest in the 7-8 years age group and this kept decreasing with the age to reach adult like values around 9-10 years of age. The finding of a significant difference between the adult group and the 7-8 years children group and the lack of such a difference between the adults and the 8-9 years and 9-10 years children group suggests a definite developmental trend of MMN latency (i.e.) decrease in the latency with increase in age.

The above results are in concurrence with earlier studies which also report of a decrease in MMN latency with increase in age. Kraus et-al. (1993) had reported that by school going age, the usual peak latency of MMN resembles the adult like response. Csepe et al. (1992) had also reported that by 10 years of age, a late negativity is the most prominent wave of the AEPs and mat it is rather stable in children, resembling the adult response. Similar results have been reported by Kraus et al. (1995) and Joustsiniemi et al. (1998).

It has been reported that shorter latency responses mature earlier or become adult like at earlier chronological ages (Auditory Brainstem Response matures by 18 months) than longer latency responses, late latency potentials are not fully developed at least by school going age (Hall, 1992). In comparison to the development of other event related potentials, MMN is reported to be developing and

maturing earlier (Alho et al. 1990; Kurtzberg et al. 1995; Pang et al 1998). The P300 potential of the late latency response has also been reported as having a definite developmental pattern. Martin et aL (1988) had reported of a significant correlation between age and latency up to 15 years of age. Pearce et al. (1989) had reported that there are significant age trends in P300 latency from 5-13 years of age which are linear. The results of the present study indicates that MMN and P300 mature at the same age. Saravanan (1996) studied the development of P300 in 7-10 year children and reported that though there was a difference in the latency values of children and adults, it did not reach statistically significant values. But, there was a significant difference between the latency of the adults and the subgroup of children i.e. 7-8 years whereas such a difference was not observed between adults and other two subgroups i.e. 9-10 and 8-9 years. Thus he also reported of a definite developmental trend in the P300 development.

b) **Duration**

Similar to latency, duration of MMN also showed a clear maturational trend. The duration of the 7-8 years children group was the largest and decreased with age and by 9-10 years of age reached adult like values. This maturational trend was seen for Cz and Pz recording sites.

Table 5 represents the duration of MMN in children and adult group for reading and no reading condition in the Cz and Pz recording sites.

Table-5: Duration of MMN in msec.

SL. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult	Cz	30				
	18-30	WR		55.83	18.53	31	108
		WOR		57.57	20.08	27	116
		Pz	30				
		WR		55.23	16.71	30	108
		WOR		56.60	21.33	28	106
2.	Children	Cz	29				
	7-10	WR		67.17	24.60	31	133
		WOR		64,48	24.96	35	141
		Pz	29				
		WR		67.03	26.12	33	139
		WOR		67.03	23.87	26	121
3.	Children	Cz	10				
	7-8	WR		80.30	26.39	52	133
		WOR		79.00	29.43	26	141
		Pz	10				
		WR		82.70	29.19	45	139
		WOR		74.90	23.53	41	121
4.	Children	Cz	* 9				
	8-9	WR		66.44	18.35	40	87
		WOR		66.44	22.29	26	98
		Pz	9				
		WR		63.67	18.35	40	87
		WOR		72.89	21.90	42	109
5.	Children	Cz	10				
	9-10	WR		54.70	24.66	31	117
		WOR		54.60	22.41	33	113
		Pz	10				
		WR		47.90	7.61	35	59
		WOR		53.90	23.31	26	106

PS: WR = With Reading; WOR = Without Reading

Table 6: Comparison between the adult and children group (2 sample "TTest)

Sl. No.	Variable	No.	Mean (msec)	S.D.	F-Ratio	Probability level
1.	Cz Latency					
	Adult	30	55.83	18.53		
					1.762	0.137
	Children	29	67.17	23.60		
2.	Pz Latency					
	Adult	30	55.23	16.71		
					2.445	0.020
	Children	29	67.03	26.21		

The results in table 6 can be summarized as follows :

i) No significant difference between the duration of children and adult at Pz recording site (P value=0.1367).

ii) A significant difference between the duration of children and adult at Pz recording site (P value=0.0199)

The results of the comparison of duration between the adult group and each of the children group is shown in table 7. The results obtained were :

i) A significant difference between adults and 7-8 years children group in terms of duration at both Cz and Pz recording sites at 0.05 level and 0.01 level respectively. (Cz P value = 0.045; Pz P value = 0.0029).

ii) No significant difference between the adult and the children groups of 8-9 years and 9-10 years at both the recording sites.

Table 7: Comparison between adult group and each children sub-group (Mann-Whitney U Test)

Sl.. No.	Variable	No.	Mean (msec)	Z-value	Probability level
1.	Cz Latency				
	Adult	30	55.23		
				-2.842	0.005
	Children (7-8 years)	10	80.70		
	Pz Latency				
	Adult	30	55.23		
				-2.982	0.003
	Children (7-8 years)	10	82.70		
2.	Cz Latency				
	Adult	30	55.83		
				-1.80	0.072
	Children (8-9 years)	9	66.44		
	Pz Latency				
	Adult	30	55.23		
				-1.333	0.182
	Children (8-9 years)	9	62.67		
3.	Cz Latency				
	Adult	30	55.83		
				0.500	0.617
	Children (9-10 years)	10	54.70		
	Pz Latency				
	Adult	30	55.23		
				1.374	0.170
	Children (9-10 years)	10	47.90		

Table 8 : Comparison of duration within the children group(Mann-Whitney U test)

Sl.. No.	Variable	No.	Mean (msec)	Z-value	Probability level
1.	Cz Latency				
	Children (7-8Years)	10	80.30	0.898	0.369
	Children (8-9 years)	9	66.44		
	Pz Latency				
	Children (7-8 years)	10	82.70	1.470	0.142
	Children (8-9 years)	9	63.67		
2.	Cz Latency				
	Children (7-8 years)	10	80.30	2.457	0.014
	Children (9-10 years)	10	54.70		
	Pz Latency				
	Children (7-8 years)	10	82.70	3.326	0.009
	Children (9-10 years)	10	47.90		
3.	Cz Latency				
	Children (8-9 years)	9	66.44	1.837	0.062
	Children (9-10 years)	10	54.70		
	Pz Latency				
	Children (8-9 years)	9	63.67	1.878	0.060
	Children (9-10 years)	10	47.90		

The results obtained when the duration of MMN within the children group was compared is depicted in table 8. It reveals that

i) There is a significant difference between the duration of MMN in the 7-8 year group and 9-10 year group at 0.01 level for both Cz and Pz recording sites (Cz P value = 0.0140; PzP value = 0.0009

ii) No significant differences between the duration of 7-8 year and 8-9 year children group and also between 8-9 year and 9-10 year children group.

Thus as seen for latency, duration of MMN too followed a similar trend (ie) greater duration for younger ages and a decrement in duration with increase in age and finally reaching adult like values by 9-10 years of age.

Kraus et al. (1995) in his study on 7-12 years children had reported of no significant differences in duration between adults and children. In an earlier study in 1993, Kraus et al. had reported of similar findings for 7-11 years children.

The results of the present study are not in concurrence with the above studies i.e. when the children (7-10 years) group was compared to the adult group as a whole, significant differences were obtained for duration in the Pz electrode placement. Moreover even when the adult group was compared to subgroups of the children group, significant differences were obtained for adults and 7-8 year group. No such differences were found for the older sub-groups.

It's possible that Kraus et al. (1993, 1995) did not find a significant difference as they considered children ranging in age from 7-12 years as one group. The results of the present study suggest that there is a need to obtain separate norms for subgroups of children.

Thus as seen for latency, duration of MMN too followed a similar trend i.e. greater duration for younger ages and a decrement in duration with increase in age and finally reaching adult like values by 9-10 years of age.

c) **Amplitude**

Amplitude of MMN for both the groups i.e. adult and children group for Cz and Pz recording can be seen in Table 9.

Table-9: Amplitude of MMN in |iV

Si.. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult 18-30	Cz	30				
		WR		2.10	1.06	0.69	4.18
		WOR		2.30	1.56	0.82	9.06
		Pz	30				
		WR		2.29	1.32	0.61	7.20
		WOR		2.30	1.44	0.87	.7.53
2.	Children 7-10	Cr	29				
		WR		2.84	1.45	0.79	6.95
		WOR		2.76	1.55	0.68	7.16
		Pz	29				
		WR		2.94	1.45	0.82	7.52
		WOR		2.99	2.01	0.63	9.16
3.	Children 7-8	Cz	10				
		WR		3.47	1.48	0.10	6.95
		WOR		4.40	1.47	1.42	7.16
		Pz	10				
		WR		3.53	1.81	1.17	7.52
		WOR		3.41	1.93	1.17	8.22
4.	Children 8-9	Cz	9				
		WR		2.95	1.44	1.00	5.28
		WOR		3.07	1.78	0.71	5.72
		Pz	9				
		WR		3.06	1.35	1.45	4.95
		WOR		3.65	2.62	1.16	9.16
5.	Children 9-10	Cz	10				
		WR		2.06	1.15	0.79	4.45
		WOR		2.26	0.88	0.82	3.48
		Pz	10				
		WR		1.95	1.11	0.68	3.34
		WOR		2.06	1.01	0.68	3.58

PS: WR = With Reading WOR = Without Reading

The values of the amplitude also clearly indicate that there is a significant relation between the age and amplitude ofMMN i.e. with increase in age, there is a reduction in the amplitude of MMN. The children in the 7-8 years group had the maximum amplitude and there was a decrease in amplitude with age till 9-10 years when it reached value similar to the adults. This was true for both the electrode site i.e. Cz and Pz.

Table 10: Comparison between the adult and children group (2 sample 'T Test)

Sl.. No.	Variable	No.	Mean µv	S.D.	F-Ratio	Probability level
1.	Cz Latency					
	Adult	30	2.10	1.06		
					1.874	0.099
	Children	29	2.84	1.45		
2.	Pz Latency					
	Adult	30	2.28	1.56		
					1.123	0.609
	Children	29	2.94	1.55		

Comparison of the amplitude between the adult group and children group was done and table 10 reveals that there was no significant difference between the adults and children group for both the recording sites.

Table 11 Comparison between adult group and each children sub-group (Mann-Whitney U Test)

Sl.. No.	Variable	No.	Mean (μv)	Z-value	Probability level
1.	Cz Latency				
	Adult	30	2.10	-2.639	0.008
	Children (7-8 years)	10	3.47		
	Pz Latency				
	Adult	30	2.28	-2.249	0.025
	Children (7-8 years)	10	3.52		
2.	Cz Latency				
	Adult	30	2.50	-1.717	0.086
	Children (8-9 years)	9	2.95		
	Pz Latency				
	Adult	30	2.28	-1.80	0.072
	Children (8-9 years)	9	3.06		
3.	*Cz* Latency				
	Adult	30	2.10	0.125	0.901
	Children (9-10 years)	10	2.06		
	Pz Latency				
	Adult	30	2.28	0.781	0.435
	Children (9-10 years)	10	1.95		

Table 11 depicts the results of the comparison of amplitude of adults and subgroups of children the results were :

i) A significant difference in amplitude was seen between the children of 7-8 years group and the adult group at 0.01 level in the Cz and at 0.05 level in Pz recording site (CzP value = 0.0083 and Pz Pvalue - 0.0245).

ii) No significant differences in amplitude between the adult and other two sub-groups of children viz. 8-9 years and 9-10 years in both the recording sites.

Table 12 : Comparison of amplitude within the children group (Mann-Whitney U test)

Sl. No.	Variable	No.	Mean (μv)	2-value	Probability level
1.	Cz Latency				
	Children (7-8Years)	10	3.47	0.408	0.683
	Children (8-9 years)	9	2.95		
	Pz Latency				
	Children (7-8 years)	10	3.53	0.490	0.624
	Children (8-9 years)	9	3.06		
2.	Cz Latency				
	Children (7-8 years)	10	3.47	2.343	0.019
	Children (9-10 years)	10	2.06		
	Pz Latency				
	Children (7-8 years)	10	3.53	2.192	0.02
	Children (9-10 years)	10	1.95		
3.	Cz Latency				
	Children (8-9 years)	9	2.95	1.551	0.121
	Children (9-10 years)	10	2.06		
	Pz Latency				
	Children (8-9 years)	9	3.06	1.877	0.060
	Children (9-10 years)	.10	1.95		

As shown in Table 12 the results indicated the significant difference between the amplitude of the 7-8 years children and 9-10 years children at 0.01 level at Cz recording and at 0.05 level at Pz recording (Cz P value = 0.0191; Pz P value = 0.02).

These findings are in concurrence with the results of Csepe et al. (1992) who reported that MMN showed a relatively large amplitude in children under 10 years of age. When compared to the adults. On the contrary, Kraus et al. (1995) reported that there was no significant difference in the onset peak amplitude in the group of 7-12 years children when compared to adults.

The results of the present study contradict the findings of Kraus et al. (1995). The reason for the contradiction could be that had the 7-12 year group taken by Kraus et al. (1995) been further divided into smaller age groups, there could have been differences in the amplitude of adults and children. Since 7-12 years children were taken as one group, there was no significant difference. Thus the findings of these studies high light on the need to study the development of MMN in smaller age groups instead of studying a wide age range.

d) Magnitude

Table 13 summarizes the magnitude of MMN for adults and children group of Cz and Pz recording sites. As expected, the magnitude was the highest for 7-8 years of age and kept decreasing with age to reach adult like values at around 9-10 years of age.

Table-13 Magnitude of MMN in µ Vmsec

Sl. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult	Cz	30				
	18-30	WR		129.19	90.59	25.54	372.02
		WOR		145.89	139.99	36.91	634.20
		Pz	30				
		WR		305.11	196.59	27.06	446.40
		WOR		263.18	168.03	27.20	572.25
2.	Children	Cz	29				
	7-10	WR		204.69	136.05	27.20	518.70
		WOR		193.28	146.71	32.76	560.58
		Pz	29				
		WR		214.63	157.14	27.06	717.24
		WOR		224.20	192.46	28.35	842.72
3.	Children	Cz	10				
	7-8	WR		281.81	140.15	57.20	518.70
		WOR		265.35	128.36	69.58	458.75
		Pz	10				
		WR		305.12	116.59	52.65	717.24
		WOR		263.18	168.03	32.39	567.18
4.	Children	Cz	9				
	8-9	WR		205.95	123.85	41.6	427.68
		WOR		224.17	180.24	46.92	560.58
		Pz	9				
		WR		203.51	123.02	62.35	410.85
		WOR		294.83	254.31	49.14	842.72
5.	Children	Cz	10				
	9-10	WR		126.37	104.20	27.20	308.88
		WOR		93.28	61.36	32.74	197.06
		Pz	10				
		WR		134.17	91.16	27.06	354.08
		WOR		121.60	105.70	28.35	377.35

PS: WR = With Reading; WOR = Without Reading

Table 14: Comparison between the adult and children group (2 sample 'T Test)

Sl.. No.	Variable	No.	Mean	S.D.	F-Ratio	Probability level
1.	Cz Latency					
	Adult	30	129.19	90.59	2.255	0.034
	Children	29	204.68	136.05		
2.	Pz Latency					
	Adult	30	140.04	196.59	-1.956	0.051
	Children	29	214.64	157.14		

The magnitude of children and adult group was compared and the results can be seen in Table 14. The results indicate a significant difference in the magnitude of adult and children group at 0.05 level for Cz and Pz recording sites (Cz pvalue = 0.0337 and Pz P value 0.0505).

Table 15: Comparison between adult group and each children sub-group (Mann-Whitney U Test)

No.	Variable	No.	Mean μv.msec	Z-value	Probability level
1.	Cz Latency				
	Adult	30	129.19	3.123	0.009
	Children (7-8 years)	10	281.81		
	Pz Latency				
	Adult	30	140.04	-2.4987	0.0125
	Children (7-8 years)	10	305.12		
2.	Cz Latency				
	Adult	30	129.19	-1.833	0.067
	Children (8-9 years)	9	205.95		
	Pz Latency				
	Adult	30	140.04	-1.667	0.096
	Children (8-9 years)	9	203.51		
3.	Cz Latency				
	Adult	30	129.19	0.3591	0.719
	Children (9-10 years)	10	126.37		
	Pz Latency				
	Adult	30	140.04	3.123	0.975
	Children (9-10 years)	10	134.18		

Table 15 reveals the results of the comparison of the magnitude of adult group and subgroup of the children group. The results were

(i) A significant difference between the adult and 7-8 years sub-group of children at 0.01 level for both Cz and Pz recording sites (Cz P value = 0.0018; Pz Pvalue = 0.0125).

(ii) No significant difference for adult group and other two subgroup viz. 8-9 years and 9-10 years.

Table 16 : Comparison of magnitude within the children group (Mann- Whitney U test)

Sl.. No.	Variable	No.	Mean	Z-value	Probability level
1.	Cz Latency				
	Children (7-8Years)	10	281.81	1.061	0.289
	Children (8-9 years)	9	205.95		
	Pz Latency				
	Children (7-8 years)	10	305.13	0.980	0.327
	Children (8-9 years)	9	203.51		
2.	Cz Latency				
	Children (7-8 years)	10	281.81	2.419	0.016
	Children (9-10 years)	10	126.37		
	Pz Latency				
	Children (7-8 years)	10	305.12	2.306	0.021
	Children (9-10 years)	10	134.18		
3.	Cz Latency				
	Children (8-9 years)	9	209.95	1.470	0.142
	Children (9-10 years)	10	126.37		
	Pz Latency				
	Children (8-9 years)	9	203.51	1.4707	0.142
	Children (9-10 years)	10	134.18		

Table 16 depicts the results of the comparison of magnitudes within the children group. The results obtained were :

(i) Statistically significant difference at 0.01 level for Cz recording and at 0.05 level for Pz recording was obtained for the comparison of magnitudes between 7-8 years and 9-10 years children.

(ii) There was no significant difference for comparison between 7-8 years and 8-9 years as well as 8-9 years and 9-10 years.

These results are similar to those of the other parameters already discussed. Greater magnitude is expected in children because of the larger amplitude and longer duration seen in them. These findings are similar to those reported by Kraus et al. (1993). They reported of significantly greater magnitude in 7-11 years children when compared to adults.

b) MMN IN Cz AND Pz RECORDING SITES

Statistical analysis was carried out to check if there was a significant difference between the mean obtained for Cz and Pz electrode placement using 2 sample T-test for adult group and Mann-Whitney 'U' test for subgroups of children. The results obtained from latency, duration, amplitude and magnitude are represented in tables 17, 18, 19 and 20 respectively. It is evident from the table that there was no significant difference between the values obtained for Cz and Pz electrode placement for all the measures.

Table 17 : Comparison of Cz and Pz electrode placement for latency in different groups (2 sample T test and Mann-whitney U-Test)

Sl.. No.	Variable	Mean (msec)	Z-value/ F ratio	Probability level
1.	Adults With reading			
	Cz	184.90		
			1.187	0.647
	Pz	186.73		
2.	Children 7-8 years With reading			
	Cz	212.5		
			0.265	0.791
	Pz	213.5		
3.	Children 8-9 years With reading			
	Cz	194.89		
			-0.265	0.791
	Pz	196.89		
4.	Children 9-10 years With reading			
	Cz	180.80		
			-3.780	0.970
	Pz	186.30		

Table 18 : Comparison of Cz and Pz electrode placement for duration in different groups (2 sample T test and Mann-whitney U-Test)

Sl.. No.	Variable	Mean	Z-value/ F ratio	Probability level
1.	Adults With reading			
	Cz	55.83	1.230	0.580
	Pz	55.23		
2.	Children 7-8 years With reading			
	Cz	80.30	-0,226	0.821
	Pz	87.70		
3.	Children 8-9 years With reading			
	Cz	66.44	0.309	0.757
	Pz	63.66		
4.	Children 9-10 years With reading			
	Cz	54.70	0.5391	0.5967
	Pz	47.9		

Table 19 : Comparison of Cz and Pz electrode placement for amplitude in different groups (2 sample T test and Mann-whitney U-Test)

Sl.. No.	Variable	Mean	Z-value/ F ratio	Probability level
1.	Adults With reading			
	Cz	2.10		
			1.559	0.243
	Pz	2.28		
2.	Children 7-8 years With reading			
	Cz	3.46		
			-3.780	0.970
	Pz	3.52		
3.	Children 8-9 years With reading			
	Cz	2.95		
			-0.177	0.860
	Pz	3.06		
4.	Children 9-10 years With reading			
	Cz	2.06		
			0.265	0.791
	Pz	1.95		

Table 20 : Comparison of Cz and Pz electrode placement for magnitude in different groups (2 sample T test and Mann-whitney U-Test)

Sl.. NO.	Variable	Mean	Z-value/ F ratio	Probability level
1.	Adults With reading			
	Cz	129.20	1.179	0.661
	Pz	140.05		
2.	Children 7-8 years With reading			
	Cz	281.81	-0.113	0.910
	Pz	305.12		
3.	Children 8-9 years With reading			
	Cz	205.95	0.309	0.757
	Pz	203.51		
4.	Children 9-10 years With reading			
	Cz	126.37	-0.378	0.706
	Pz	134.18		

c) MMN IN READING AND NO READING CONDITIONS

MMN waveforms were recorded for two conditions (viz) reading and no reading. To compare these conditions, for the adult group 2 Sample 'T ' Test was uses whereas for children group Mann-Whitney U Test was used.

Table 21 : Comparison of Latency between reading and no reading in adults and children.

Sl.. No.	Variable	No.	Mean (msec)	Z-value/ F ratio	Probability level
1.	Cz latency Adults	30			
	With reading		184.90	1.324	0.4549
	Without reading		181.87		
	Pz latency Adults	30			
	With reading		186.73	1.320	0.460
	Without reading		183.50		
2.	Cz latency Children (7-8 years)	10			
	With reading		212.50	-7.559	. 0.9397
	Without reading		212.10		
	Pz latency Children	10			
	With reading		213.50	0.113	0.9097
	Without reading		211.40		
3.	Cz latency Children (8-9 years)	9			
	With reading		194.89	0.839	0.402
	Without reading		184.56		
	Pz latency Children	9			
	With reading		196.89	0.871	0.623
	Without reading		184.78		
4.	Cz latency Children (9-10 years)	10			
	With reading		180.80	-0.340	0.733
	Without reading		184.90		
	Pz latency Children	10			
	With reading		187.30	0.416	0.678
	Without reading		187.10		

Table 21 represents the comparison of latency ofMMN in reading and no reading conditions. Results indicated no significant difference for any of the groups for reading and no reading condition.

Table 22 : Comparison of Duration in reading and no reading condition in adults and children.

Sl.. No.	Variable	No.	Mean (msec))	Z-value/ F ratio	Probability level
1.	Cz latency Adults With reading	30	55.83	1.420	0.351
	Without reading		57.56		
	Pz latency Adults With reading	30	55.23	1.529	0.195
	Without reading		56.60		
2.	Cz latency Children (7-8 years) With reading	10	80.30	0.227	0.821
	Without reading		79.00		
	Pz latency Children With reading	10	82.70	0.491	0.623
	Without reading		74.90		
3.	Cz latency Children (8-9 years) With reading	9	66.44	0. 415	0.965
	Without reading		66.44		
	Pz latency Children With reading	9	63.67	-0.883	0.377
	Without reading		72.89		
4.	Cz latency Children (9-10 years) With reading	10	180.80	-0.340	0.733
	Without reading		184.90		
	Pz latency Children With reading	10	187.30	0.416	0.678
	Without reading		187.10		

Table 22 represents the comparison of amplitude for the two conditions and it revealed no significant difference for any of the groups.

Table 23 depicts the comparison of amplitude for reading and no reading conditions. The results were as follows

i) Significant difference for amplitude in reading Vs no reading condition for adults was seen at 0.05 level in the Cz recording site whereas such a difference was not seen at the Pz recording. (Cz P value = 0.03; Pz P value= 0.6544)

ii) None of the other groups showed a difference between the reading and no reading conditions at any recording site.

The comparison of the magnitude for both the conditions is represented in table 23. The results revealed a

i) Significant difference between the reading and no reading condition for adults at 0.05 level for the Cz recording site only (Cz P value = 0.0221; Pz P value= 0.2293)

ii) No significant difference for any of the subgroups of children at Cz or Pz electrode placement.

Table 23 : Comparison of Amplitude in reading and no reading condition in adults and children.

Sl.. No.	Variable	No.	Mean (μv)	Z-value/ F ratio	Probability level
1.	Cz latency Adults	30			
	With reading		2.10	2.239	0.033
	Without reading		2.30		
	Pz latency Adults	30			
	With reading		2.29	1.183	0.654
	Without reading		2.30		
2.	Cz latency Children (7-8 years)	10			
	With reading		3.46	0.567	0.571
	Without reading		3.39		
	Pz latency Children	10			
	With reading		3.53	0.378	0.706
	Without reading		3.41		
3.	Cz latency Children (8-9 years)	9			
	With reading		2.95	-8.830	0.930
	Without reading		3.07		
	Pz latency Children	9			
	With reading		3.06	-8.830	0.930
	Without reading		3.65		
4.	Cz latency Children (9-10 years)	10			
	With reading		2.06	-0.756	0.450
	Without reading		2.26		
	Pz latency Children	10			
	With reading		1.95	-0.378	0.706
	Without reading		2.06		

Table 24 : Comparison of Magnitude in reading and no reading in adults and children.

Sl.. No.	Variable	No.	Mean (μv.msec)	Z-value/ F ratio	Probability level
1.	Oz latency Adults	30			
	With reading		129.20	2.388	0.022
	Without reading		145.90		
	Pz latency Adults	30			
	With reading		140.05	1.372	0.229
	Without reading		133.11		
2.	Cz latency Children (7-8 years)	10			
	With reading		281.81	0.302	0.762
	Without reading		265.35		
	Pz latency Children	10			
	With reading		305.12	0.436	0.650
	Without reading		263.18		
3.	Cz latency Children (8-9 years)	9			
	With reading		205.95	0.132	0.894
	Without reading		224.17		
	Pz latency Children	9			
	With reading		203.51	-0.486	0.627
	Without reading		294.83		
4.	Cz latency Children (9-10 years)	10			
	With reading		126.36	0.378	0.706
	Without reading		93.29		
	Pz latency Children	10			
	With reading		134.18	0.529	0.60
	Without reading		121.61		

The comparison of the magnitude for both the conditions is represented in table 24. The results revealed

i) A significant difference between the reading and no reading condition for adults at 0.05 level for the Cz recording site only (Cz P value = 0.0221; Pz P value= 0.2293)

ii) No significant difference for any of the subgroups of children at Cz or Pz electrode placement.

The adult group showed a significant difference in amplitude and magnitude for reading and no reading condition for Cz recording. From Tables 25, 26, 27 and 28, it can be seen that the waveform detectability was better for the reading condition in children of 7-8 yers. In adults, waveform was detectable better in the no reading condition. For the children of 8-9 years, such a difference was not seen whereas for 9-10 years old children, a pattern similar to the adults was seen.

For a better detectibility ofMMN for intensity deviations, a little amount of passive attention to the auditory stimuli is necessary (Naatanen, et al. 1993). In adults and older children, it could be that due to reading, this passive attention was being diverted significantly and hence the MMN was not detectable better in the reading conditioa in the no reading since this passive attention to the auditory stimulus was present, there was a better detectability of waveforms. In the 7-8 yers group of children, the MMN was detectable better in the reading condition than in the no reading condition. In the no reading condition, thre was much more attention being paid to the auditory stimuli which

reduced the detectability of MMN and this was evident by the presence of P300 in 6 out of 10 children of this age range. Lang et al. (1995) have reported that presence of P_{300} indicates that either the stimulus was too obstrusive or the subject was paying a lot of attention to the stimuli. In this case, since the difference between the 2 stimuli was only 5 dB and since it did not elicit an : P_{300} in other subjects, the possibilityof the stimuli being too obstrusive is ruled out. Thus, the other possibility that the children of 7-8 years were paying too much attention to the auditory stimuli holds good.

Table-25 : Latency of MMN in msec.

Sl.. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult 18-30	Cz	30				
		WR		184.90	29.09	140	294
		WOR		181.86	25.28	121	226
2.	Children 7-10	Cz	29				
		WR		205.31	68.61	140	522
		WOR		194.66	33.87	123	258
3.	Children 7-8	Cz	10				
		WR		212.50	37.88	160	258
		WOR		212.10	40.27	154	258
4.	Children 8-9	Cz	9				
		WR		194.89	28.61	150	266
		WOR		184.56	24.82	123	213
5.	Children 9-10	Cz	10				
		WR		180.80	27.95	140	216
		WOR		184.90	25.00	147	219

PS: WR = With Reading; WOR = Without Reading

Table-26: Duration of MMN in msec.

Sl.. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult 18-30	Cz	30				
		WR		55.83	18.53	31	108
		WOR		57.57	20.08	27	116
2.	Children 7-10	Cz	29				
		WR		67.17	24.60	31	133
		WOR		64,48	24.96	35	141
3.	Children 7-8	Cz	10				
		WR		80.30	26.39	52	133
		WOR		79.00	29.43	26	141
4.	Children 8-9	Cz	9				
		WR		66.44	18.35	40	87
		WOR		66.44	22.29	26	98
5.	Children 9-10	Cz	10				
		WR		54.70	24.66	31	117
		WOR		54.60	22.41	33	113

PS: WR = With Reading; WOR = Without Reading

Table-27: Amplitude of MMN in µv

Sl.. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult 18-30	Cz	30				
		WR		2.10	1.06	0.69	4.18
		WOR		2.30	1.56	0.82	9.06
2.	Children 7-10	Cz	29				
		WR		2.84	1.45	0.79	6.95
		WOR		2.76	1.55	0.68	7.16
3.	Children 7-8	Cz	10				
		WR		3.47	1.48	0.10	6.95
		WOR		4.40	1.47	1.42	7.16
4.	Children 8-9	Cz	9				
		WR		2.95	1.44	1.00	5.28
		WOR		3.07	1.78	0.71	5.72
		16					
5.	Children 9-10	Cz	10				
		WR		2.06	1.15	0.79	4.45
		WOR		2.26	0.88	0.82	3.48

PS: WR = With Reading; WOR = Without Reading

Table-28: Magnitude of MMN in µVmsec

Sl.. No.	Age in years	Electrode site	Sub-jects	Mean	S.D.	Min.	Max.
1.	Adult 18-30	Cz	30				
		WR		129.19	90.59	25.54	372.02
		WOR		145.89	139.99	36.91	634.20
2.	Children 7-10	Cz	29				
		WR		204.69	136.05	27.20	518.70
		WOR		193.28	146.71	32.76	560.58
3.	Children 7-8	Cz	10				
		WR		281.81	140.15	57.20	518.70
		WOR		265.35	128.36	69.58	458.75
4.	Children 8-9	Cz	9				
		WR		205.95	123.85	41.6	427.68
		WOR		224.17	180.24	46.92	560.58
5.	Children 9-10	Cz	10				
		WR		126.37	104.20	27.20	308.88
		WOR		93.28	61.36	32.74	197.06

PS: WR = With Reading; WOR = Without Reading

Thus, the present study outlines a developmental pattern of MMN in children aged between 7-10 years and adds on to the already present literature regarding the maturation of MMN i.e. MMN matures 9-10 years of age. Therefore, even when the intensity deviations are used for MMN elicitation, the development and maturation of MMN is similar to what is reported when frequency deviations or speech stimuli are used. The results emphasize the need for age appropriate norms for children younger than 8 years. The results also indicate that reliable MMN can be picked up from either Cz or Pz electrode and the testing can be carried out without reading for adults and with reading for children.

SUMMARY AND CONCLUSION

The Mismatch Negativity (MMN) is a negative component of the event related potential (ERP) elicited by any discriminable change in the auditory stimulation in the latency range of 100-250msecs. It has been reported to be distributed largely over the supratemporal auditory cortex. However, it has been reported that MMN has several generator sites in the right hemispheres.

It is best recorded with an oddball paradigm and is not affected by attention, unlike P300. It is however influenced by other factors such as stimulus deviance, pobability of stimulus, age.

The current study was undertaken to investigate if there was any age related variation in the latency, duration, amplitude and magnitude on comparing children and adults. It was carried out to determine if there was any significant difference between the Cz and Pz recording in adults and children. In addition to these, reading and no reading conditions were compared in both adults and children to see if there was any significant difference in terms of latency, duration, amplitude and magnitude.

Subjects for the study comprised of normal hearing adults (18-30 years) and children (7-10 years). The children were further subdivided into three groupus viz. 7-8 years; 8-9 years and 9-10 years.

Auditory "oddball" paradigm was used to record MMN of both the groups. The frequency for both the standard and target tone

was 1000kHz. MMN was recorded for deviations in intensity (i.e.) standard tone was 60dBnHL (as given in APPENDIX I) and target tone was 65dB nHL with a probability of 80% and 20% respectively. The recordings were done in two conditions viz. reading and no reading conditions. MMN was recorded at Cz and Pz electrode sites. All waves were analysed and subjected to statistical analysis.

The results revealed

a) There was a clear developmental trend in the MMN latency (i. e.) latency decreased with increase in age, it being maximum for the 7-8 year children group and the minimum for the adult group. There was a significant difference in terms of latency between the adult group and the 7-8 year children group, whereas the other two groups (i.e.) 8-9 year and 9-10 year did not show any significant difference. Within the children group too, there was a significant difference between 7-8 year and 9-10 year subgroups. The other comparisons between the 7-8 year and 8-9 year groups and 8-9 year and 9-10 year groups did not show any statistically significant values.

b) There was also a clear maturational pattern in terms of duration of MMN. The duration of MMN was the highest in children of 7-8years followed by the 8-9 years. The children in 9-10 years range had duration similar to the adults.

When the adult and each of the subgroup of children was compared, it was found that the duration of MMN revealed statistically

sginificant difference only for the adult group and 7-8 year subgroup of children. When the other two groups were compared with adults no such difference was obtained.

When the children subgroups were compared among themselves, it was found that the 7-8 year group differed significantly only from the 9-10 year subgroups for duration. Such a difference was not seen when it was compared with the 8-9 year group. Also the comparison of 8-9 year and 9-10 year subgroups did not reveal any statistically significant difference.

c) The amplitude of MMN also showed a definite developmental pattern with the children in the age range of 7-8 years having the highest amplitude whereas the adult group had the least amplitude.

There was no significant difference between the adults and children for MMN amplitude.

However, there was a difference between the adults and 7-8 year subgroup. Such a difference was absent for other comparisons. Also a clear developmental trend was seen within the children groups. The amplitude comparison of 7-8 year and 9-10 year subgrous of children was statistically significant whereas no such significance was not seen for comparison between the 8-9 year subgroup with the 9-10 year and 7-8 year subgroups.

d) Magnitude too, like the other measures showed a developmental pattern with children having greater magnitudes than adults.

There was a significant difference in terms of magnitude between the adult groups and the 7-8 year children group, whereas the other two groups (i.e.) 8-9 year and 9-10 year did not show any significance difference.

Within the children group too, there was significant difference between 7-8 year and 9-10 year subgroups. The other comparisons between other subgroups did not reach statistically significant values.

e) There was no significant difference between the measures in the Cz and Pz recording (i.e.) no statistically significant difference existed at the recording sites.

f) When reading and no reading conditions were compared, there was a difference in terms of amplitude and magnitude for Cz recording site only in adults and such a difference was not seen in children.

Thus, MMN also shows a developmental trend and is very similar to that of P300. This study also highlights the need for considering smaller age groups rather than grouping children of different ages in one group while investigating the maturation of MMN. MMN is an objective tool for studying audiotry processing. However, normative data has to be established before using it on clinical population. This study reaffirms the importance of age appropriate norms for late latency event related potential MMN.

Limitations of the study

1. Only 30 subjects in each group were considered.

2. Two electrode placements i.e. Cz and Pz were considered for recording. Other electrodes (viz) F_4, Fz, F_3, C_4, C_3 could have been considered along with two EOG electrodes.

3. Only 500 stimuli were averaged.

4. Puretones with intensity deviations were used could be done with speech stimuli.

5. Children from 7-10 years were considered. Younger age groups could have been taken.

6. Reading was used as abstractor. Watching a video could have been used to reduce eye movements.

APPENDIX

Calibration of nHL

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

A group often normal hearing subjects (5 males,5 females) were taken. The behavioural threshold for clicks \vs 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 OdB nHL for that stimulus. The nHL value obtained value for test room was 30 dB SPL.

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