Prevalence of mismatch negativity with tonal stimuli in normal-hearing individuals

Himanshu Kumar Sanju, Prawin Kumar

Department of Audiology, All India Institute of Speech and Hearing, Mysore, Karnataka, India

Correspondence to Himanshu Kumar Sanju, Department of Audiology, All India Institute of Speech and Hearing, Mysore-6, Karnataka, India
Tel: +91 740 609 3279;
e-mail: himanshusanjuaiish@gmail.com

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Electrophysiological measures are one of the objective modes of assessment to check the integrity of the auditory function. The endogenous potentials like mismatch negativity (MMN) are responses which are due to internal events such as cognition or perception. In clinical practice and researches it was observed that MMN not present in all normal hearing individual. So, there is a need to study prevalence of MMN in normal population, which helps the researchers and clinicians in interpreting clinical findings. 50 participants recruited in the age range of 18-25 years. MMN was recorded with pair of stimuli. The pair was having /1000Hz/ and /1100Hz/ with /1000Hz/ as frequent stimulus and /1100Hz/ as the infrequent stimulus. Out of 50 normal hearing subjects, MMN was present only in 33 normal hearing subjects (66%). So clinician should be cautious during interpretation of clinical findings using MMN in abnormal population.

Keywords:
mismatch negativity, prevalence, tonal

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Introduction

Electrophysiological measures are one of the objective modes of assessment to check the integrity of the auditory function. These measures complement the information provided by the behavioral measures. An auditory evoked potential is one of the electrophysiological measures that describe a series of electrical changes occurring in the peripheral and central nervous system, usually related to the sensory pathways. The auditory evoked potential is further classified as endogenous and exogenous potentials. The exogenous potentials are primarily evoked by some external event-related dimension of the stimulus. The endogenous potentials such as mismatch negativity (MMN) are responses that are due to internal events such as cognition or perception.

MMN was first described by Näätänen *et al.* [1] in 1978. The brain is able to perceive even a minute change in acoustic environment. MMN has been gaining impetus as a measure to assess discrimination. Näätänen and Escera [2] defined MMN as 'an electric brain response, a negative component of the event-related potential, elicited by any discriminable change (deviant) in some repetitive aspect of auditory stimulation (standard), usually peaking around at 100–200 ms from onset'. MMN is elicited when a discriminable sound changes in intensity, duration, frequency, or phase of tone burst stimuli. It is also observed for complex change in phonemes [3]. MMN is the only objective measure of central auditory processing that may accurately correlate with behavioral perceptual measures [4]. It is an objective measure of the duration of echoic memory [5]. MMN is also an objective index of general brain degeneration, and the gross functional state of the brain can be obtained using MMN [6]. MMN can be evoked even in the absence of attention and is easy to administer [7]. The MMN reflects the central code of stimulus change. Its amplitude and latency are related to the degree to which the deviant stimuli differ from the standard stimuli, not the absolute levels of the deviant or standard stimuli. Generally, the larger the acoustic difference, the earlier and larger is the MMN, although there may be a ceiling effect in amplitude with larger difference [8]. Kasai *et al.* [9] recorded MMN for tonal and phonetic stimuli, which showed no effect in amplitude, latency, or laterality in relation to sex for either tonal or phonetic MMN.

In clinical practice and studies, it was observed that MMN is not present in all normal-hearing individuals. Thus, there is a need to study the prevalence of MMN in the normal population, which would help the researchers and clinicians in interpreting clinical findings.

Materials and methods

Participants

A total of 50 participants in the age range of 18–25 years were recruited. Participants were selected

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from a private science college. Informed written consent was obtained from all participants selected for the study.

Participant selection criteria

All participants had normal hearing thresholds as defined by pure-tone thresholds of less than 15 dBHL at 250–8000 Hz. Furthermore, they had normal middle ear function as revealed with the middle ear analyzer. Participants with any other otological, neuromuscular, and neurological problems were excluded from the study.

Testing environment

Electrophysiological tests were carried out in a sound-treated room where the noise level was as per the guidelines in ANSI S3.1 (1999). The testing rooms were well illuminated and air conditioned for the comfort of the experimenter, as well as the participant.

Instrumentation

A calibrated double-channel clinical audiometer (Orbitor-922, GN Otometrics, North America) was used for pure-tone audiometry. A calibrated GSI-Tympstar (Grason-Stadler, 7625 Golden Triangle Drive, Suite F, Eden Prairie MN 55344) Immittance meter was used for tympanometry and reflexometry. The Intelligent Hearing System with smart electrophysiology (EP) was used to record MMN.

Procedure

Pure-tone thresholds were obtained using a modified version of Hughson and Westlake procedure across octave frequencies from 250 to 8000 Hz for air conduction and frequencies from 500 through 1000, 2000, and 4000 Hz for bone conduction. The middle ear analyzer (GSI-Tympstar) was used to carry out tympanometry using a probe-tone frequency of 226 Hz and to obtain ipsilateral and contralateral acoustic reflexes thresholds at 500, 1000, 2000, and 4000 Hz.

MMN was recorded with a pair of stimuli. The pair included 1000 and 1100 Hz, with 1000 Hz as the frequent stimulus and 1100 Hz as the infrequent stimulus. The total duration of the stimuli was 200 ms with 30 ms rise–fall time and a plateau of 140 ms. The stimuli were made with the help of Aux Viewer program (Solvusoft Corporation, ATTN: [product name] Customer Service, 848 N. Rainbow Blvd. #3321, Las Vegas, NV 89107). The wave file was then converted to stimulus file for AEPs using the software 'Stimconv' provided by the Intelligent Hearing System (6860 SW 81st Street, Miami, FL 33143, USA). MMN was recorded in a vertical montage with 'Fz' as the positive electrodes referenced to the nape of the neck. The ground electrode was placed on the lower forehead. A second channel was used to record the eye blink response. The sweeps with large eye blink artifacts were eliminated from the averaging. Stimuli were presented in the oddball paradigm, with the probability of standard and deviant stimulus as 80 and 20% at 70 dBnHL, respectively. The stimuli were presented in the rarefaction polarity with a repetition rate of 1.1/s. The response was averaged for 150 sweeps (150 infrequent stimuli+the corresponding number of frequent stimuli) from -50 to 500 ms (with reference to stimulus onset). The band pass filter was set to a frequency between 0.1 and 30 Hz, and it was amplified up to 50 000 times. Stimuli were presented binaurally. The participants were seated comfortably to avoid muscular artifacts and were made to watch a silent movie to promote passive listening. The participants were instructed not to pay attention to the auditory stimuli. The skin surface of the target electrode sites was cleaned, and disc electrodes were placed. The absolute impedance was less than 5 kΩ, and interelectrode impedance was less than 2 kΩ when recording MMN. Apart from recording MMN in the conventional paradigm for each stimulus pair, late latency responses (LLRs) were also recorded for the infrequent stimulus for 150 presentations maintaining the same recording parameters as it was for MMN.

Response analysis

Conventional MMN recording was obtained in the oddball paradigm, which consisted a waveform for the frequent and the infrequent stimulus. This was followed by a second recording, which was the conventional LLR for the infrequent stimulus at the rate of 1.1/s, averaged for 150 sweeps. The LLR obtained for the infrequent stimulus was later used to analyze MMN by comparing it with the infrequent waveform of the conventional oddball paradigm. This paradigm was adopted to rule out any chance of error in MMN parameters due to difference in the LLRs elicited by the two stimuli of the oddball paradigm and also to reduce the N1 effect [10]. MMN was located in the difference wave to obtain its onset latency, peak latency, offset latency, peak amplitude, and the area under curve.

For the identification of the MMN true response through visual detection, MMN should be the first negative trough in the latency range of N_1–P_2 or P_2–N_2 complex of LLR of amplitude more than -0.3 μV and a positive peak should follow the negative peak. If an extra negativity occurred in the P_1 area, it was ignored.

Statistical analysis

Descriptive statistics was performed to determine the mean and SD for all parameters of MMN (onset latency, offset latency, peak latency, peak amplitude, and area under the curve) using SPSS, version 17.

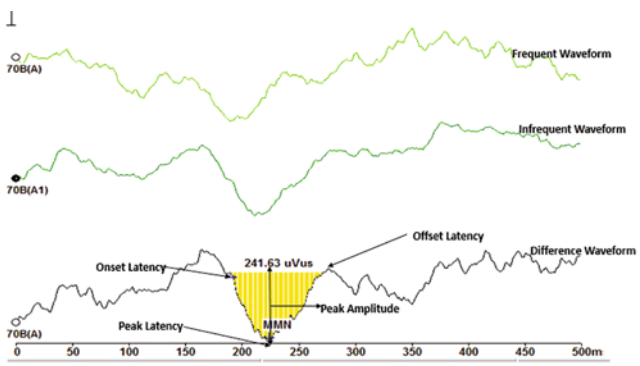
Results

Out of 50 participants, MMN was present only in 33 participants (66%). Hence, further statistical analysis was carried out only for 33 participants. The different measures of MMN – that is, onset latency, offset latency, peak latency, peak amplitude, and area under curve – were extracted from the MMN waveform through visual inspection for each participant (Fig. 1, Tables 1 and 2).

Discussion

The present study showed that MMN was present only in 66% of the participants. The absence of MMN in 34% of the population may be due to poor signal-to-noise ratio and attention to stimuli. MMN responses also depend on the cognition of the participant. Heterogeneity in the cognition of normal population can also be a reason for the absence of MMN in 34% of the population. Pulvermüller and Shtyrov [11] reported MMN as a tool for studying higher cognitive processes. The present study highlights that the finding of MMN in clinical population should be interpreted cautiously, as it was seen that there is a possibility of absence of MMN even in normal-hearing individuals. Similarly, MMN was studied by Koelsch *et al.* [12] on professional violinists and nonmusicians. The results showed that a distinct MMN was evoked in professional violinists but MMN was absent in nonmusicians. Previous studies have also reported MMN to be robust at the group level, but identification of MMN was difficult at the individual level [13–16]. Dalebout and Fox [16] also reported that MMN identification rate was too low (29%) to allow reliability to be evaluated. Lang *et al.* [13] reported that various physiological factors (attention, alertness, and topographic distribution) can also effect MMN in normal individuals, which made the interpretation of results difficult among audiologists in clinical population. In a similar study conducted by Kurtzberg *et al.* [17], they showed that unfavorable signal-to-noise ratio of individual MMN data limits its clinical applicability. The present study showed the need of an alternative technique for the identification of MMN.

Figure 1



A sample waveform of mismatch negativity along with the response measures.

Table 1 The mean and SD of onset latency, offset latency, and peak latency

Parameters	Onset latency (ms)		Offset latency (ms)		Peak latency (ms)	
	Mean	SD	Mean	SD	Mean	SD
	152.82	22.67	266.52	36.51	206.05	23.98

Table 2 The mean and SD of peak amplitude and area under curve

Parameters	Peak amplitude(μV)		Area under curve (μVμs)	
	Mean	SD	Mean	SD
	4.02	1.24	214.73	113.58

Conclusion

The present study showed that the prevalence of MMN is 66% only with tonal stimuli even in normal-hearing individuals. Therefore, the clinician should be cautious during interpretation of clinical findings in abnormal population.

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Conflicts of interest

There are no conflicts of interest.

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