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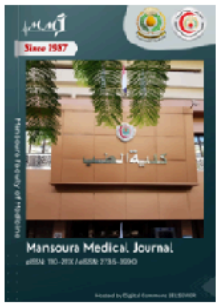

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MISMATCH NEGATIVITY IN AUDITORY NEUROPATHY PATIENTS

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ABSTRACT

Mismatch negativity (MMN), is a negative component in the auditory event-related potential. There has been increased interest in using the MMN as a clinical diagnostic tool because it might provide an objective neural measure of auditory discriminability. Auditory neuropathy (AN) is characterized by a paradoxical absence of auditory brainstem evoked potentials with presence of otoacoustic emissions, in patients whose puretone thresholds were slightly elevated. The present study was designed to investigate the detectability of MMN in cochlear hearing loss and AN patients and to test the effectiveness of MMN as an indicator of auditory discrimination at cortical level, particularly in patients with AN, if any. This study consisted of sixty subjects divided into three groups: (Group 1) 20 AN patients, (group 2) 20 patients with bilateral moderate SNHL of cochlear origin and (group 3) 20 normal peripheral hearing subjects. All participants were submitted to: full medical history, otoscopy, basic audiological evaluation, TEOAEs, ABR for neuro-otologic diagnosis and MMN testing. The results of the present study demonstrated that SNHL had a significant impact on the timing of the brain processes involved in the detection and discrimination of stimuli. Moreover, no significant differences were found between AN patients and patients with cochlear hearing loss as far as MMN latencies.

Key words : Mismatch negativity test, auditory neuropathy.

INTRODUCTION

Mismatch negativity (MMN), a negative component in the auditory event-related potential (Naatanen et al. 1978), is thought to index automatic processes involved in sensory or

echoic memory. It is elicited by infrequent "deviant" stimuli occasionally replacing frequently occurring "standard," stimuli (Naatanen, 1990, 1995; Naatanen and Winkler, 1999). The MMN is generated in the primary auditory cortex (Javitt et al. 1994), but the secondary auditory cortex may be activated as the stimulus deviance increases (Naatanan and Alho, 1995). A frontal lobe component may be activated and is thought to reflect the passive drawing of attention (Naatanen, 1995). MMN likely reflects the N-methyl-D aspartate channel current influx in the cortical layers II and III (Umbricht, 2000).

Auditory neuropathy (AN) was first noted about 2 decades ago when researchers found a paradoxical absence of auditory brainstem evoked potentials in patients whose pure-tone thresholds were slightly elevated (David and Hirsh, 1979; Worthington and Peters, 1980; Kraus et al., 1984; Soliman, 1987). Later studies showed that these patients had normal cochlear outer hair cell function, indicated by the presence of cochlear microphonics and otoacoustic emissions (Berlin et al., 1993; Starr et al. 1996). Thus, different from the conventional cochlear loss, AN preserves the outer hair cell function but disrupts the neural synchrony in the auditory nerve.

At present, the exact site of lesion and pathology that disrupts the neural synchrony is not known and may include loss of inner hair cells, abnormal synaptic function, and/or demyelination in the auditory nerve fibers. Isolated IHC damage does not explain the discrepancy between audiometric findings and ABR in AN patients. Eighth nerve affection is evidenced in AN patients by the highly distorted ABRs and by signs of peripheral neuropathy in some patients (Soliman, 1987; Starr et al. 1991; and Rance et al. 1999).

Previous studies including psychphysical measurements were conducted on such patients in an attempt to delineate the possible sites of affection (Starr et al., 1991; Soliman et al., 2002). Soliman et al. (2002) concluded that in AN patients, there was significant temporal processing deficit which may be merely peripheral (at the level of IHC and /or auditory nerve) or is combined with central affection. Such patients could not gain benefit from conventional amplification. Cochlear implants were tried to

solve this problem by stimulating the spiral ganglion cells directly (Shallop et al. 2001).

There has been increased interest in using the MMN as a clinical diagnostic tool because this deviant-evoked negativity might provide an objective neural measure of auditory discriminability. One idea has been to employ the MMN as a test of the auditory system's ability to transmit the acoustic information important for understanding spoken language (Picton, 1995; Naatanen, 1995; Kraus et al., 1995). To date, the MMN has been used to assess the efficacy of phoneme discrimination training and related neural plasticity (Kraus, et al., 1995; Tremblay et al., 1997), and some investigators have proposed using MMN to monitor the effectiveness of hearing aid therapy (Picton, 1995) and cochlear implants (Ponton and Don, 1995).

The present study was designed to investigate the detectability of MMN in cochlear hearing loss and AN patients and to test the effectiveness of MMN as an indicator of auditory discrimination at cortical level, particularly in patients with auditory neuropathy, if any.

SUBJECTS AND METHODS

A. Subjects:

This study consisted of sixty subjects divided into three groups:

Group 1 : 20 patients diagnosed as AN, selected according to the following criteria:

a- Bilateral mild to moderate low frequency SNHL.

b- Poor speech discrimination scores disproportionate to the degree and configuration of hearing loss.

c- Normal middle ear pressure with elevated or absent acoustic reflexes.

d- Preserved transient evoked otoacoustic emissions (TEOAEs).

e- Bilateral absent or severely distorted auditory brainstem responses (ABR).

f- Normal MR imaging of the brain.

Group 2 : 20 subjects with bilateral moderate cochlear hearing loss.

Group 3 : 20 subjects with bilateral normal peripheral hearing.

B. Methods :

All participants in the study were submitted to the following: full medical history, otoscopy, basic audiological evaluation in the form of pure-tone audiometry, speech audiometry and immittancemetry. TEOAEs, ABR for neurootologic diagnosis at an intensity level of 90 dBnHL and MMN testing.

MMN test :

All subjects were tested while resting comfortably in a supine position inside a sound booth. Subjects were instructed to lie as quietly as possible while reading a book, to have control over the level of arousal and to minimize the subject's attention to test stimuli.

Electrode montage :

The recording of neuro-electrical activity was accomplished from Fz/A1-A2 (linked) with ground electrode at Fpz pursuant to the 10-20-electrode system (Jasper, 1958). Prior to electrode placement, the skin at the electrode sites was cleaned with alcohol and scrubbed by an abrasive material to minimize skin impedance. Inter-electrode impedance was maintained below 3 Kohms throughout the recording session.

Stimulus parameters :

MMN was recorded by binaural presentation of 750 Hz tone-burst (served as the standard), randomly replaced by 1000 Hz tone-burst (as the deviant) in 20% of testing time. The tones were 20 msec in duration with rise and fall times of 2 msec. The stimuli were delivered through TDH-39 earphone, presented at 75 dBnHL, at a rate 0.7/sec.

Recording parameters :

The neuroelectrical activity picked up from the surface electrodes was amplified (x 30.000), filtered at 0.1-30 Hz with 12-dB/octave roll off. The used time window was 500 msec post-stimulus onset with 50 msec pre-stimulus. The evoked responses were collected in 4 separate blocks, each consisted of 200 stimuli (40 deviant and 160 standard).

Data analysis (figure 1) :

Because the MMN is by definition, elicited only by the deviant stimulus, a difference wave was computed by subtracting the individual responses to the standard stimuli from the response to the deviant stimuli. The MMN was identified visually as a relative negativity in the difference waveform following the N1 with a latency range of 150-300 msec.

MMN response parameter measurements:

1. Onset latency (L1): measured (in msec) from the stimulus onset to the onset of the response.
2. Peak latency (L2): measured (in msec) from the stimulus onset to the maximum negative peak of the response.
3. Offset latency (L3): measured (in msec) from the stimulus onset to the offset of the response.
4. Peak amplitude (A1): measured (in microvolts) from the baseline to the maximum negative peak of MMN.
5. Onset to peak amplitude (A2): measured (in microvolts) from the onset point to the maximum negative peak of MMN.
6. Peak to offset amplitude (A3): measured (in microvolts) from the maximum negative peak of MMN to the offset point.

Statistical procedure :

Results were entered into a computer and analyzed statistically using SPSS version 10.0. Descriptive statistics was performed for the three groups. One way ANOVA test was done to compare MMN latency and amplitude, among the three groups. Post Hoc test was done to validate the correlation between the three groups. Probability of $P < 0.05$ was considered statistically significant.

RESULTS

Demographic data of the studied three groups were illustrated in table (1). They were age and sex matched. Their mean pure tone thresholds were illustrated in figure (2).

Speech discrimination, TEOAEs, and ABR findings:

Group I (AN patients) :

Their speech recognition scores ranged from 0% to 40% correct with an average of 16% correct. All subjects had measurable TEOAEs, with absent ABR. In addition, MR imaging of the brain was normal in all 20 patients tested.

Group II (Cochlear HL patients) :

Their speech recognition scores ranged from 76 % to 100 % correct with an average of 84 % correct. All subjects had absent TEOAEs, but ABR revealed well identifiable and repeatable waves with normal absolute and interpeak latencies.

Group III (Normal hearing subjects) :

Their speech recognition scores

were 100 % correct with measurable TEOAEs and normal ABR.

MMN response parameters :

Comparing the MMN response obtained from the studied three groups, we found statistically significant prolongation of L1, L2, and L3 among the three groups. Post Hoc test detected that this significant difference is between the control group and both the cochlear HL and AN patients. There was no significant difference between AN and cochlear loss patients as far as MMN latencies and amplitudes (tables 2 &3).

Table (1): Demographic data of all three groups.

Groups	I (AN)	II Moderate SNHL	III Norms
Number	20	20	20
Gender	12 females 8 males	10 females 10 males	10 females 10 males
Age (years) Range: Mean:	 14 – 40 26	 14 – 33 25	 15 – 44 27.9

Table (2): Group effect on MMN latency measures (msec) using ANOVA test.

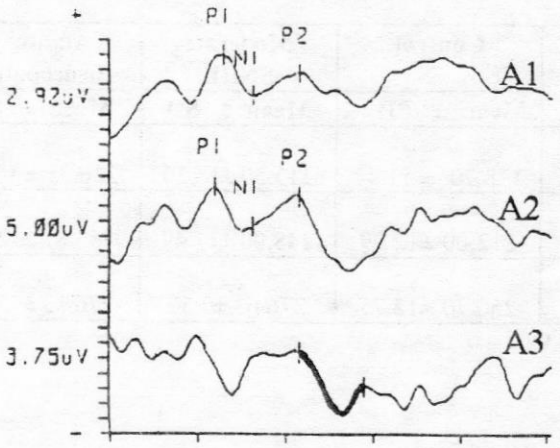
	Control	Moderate SNHL	Auditory neuropathy	F	Sig.
	Mean ± SD	Mean ± SD	Mean ± SD		
L1	178.70 ± 11.41	213.50 ±13.30	226.95 ± 16.55	35.19	0.000*
L2	212.00 ±12.99	248.00 ±17.49	253.81 ±12.25	27.08	0.000*
L3	250.70 ±12.75	276.63 ±9.57	276.63 ±13.07	17.39	0.000*

* $P < 0.05$

Table (3): Group effect on MMN amplitude measures (microvolts)nusing ANOVA test.

	Control	Moderate SNHL	Auditory neuropathy	F	Sig.
	Mean ± SD	Mean ± SD	Mean ± SD		
A1	5.69 ±1.58	5.20 ±0.88	5.12 ±1.62	0.522	0.598
A2	3.62 ±1.89	3.56 ±1.08	4.19 ±1.40	0.599	0.556
A3	5.88 ±2.21	5.44 ±0.75	4.20 ±2.43	2.191	0.129

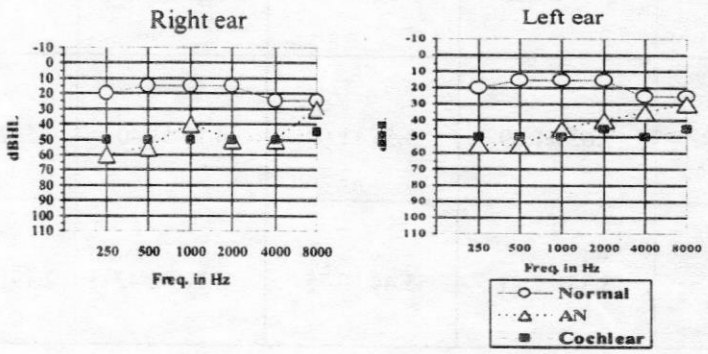
Figure (1): MMN trace recorded from a normal subject



(A1) Response to standard stimuli, (A2) Response to deviant stimuli,

(A3) Difference wave.

Figure (2): Mean pure tone thresholds of the three groups:



DISCUSSION

Cortical event-related potentials has been successfully used to assess the cognitive processes involved in the detection and discrimination of complex stimuli as speech sounds, in normal-hearing subjects (Martin et al., 1999). There has been increased interest in using the MMN as a clinical diagnostic tool because this deviant-evoked negativity might provide an objective neural measure of auditory discriminability. MMN is used as a test of the auditory system's ability to transmit the acoustic information important for understanding spoken language (Picton, 1995; Naatanen, 1995; Kraus, et al., 1995).

In the present study, MMN latencies were significantly prolonged for the two hearing-impaired groups (AN and cochlear hearing loss) in comparison to those obtained from the normal hearing subjects. This agreed with Korczak et al. (2005). They suggested that the brain is not processing the acoustic signals with the same degree of accuracy and effectiveness as it is in individuals with normal-hearing sensitivity. There was no statistically significant difference between the cochlear HL and AN patients as regards latency measures of MMN. This specific pattern of electrophysiological finding provide evidence that the signal has been neurally coded at the level of the cortex and the brain is able to discriminate the acoustic changes present in the signal on a preattentive level.

As regard the MMN amplitude, there was no statistically significant difference among the three groups. This agreed with previous studies that attributed this variability to the dependence of MMN amplitude on the level of alertness of the subject (Lang et al., 1995 and Morr et al. 2002).

The results of the present study demonstrated that SNHL had a significant impact on the timing of the brain processes involved in the detection and discrimination of stimuli. In AN patients, MMN provide useful information regarding higher-level (cortical) responsiveness to auditory stimuli. Further extensive studies of cortical evoked potentials are recommended in AN patients, specially MMN using speech stimuli in order to provide insight into the early and later cognitive processes that underlie the detection and discrimination of speech.

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الملخص العربى
موجة عدم التوافق السالبة فى مرض إعتلال العصب السمعى

ملخص البحث :

تمثل موجة عدم التوافق السالبة وسيلة إكلينيكية وموضوعية لتقييم التمييز السمعى.

يتميز مرضى إعتلال العصب السمعى بوجود ضعف سمعى للنغمات النقية مع إختفاء الاستجابة السمعية المثارة لجذع المخ فيما يظل الإنبعاث الصوتى للأذن الداخلية فى حالته الطبيعية.

صمم هذا البحث لدراسة موجة عدم التوافق السالبة فى ٦٠ شخص قسموا إلى ثلاث مجموعات : المجموعة الأولى : تشتمل على ٢٠ مريض من مرضى إعتلال العصب السمعى. المجموعة الثانية : ٢٠ مريض من مرضى ضعف السمع الحسى (القوقعى) والمجموعة الثالثة : من ٢٠ شخص من ذوى السمع الطبيعى.

ولقد تم فحص كل هؤلاء الأشخاص على النحو التالى :-

تاريخ مرضى شامل، فحص الأذن بالمنظار، تقييم السمع الأساسى، الإنبعاث الصوتى للأذن الداخلية. الاستجابة السمعية المثارة لجذع المخ واختبار تسجيل موجة عدم التوافق السالبة.

وأظهرت نتائج هذا البحث أن ضعف السمع الحسى / عصبى له تأثير بالغ على توقيت التفعيل الدماغى المسئول عن التنبيه والتمييز للمؤثرات. بالإضافة لهذا لم يتلاحظ وجود إختلاف جوهرى بين مرضى إعتلال العصب السمعى ومرضى ضعف السمع القوقعى من حيث زمن حدوث موجة عدم التوافق السالبة.