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The mismatch negativity cortical evoked potential elicited by speech in cochlear-implant users *

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The mismatch negativity (MMN) event-related potential is a non-task related neurophysiologic index of auditory discrimination. The MMN was elicited in eight cochlear implant recipients by the synthesized speech stimulus pair /da/ and /ta/. The response was remarkably similar to the MMN measured in normal-hearing individuals to the same stimuli. The results suggest that the central auditory system can process certain aspects of speech consistently, independent of whether the stimuli are processed through a normal cochlea or mediated by a cochlear prosthesis. The MMN shows promise as a measure for the objective evaluation of cochlear-implant function, and for the study of central neurophysiological processes underlying speech perception.

Cochlear implants; Auditory evoked potentials; Mismatch negativity; Event-related potentials

Introduction

A cochlear implant encodes sound electronically and then bypasses an undeveloped or damaged inner ear to provide direct electrical stimulation to the auditory nerve. To individuals who are deaf and cannot benefit from conventional hearing aids, this electrical stimulation provides a sensation of hearing. Cochlear implants have become an accepted medical treatment for individuals with profound bilateral sensorineural hearing loss.

Cochlear implant recipients exhibit great variability in the way they use the information provided by an implant. Their speech perception abilities can range from the simple detection of sound to the ability to converse on the telephone. This variation in speech perception ability among users cannot be explained fully. Implant success is somewhat related to the length of time a person has been deaf and whether the deafness occurred before or after the acquisition of speech and language. Other factors, such as the status of the cochlea (Gantz et al., 1988a), the number of surviving nerve fibers (Galey, 1984), basic psychophysical skills (Cazals et al., 1990), or the type of device implanted (Gantz et al., 1988b), also influence implant success but cannot account sufficiently for the variation in patient performance.

The wide range of speech perception abilities exhibited by cochlear implant recipients may depend in part upon differences in the central auditory processing abilities of implant users. One way to assess central auditory function in these individuals is to measure speech-evoked cortical potentials. In particular, measuring cortical potentials that reflect auditory discrimination may provide insight into the central mechanisms underlying speech perception. Moreover, if those cortical potentials can be recorded from cochlear implant users, comparing the potentials to the responses measured in normal listeners should indicate whether the brain's response to speech mediated by a cochlear implant is similar to the brain's response to speech processed by a normal cochlea.

From a theoretical standpoint, the presence of cortical potentials in cochlear implant users may provide a unique window for viewing the central auditory system. The electrical signals from a cochlear implant are crude in comparison to the output of the thousands of receptor cells in a normal cochlea. Cortical potentials may show how the central auditory system makes use of the limited information from an implant, and how

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the central auditory system adapts to process signals that are different from its normal input.

The mismatch negativity (MMN) is an event-related auditory potential that reflects the neurophysiologic processing of stimulus differences (Näätänen et al., 1978). Because it originates in higher auditory and non-auditory centers (Csépe et al., 1987; 1988; Näätänen and Picton, 1987; Hari et al., 1984; Alho et al., 1986; Sams et al., 1991; Giard et al., 1990), it provides a way to investigate the central auditory processes underlying discrimination. The MMN is elicited using an oddball paradigm in which a deviant, or rare, stimulus is presented within a series of homogeneous, or standard, stimuli. In normal listeners, the MMN is exquisitely sensitive to fine differences in acoustic parameters, including small changes in intensity, frequency, and location of a sound source (Sams et al., 1985; Näätänen et al., 1987; Paavilainen et al, 1989; Näätänen, 1990; Novak et al., 1990).

The MMN response is automatic and requires no behavioral task on the part of the subject. During testing, the subject's attention is occupied by another task, usually employing another sensory modality (such as reading a book or watching a television screen), so that the auditory stimuli are ignored. Although affected by attention (Woldorff and Hillyard, 1991; Woods et al., 1992; Alho et al., 1992), the MMN does not require conscious attention to the stimuli (Näätänen, 1990) and therefore provides an objective measure of the discrimination of stimulus differences. Consequently, it may permit an objective analysis of sensory processing and discrimination in patients who cannot attend to acoustic stimuli.

The P300, another late event-related potential, has been measured in cochlear-implant users in response to acoustic stimulus pairs presented in an oddball paradigm (Oviatt and Kileny, 1991; Kaga et al., 1991). However, the MMN and P300 represent neurophysiological mechanisms that are quite different. The MMN is a sensory response which largely reflects the activity of auditory cortex neurons in response to small acoustic stimulus differences. The P300 is a more general multimodality, cognitive response that originates from multiple auditory and non-auditory structures. It generally requires attention and a behavioral response, and is not sensitive to small stimulus differences (Harrison et al., 1988; Halgren et al., 1986; Buchwald, 1989).

In this investigation, acoustically well-defined synthetic speech stimuli were used to elicit the MMN in cochlear implant recipients in order to ascertain whether the MMN was present in these patients and whether the response was similar to the MMN measured in normal listeners. The investigation was unique because the MMN has never been measured in implanted patients and because synthetic speech stimuli have rarely been used to elicit auditory evoked potentials of any type in these individuals. Identifying the MMN in cochlear implant recipients provides an opportunity to assess the role of central auditory structures in the processing of speech stimuli. In addition, the MMN results can indicate how the brain discriminates well-defined electrically encoded speech parameters, thereby furthering knowledge of the minimal cues required for processing speech via a cochlear implant. Finally, characterizing the MMN in implant recipients may provide the basis for developing a non-invasive objective tool for assessing implant performance in patients who cannot undergo conventional behavioral testing (e.g., young deaf children).

Methods

Subjects

The MMN was measured in eight cochlear implant recipients who were considered to be 'good' users based upon subjective reports of satisfaction, their everyday communication competence, and their ability to understand monosyllabic words in an open-set task (NU-6 word list). Subjects included five men and three women ranging in age from 34 to 81 years (average age = 56 years). Etiologies of hearing loss were progressive sensorineural loss of unknown origin ($N = 4$), far-advanced otosclerosis ($N = 2$), Meniere's disease ($N = 1$), and temporal bone fracture ($N = 1$). All subjects had 22-channel implants (Cochlear Corporation), which they had been wearing for at least six months. The MMN also was evaluated in one 'poor' 22-channel implant user. This 49-year-old woman, who had a progressive hearing loss of unknown origin, was unsatisfied with the device, used it infrequently, and was unable to understand open-set speech materials.

22-channel cochlear implant

The 22-channel cochlear implant system is designed specifically to select and deliver relevant speech information to the recipient. The speech processor extracts the fundamental frequency (voice pitch), the first and second formants (the frequency bands of acoustic energy that are characteristic of specific phonemes), and additional high-frequency information from the acoustic signal which it encodes and sends, as a set of electrical pulses, to electrodes implanted in the cochlea. The fundamental frequency is coded as the rate of stimulation, and the formant frequencies and high-frequency information determine which of the 22 electrodes are stimulated. The amplitude of the formants determines the amount of current delivered to the selected electrodes (Blamey et al., 1987; Koch et al., 1990).

Stimuli

The MMN was elicited by two computer-generated stop consonants /da/ and /ta/. The two stimuli were generated using a Klatt (1980) digital speech synthesizer on a DEC VAX computer. The consonants were composed of five formants and differed primarily in voice onset time. Total stimulus duration was 100 ms. All subjects (except the 'poor' user) discriminated these stimuli behaviorally.

The fundamental frequency (F_0) began at 103 Hz and fell to 84 Hz for /da/ and /ta/. The starting frequencies of F_2 and F_3 for the transient portion of both stimuli were 1398 Hz and 2599 Hz, respectively. The starting frequency for F_1 was 220 Hz for /da/ and 529 Hz for /ta/. The center frequencies of the formants for the steady-state vowel portions of both stimuli were 720 Hz (F_1), 1240 Hz (F_2), 2500 Hz (F_3), 3600 Hz (F_4), and 4500 Hz (F_5). F_4 and F_5 were constant through both the transient and steady state portions of both stimuli. For /da/, the onset of voicing began at 0 ms. For /ta/, the frication/aspiration began at 0 ms and lasted for 15 ms, at which time the onset of voicing began. The amplitude of voicing was constant up to 90 ms and fell linearly to 0 dB in the last 10 ms for both stimuli. The peak amplitudes of the stimuli were within 0.5 dB of each other.

Files from the Klatt synthesizer were downloaded to a PC-based stimulus delivery system which output the signals through a 12-bit D/A converter. That system controlled time of delivery, the stimulus sequence, and the stimulus intensity. It also triggered a PC-based evoked potential averaging system for stimulus onset and indicated whether the trial contained a standard or deviant stimulus.

The stimuli were presented using an oddball paradigm where /da/ was the standard stimulus (probability of occurrence = 85%) and /ta/ was the deviant stimulus (probability of occurrence = 15%). The interstimulus interval was 1 s. Stimuli were presented in a pseudorandom sequence with at least three standard stimuli separating presentations of deviant stimuli. Twenty standard stimuli preceded the presentation of the first deviant stimulus. Responses to standard stimuli immediately following deviant stimuli were excluded from the standard-stimulus average.

The stimuli were delivered through a speaker placed approximately five feet in front of the subject. Stimulus intensity was 65–70 dB SPL at the microphone input to the speech processor. The distance from the speaker to the subject eliminated the possibility that electrical stimulus artifact would be picked up by the recording electrodes. Prior to the test session, each subject was asked to adjust the sensitivity control of the speech processor so that the stimuli were heard comfortably. Subjects watched captioned videotapes so that they would not attend to the stimuli and would remain awake.

Response recording

The MMN was recorded from Fz/earlobe contralateral to the implant, with the ground electrode on the forehead. Eye movements were monitored with a supraorbital electrode referenced to the contralateral mastoid or a bipolar electrode montage (supraorbital-to-lateral canthus). Prior to data collection, subjects were instructed to blink and move their eyes while amplifier settings were adjusted to ensure detection of eye movements (artifact level ± 163–245 μV). Averaging was suspended automatically when the eye channel registered movement.

The evoked responses were collected in blocks of 25 deviant stimuli and approximately 140 standard stimuli. Eight blocks (1200 standard and 200 deviant stimuli) were run in each stimulus condition for each subject. Evoked potentials were averaged separately for the deviant and standard stimulus presentations. The MMN should occur in response to the deviant stimulus only when it is presented in the oddball paradigm and not when the deviant stimulus is presented alone (Kraus et al., 1992). Therefore, as a control, eight blocks of 25 presentations of /ta/ were presented alone (/ta/-alone condition), also at 1/s. As a final control, responses were recorded when the implant system's speech processor was turned off to verify that no replicable evoked potentials were present.

The recording window included a 50 ms pre-stimulus period and 500 ms of post-stimulus time, with a total of 512 sampling points/sweep (A/D conversion rate = 1074/s). Responses were analog bandpass filtered on-line from 0.1 to 100 Hz (12 dB/octave) and digitally lowpass filtered off-line at 40 Hz with a Blackman filter. Averaged response waveforms were converted to ASCII format and transferred to a spreadsheet for analysis.

Individual-subject data analysis

For each subject, responses from a total of eight stimulus blocks each for the /da/ and /ta/ in the oddball paradigm and eight blocks for the /ta/-alone condition were used in the analysis. An individual grand average of those eight blocks was computed. Thus the individual grand averages consisted of a total of 1200 responses to the standard /da/ stimulus and 200 responses each to the deviant /ta/ and /ta/-alone stimuli.

Because the MMN is, by definition, elicited only by the deviant stimulus, a difference wave was computed by subtracting the individual grand average response to the standard stimulus from the response to the deviant stimulus. Likewise, a difference wave was computed by subtracting the response to the /ta/-alone stimulus from the response to the deviant /ta/ stimulus.

The morphologies of the standard, deviant, /ta/-alone, and difference waveforms (deviant minus standard, deviant minus /ta/-alone) were examined and assessed relative to the previously described morphology of speech-evoked MMNs (Aaltonen et al., 1987; Sams et al., 1990; Kraus et al., 1992). The MMN was identified visually as a relative negativity following the N1, within a latency range of 150–300 ms. The MMN (about 100 ms in duration) was apparent in the deviant and the difference waveforms, while the N1 was apparent in the standard, deviant, and /ta/-alone waveforms.

Statistical tests were performed on the individual responses to ensure that the MMN identified visually was indeed a significant negative deflection. Using the subject's grand average difference waveforms, a latency (in milliseconds) was determined for the onset, offset, and peak (point of maximum negativity) of the MMN. MMN onset and offset typically were the adjacent positive peaks. Using the contributing difference waves, *t*-tests were performed comparing the amplitudes of five-millisecond periods flanking the three marked latencies (onset, peak, offset). Likewise, *t*-tests were performed on the individual deviant (oddball paradigm) and deviant minus /ta/-alone difference waveforms comparing the amplitudes at the same three latency points identified above. An MMN was considered to be present for that individual if the amplitude of the peak was significantly different from the onset or offset amplitudes of the MMN in both the deviant minus standard and deviant minus /ta/-alone conditions.

Group data analysis

The MMN data also were analyzed for the eight good-user subjects as a group. Grand averages were computed across subjects. A grand average of the difference waveform (deviant minus standard) was calculated. A point-by-point *t*-test of the values of the contributing waveforms determined the latency duration over which the grand averages were significantly different from zero (i.e., a significant difference between the standard and deviant waveforms). A significant negativity (seen in the grand average difference wave) following the N1 (seen in the grand average standard and deviant waveforms) was defined as the group MMN. A similar analysis was performed on the deviant (oddball paradigm) minus /ta/-alone difference waveforms because the MMN should occur in response to the deviant stimulus only when it is presented in the oddball paradigm and not when the deviant stimulus is presented alone.

The group data analysis included comparisons of MMN peak latencies and MMN duration, with duration being defined as the offset minus the onset latency for each subject. The MMN magnitude was measured on the individual grand averages in the following two ways: (1) by measuring the amplitude from the preceding peak to the midpoint of the MMN (onset-to-peak) and from the midpoint to the end of the MMN waveform (peak-to-offset) and (2) by measuring the area of the MMN waveform. To measure the area of the MMN, a line was drawn between the onset and offset of the MMN in the difference wave. The enclosed area of the difference waveform was measured in ms × μV.

Results

Intra-subject statistical testing indicated that an MMN was present in each of the eight 'good' cochlear implant users in response to the synthesized speech stimuli. Fig. 1 shows the averaged response to the standard stimulus /da/, the averaged response to the deviant stimulus /ta/, and the difference wave for a representative cochlear implant subject. The MMN response is evident in the response to the deviant stimulus and is seen in the 200 ms region of the difference waveform. Also evident in the response to both standard and deviant stimuli is the classic N1 wave at about 100 ms (Davis, 1939).

Fig. 2 (top) shows the grand average MMN difference wave for all eight good implant subjects. The cross-hatched area represents the presence of a statistically significant difference between the difference wave and zero. The analysis clearly shows the response area of the MMN, which occurs around 200 ms. Fig. 2 (bottom) shows the grand average difference wave for a group of ten normal-hearing adults. The similarity in

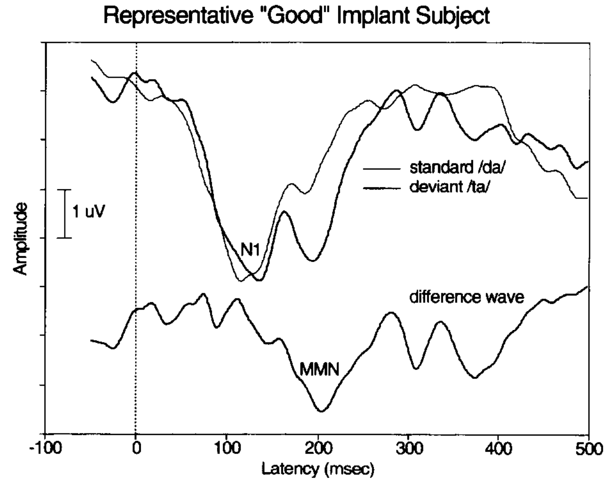

Fig. 1. Speech-evoked MMN responses from a 'good' cochlear implant subject. Averaged responses for a representative 'good' cochlear implant subject to the standard stimulus /da/, the deviant stimulus /ta/, and the difference wave obtained by subtracting the standard from the deviant waveform. The MMN occurs around 200 ms. Note the N1 at about 100 ms.

TABLE I

Statistical analysis of MMN significance in individual subjects

	Deviant – standard				Deviant rare – deviant alone			
	onset/peak		peak/offset		onset/peak		peak/offset	
subj.	amp (μV)	t	amp (μV)	t	amp (μV)	t	amp (μV)	t
CC	1.20	2.63 **	1.84	6.66 **	0.11	0.23	0.99	2.27 **
GW	1.02	2.08 **	1.88	4.08 **	1.88	3.02 **	2.97	5.31 **
RP	2.43	3.84 **	3.06	5.27 **	1.87	2.20 **	0.72	0.97
SA	1.10	3.49 **	1.05	2.76 **	2.55	7.30 **	1.68	3.79 **
SW	2.93	3.03 **	2.89	2.91 **	3.95	3.96 **	4.63	4.80 **
TB	1.36	2.65 **	2.65	5.16 **	0.86	1.00	2.28	2.48 **
TL	2.61	7.25 **	2.37	6.12 **	1.26	2.1 **	2.61	4.25 **
WP	1.16	1.80 *	1.78	3.10 **	1.46	1.92 *	0.79	1.26
DT	0.70	1.29	0.67	1.54	1.30	2.92 **	0.67	0.99

** Indicates significance at $P < 0.001$; * indicates significance at $P < 0.05$.

responses between the cochlear implant subjects and normal listeners is evident in comparing the top and bottom of Fig. 2.

A similar analysis compared the response to /ta/ when it was the deviant stimulus in the oddball paradigm and when /ta/ was presented alone. Subtraction of the grand averages of those two waveforms showed a negativity at the same latency as the MMN in Fig. 2, thereby demonstrating that the negativity to /ta/ occurred only when it was the deviant stimulus in the oddball paradigm. Like the MMN, this negativity peaked at 230 ms and the /ta/-deviant and /ta/-alone waveforms were significantly different over a 50 ms latency region. These results indicate that the negativity seen in the difference waveform truly represents a neurophysiologic mismatch response to stimulus differences and that the MMN is not simply a response to the peripheral processing of the acoustic differences.

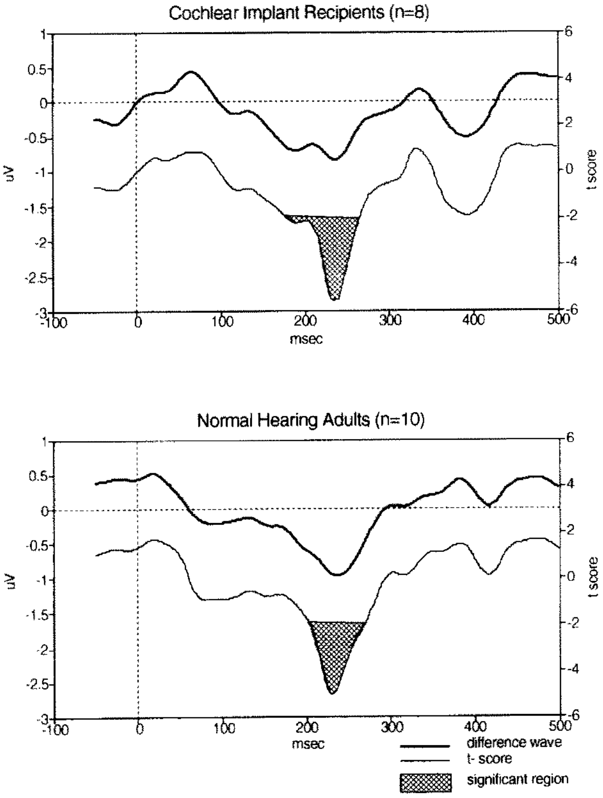

Fig. 2. Grand average MMN difference waveforms for eight 'good' cochlear implant subjects (top) and ten normal-hearing adults (bottom). The bolder trace represents the grand average waveform obtained by subtracting the response to the standard stimulus from the response to the deviant stimulus. The bottom trace shows the t-scores and the significant MMN range ($P < 0.05$).

Intra-subject statistical testing indicated that an MMN was present in each of the eight good users (Table I). By the criteria specified above, the MMN was present in each individual in the deviant minus standard condition as well as in the corresponding control deviant /ta/ minus /ta/-alone condition.

The single 'poor' implant user did not have a statistically significant MMN in response to the /da/-/ta/ stimulus pair (Table I, subject DT). Interestingly, she did have a significant MMN to the stimulus pair /da/ and /di/ (behavioral discrimination was above chance). The spectral components of /da/ and /di/ are very different from each other (somewhat like two pure tones) and are processed more distinctly by the 22-channel implant system than the differences in /da/-/ta/. Most 22-channel implant recipients can hear the difference between /da/ and /di/ easily.

Latency

The MMN latency values for each cochlear implant user are shown in Fig. 3. Mean latency was 220 ms (±27 ms). Duration measurements, indicating the beginning and ending of the MMN response, are also shown in Fig. 3 for each subject. Mean duration was 121 ms (±26 ms).

Amplitude

Individual amplitude values (onset-to-peak and peak-to-offset) for each subject are shown in Fig. 4.

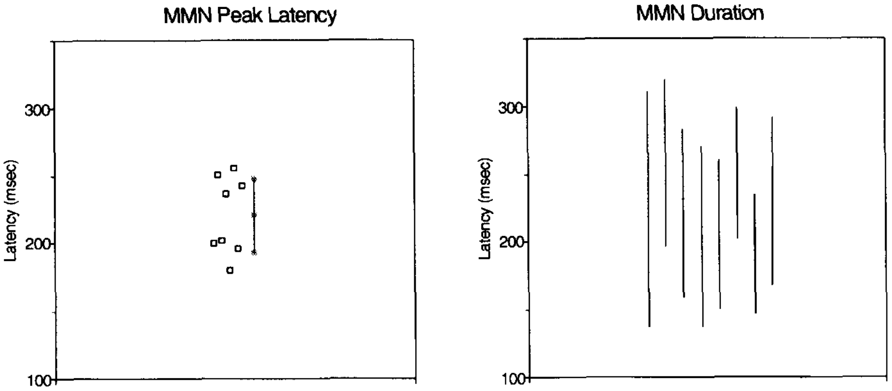

Fig. 3. MMN peak latency (±1 S.D.) and latency duration for individual subjects. Each vertical line = 1 subject.

Mean amplitudes were 1.7 uV (±0.7μV) and 2.2 uV (±0.6μV) onset-to-peak and onset-to-peak, respectively. MMN mean area was 134.9 ms × μV (60 ± 1 S.D.). Individual subject values are shown in Fig. 4.

Discussion

The results reported here are important for several reasons. First, this is the first evidence that the MMN cortical response exists in 'good' cochlear-implant patients in response to speech stimuli. The MMN waveforms in good cochlear-implant users are strikingly similar to those recorded from normal listeners. That similarity implies that the central auditory system's response to these speech stimuli is consistent, independent of whether the stimulus is processed through a normal cochlea or mediated by a cochlear implant. Remarkably, despite the limited input provided by an implant (compared to a normal cochlea), the brain appears to process the signals in a relatively normal fashion.

Second, the MMN provides an objective measure of the central auditory system's discrimination of acoustic differences. The absence of an MMN in the 'poor' implant user suggests that the MMN may reflect behavioral speech discrimination ability, although this relationship needs to be determined by future studies.

Finally, the ability to measure the MMN in cochlear implant recipients indicates that the response might be used to evaluate the success of implantation in a more objective manner than is practiced currently. Because the MMN specifically reflects central auditory processing and is not dependent on attention, the results suggest that the MMN could be developed as an objective measure of the neurophysiological events underlying speech discrimination in implanted individuals. A subsequent study is underway that will correlate the MMN response to psychophysical speech discrimination abilities in order to define that relationship more clearly.

Because of its involuntary nature, the MMN might be particularly useful as a tool for evaluating cochlear implant function in young deaf children. In addition, because the MMN appears to be an effective neurophysiologic index of fine acoustic stimulus processing, it may provide a neurophysiologic basis for the design

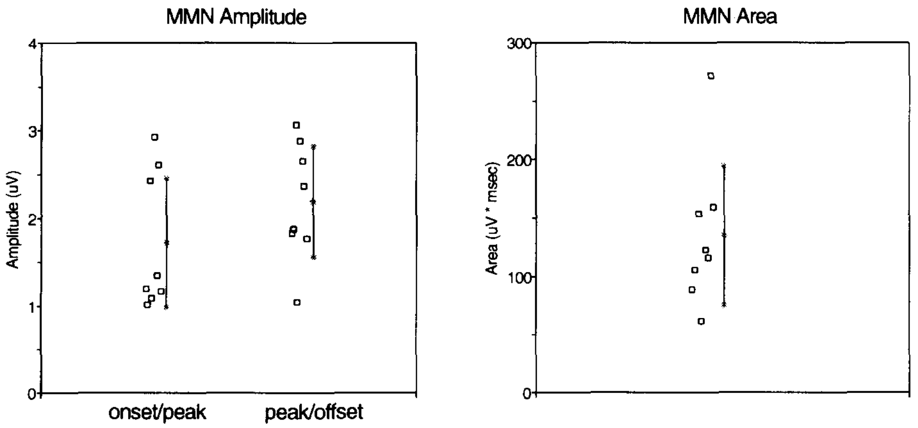

Fig. 4. MMN magnitude (amplitude and area) is shown for individual subjects. Solid lines indicate ± 1 S.D.

of cochlear implant rehabilitation programs and signal-processing strategies.

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