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Identification of the Mismatch Negativity in the Responses of Individual Listeners

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Abstract

The mismatch negativity (MMN) was recorded from normal adults in three stimulus conditions: two contrast conditions and a control condition in which standard and deviant stimuli were identical. Averaged waveforms were analyzed by examiners blind to the evoking stimulus condition. Hit rates, a false alarm rate, and *d'* values were determined based on the number of MMNs identified in each condition. Hit rates were low and the false alarm rate was relatively high, resulting in unacceptably small *d'* values. The relationship between MMN findings and corresponding behavioral discrimination data for individual listeners was not systematic. Factors that may contribute to ambiguity and error in MMN data analysis are discussed.

Key Words: Auditory evoked potentials, central auditory processing, mismatch negativity

Abbreviations: ABR = auditory brainstem response, C_z = vertex, F_z = 30 percent of the distance between nasion and inion at the midline, MLR = middle latency response, MMN = mismatch negativity, SNR = signal-to-noise ratio

The mismatch negativity (MMN) is an event-related component of the larger auditory evoked response that reflects the detection of acoustic change by mechanisms within the central auditory system. The MMN is elicited using an oddball paradigm in which a repetitive string of standard stimuli is occasionally interrupted by a deviant (i.e., "oddball") stimulus. The paradigm is based on the premise that a neural trace or "template" is formed to represent the standard stimulus and held in short-term memory (Näätänen, 1995). When preattentive detection of a mismatch between the deviant stimulus and the template for the standard stimulus occurs, the evoked response pattern is altered. Creating separate averages of single responses to standard stimuli and deviant stimuli allows the MMN to be visualized as a negative deflection in the deviant waveform relative to the standard waveform.

Much of the MMN's appeal stems from the fact that it is passively elicited, requiring neither attention to the evoking stimuli nor a behavioral response from the listener. Because the presence of an MMN indicates that mechanisms within the central auditory system have differentiated the deviant stimulus from the standard stimulus, independent of listener attention or response, the MMN has been conceptualized as an electrophysiologic correlate of suprathreshold auditory discrimination ability (Näätänen et al, 1978; Kraus et al, 1993b, 1996; Kraus, 1996).

Although the MMN is used only as a research tool at the present time, there is hope that it will have utility as a clinical tool for objectively assessing the perceptual abilities of individual listeners. For example, it is possible that the MMN could be used to assess the auditory discrimination abilities of individuals who cannot be tested using more conventional means. It also is conceivable that absence of an MMN in a particular stimulus context could be used to identify individuals with deficits at the auditory level of processing (e.g., the level at which an acoustic waveform is transformed into a neurally encoded representation) as distinct from those with deficits that originate at higher levels (Dalebout and Stack, 1999). In the latter

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case, the MMN would function as a diagnostic test and information about its performance characteristics would be necessary.

The MMN is not without limitations, perhaps the most serious of which is a signal-to-noise ratio (SNR) frequently poor enough to obscure the response in individual listeners. The poor SNR is the result of several converging factors, including (but not limited to) the small magnitude of the response, the considerable physiologic noise within the bandpass filter settings used to record the response, the subtraction procedure from which the response typically is derived, and the heavy dependence of the response on the listener's level of alertness. To a large extent, noise is averaged out in group data, but the responses of individual listeners tend to remain noisy due to the smaller number of single trials included in the averaged waveforms. Despite attempts to control factors known to degrade the SNR (e.g., providing the listener with an activity designed to minimize drowsiness, using automatic artifact rejection to eliminate contaminated single trials, increasing the number of responses to deviant stimuli included in averaged responses, etc.), the interpretation of data from individual listeners remains difficult (Kurtzburg et al, 1995; Lang et al, 1995; McGee et al, 1997; Ponton et al, 1997). As a result, validation (i.e., confirmation) of the MMN response is particularly important.

In the case of the more familiar auditory brainstem response (ABR) and middle latency response (MLR), response validity is judged by the presence of an expected waveshape that can be replicated (McGee et al, 1997). This requires an evoked response that is sufficiently (a) robust to be obtained within a reasonable amount of time and (b) invariant to be obtained in subsequent testing. McGee et al concluded that the ABR and MLR meet both requirements. Cortical evoked responses are more variable on test–retest due to a number of factors, not the least of which is the flexible nature of sensory processing at the cortical level. That is, as higher levels of the auditory system are engaged, inputs are not automatically switched to outputs; instead, processing is dynamic, subject to the formation of different hypotheses about the environment and the allocation of available resources to various tasks (Dalebout and Robey, 1997). Nonetheless, the cortical potentials N_1 and P_{300} are robust enough to allow valid responses to be readily recognized (McGee et al, 1997) and sufficiently invariant to be replicable (Dalebout and Robey, 1997). In contrast, the MMN is not robust enough to make replication practical as a means of validation, and its stability has yet to be adequately determined.

McGee et al (1997) evaluated a variety of techniques for validating the MMN response in individual listeners. The techniques included methods based on the measurement of waveform characteristics, mathematical analyses of the waveform, and statistical tests. Three experimental conditions were used for data collection: a control condition in which standard and deviant stimuli were identical, a relatively easy mismatch condition, and a more difficult mismatch condition. The control condition allowed the false positive rate (i.e., the rate at which the MMN was identified in the absence of a stimulus contrast) associated with each set of validation criteria to be determined. Stimuli were drawn from a synthetic speech continuum that ranged from /wɑ/ to /bɑ/. Listeners were 86 normal children; however, data compared across the three conditions were not necessarily obtained from the same listeners. Behavioral discrimination data for individual listeners were not provided.

McGee et al (1997) compared 17 combinations of validation criteria on the basis of "hit rate" (i.e., the percentage of presumably correct identifications of the MMN in the contrast conditions), "false alarm rate" (i.e., the percentage of incorrect identifications of the MMN in the control condition), and d' value. d' is a statistic that incorporates both hit rate and false alarm rate; more accurate tests are associated with larger d' values (Swets, 1964). The most advantageous validation method was one in which criterion values for waveform characteristics were used. Specifically, an onset latency criterion of less than 235 msec combined with an area criterion of greater than 225 msec $\times$ μV produced a hit rate of 71.1 percent for the easy contrast condition, a hit rate of 62.7 percent for the difficult contrast condition, and a false alarm rate of 15.8 percent for the control condition. Resultant d' values were 1.56 and 1.33 for the easy and difficult contrast conditions, respectively. Three other combinations of validation criteria produced d' values that were slightly better; however, the larger d' values were attributable to lower false alarm rates, achieved at the expense of undesirably low hit rates (26%, 27%, and 57% in the easy contrast condition).

Information regarding identification of the MMN in the responses of normal listeners is critical for evaluating its clinical potential. For example, if the hit rate of the MMN is no better than 70 percent (Kurtzburg et al, 1995; Lang et al, 1995; McGee et al, 1997), the ability to identify an auditory perceptual disorder based on its absence will be limited since the MMN will not be detected in 30 percent of normal listeners. Similar findings led Lang et al (1995) to conclude that "a missing MMN apparently cannot be interpreted as a pathologic finding in adults" (p. 129). Moreover, if the false alarm rate is as high as 16 percent, test performance will be degraded further because approximately 16 percent of listeners with auditory perceptual deficits will be classified as normal.

The purpose of the present study was to estimate the probabilities of correctly and incorrectly identifying the MMN in the individual responses of normal listeners. That portion of the McGee et al (1997) study in which criterion values for MMN onset latency and area were used to validate responses was repeated using adults as listeners. The McGee et al study was extended by comparing MMN findings to corresponding behavioral discrimination data in individual listeners.

METHOD

Listeners

Thirty college students served as listeners in the study (mean age = 23 years). Each was in good health with a negative history of learning disabilities, neurologic disorders, and significant head trauma (defined as head trauma resulting in unconsciousness for a period of 2 minutes or longer). In addition, each had normal hearing sensitivity bilaterally as defined by pure-tone thresholds of 20 dB HL or better at 500 through 8000 Hz.

Stimuli

Standard and deviant stimuli were taken from a nine-item, five-formant continuum varying in place of articulation from /da/ to /ga/, synthesized using a modified version of the Klatt (1980) speech synthesizer on a personal computer. Stimulus parameters were based on the description provided by Sharma et al (1993) and have been described elsewhere (Dalebout and Stack, 1999). All stimuli were synthesized at a 10-kHz sampling rate with 16-bit quantization. Syllables on the continuum differed only in the starting frequency of the second and third formant (F2, F3) transitions. The endpoints of the continuum were modeled after the control stimuli described in the study of Walley and Carrell (1983). The center frequencies of the formants for the steady-state vowel were set at 720 Hz (F1), 1240 Hz (F2), 2500 Hz (F3), 3600 Hz (F4), and 4500 Hz (F5). The starting frequency of F1 was 220 Hz and the transition duration to steady-state frequency was 35 msec. The F2 starting points varied in equal steps from 1700 Hz (endpoint of /da/) to 1640 Hz (endpoint of /ga/). The starting frequencies for F3 varied in equal steps from 2800 Hz (endpoint of /da/) to 2100 Hz (endpoint of /ga/). The transition durations for F2 and F3 were 40 msec. The trajectories of the first three formants were linear from the starting point to the steady-state value of the vowel. The fourth and fifth formants were steady state throughout. The total stimulus duration was 90 msec. Fundamental frequency began at 103 Hz, increased linearly to 125 Hz at 35 msec, then decreased to 83 Hz after 55 msec. The peak amplitudes of the stimuli were normalized to be identical. The amplitude of the voicing was constant for 80 msec, then fell linearly to 0 dB in the last 10 msec. The parameters of the experimental stimuli are shown in Figure 1.

Token pairs were taken from this continuum to create the three stimulus conditions used in the study. The continuum endpoints (i.e., steps 1 and 9) formed the "easy" contrast condition,

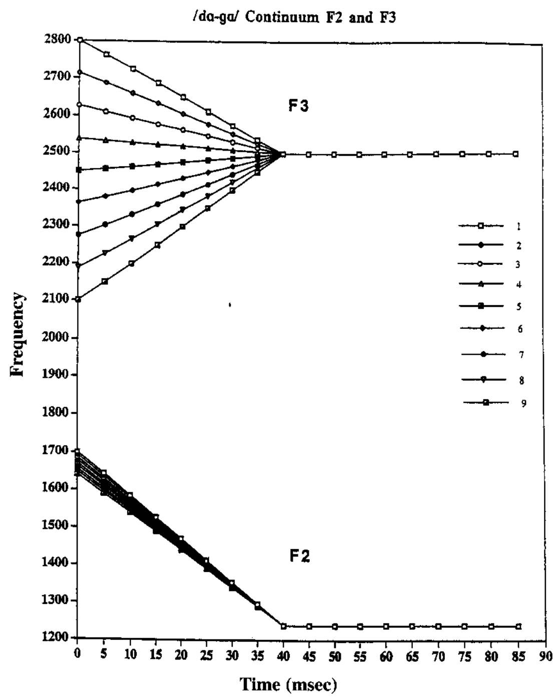

Figure 1 Parameters of the nine synthetically generated syllables forming the experimental /da/-/ga/ stimulus continuum.

while steps 3 and 7 were chosen to form the "difficult" contrast condition. Previous testing in our laboratory has indicated that the 3–7 contrast straddles the phonemic boundary of nearly all normal listeners, rendering discrimination difficult but better than chance. The third token pair was composed of identical syllables (both step 9) and formed the control condition.

Prior to initiation of the study, listeners were coded by number. The three stimulus conditions were coded in a manner that allowed presentation order to be counterbalanced during data collection but did not allow waveforms to be matched to stimulus condition during data analysis.

Mismatch Negativity

Recording parameters and conditions were similar to those that have been described previously (Dalebout and Stack, 1999). Data acquisition and stimulus presentation were accomplished using NeuroScan software (SCAN and STIM packages) on two personal computers. During data collection, listeners reclined in a sound-attenuating, electromagnetically shielded chamber manufactured by the Industrial Acoustics Company. To maintain alertness and minimize attention to the test stimuli, listeners watched videotaped movies of their own choosing. Videotape audio levels averaged 40 dB SPL (A-weighted scale), measured at the listener's left ear. Experimental stimuli were presented to the right ear at 72 dB SPL through an Etymotic ER-3A insert earphone. The interstimulus interval was 1.1 seconds and the probability ratio between standard and deviant stimuli was 85/15. Stimuli were presented in pseudorandom sequences with the constraints that (a) the sequence always started with at least three standard stimuli and (b) a minimum of three standard stimuli separated deviants thereafter. Evoked responses were recorded at F_z, C_z, and both mastoids, with the nose as reference and the forehead as ground. Eye artifact was recorded with a bipolar electrode montage, using supraorbital and infraorbital electrodes around the left eye. Single trials contaminated by eye movement (± 100 μV) were eliminated from the averaged responses.

The recording window included a 100-msec prestimulus period and 450 msec of poststimulus time. A total of 275 points was averaged in a 550-msec time window, resulting in a sampling rate of 500 points/sec. Evoked responses were bandpass analog filtered online from 0.1 to 100 Hz. Single trial responses were referenced to the prestimulus baseline prior to averaging. Responses elicited by standard stimuli and deviant stimuli were averaged separately, within stimulus condition, for each listener. Responses to standard stimuli following deviants were excluded from standard response averages. After averaging, linear trends were removed from the data and responses were digitally lowpass filtered at 30 Hz. Finally, each listener's standard waveform was subtracted from the corresponding deviant waveform to create difference waveforms for each condition.

Waveforms were analyzed for the presence of a MMN by examiners blind to the evoking stimulus condition. Although data were recorded from several electrode sites, only F_z data are reported here. The MMN was defined as (a) a relative negativity following N_1 onset (N_1 was required in both the standard and deviant waveforms), with (b) an onset latency of less than 235 msec and (c) an area greater than 190 msec $\times$ μV. These criterion values were based on the model provided by McGee et al (1997) but were specific to our data set. To account for the differences in stimuli, recording parameters, and subject sample that exist between the two studies, the criterion values that produced the most desirable d' value in our data set were used.

MMN onset and offset were defined as the positive peaks preceding and following the visually identified negativity in the difference waveform (Kraus et al, 1993d; Sharma et al, 1993). Selection of these peaks was based on an examination of the difference waveform, as well as the standard and deviant waveforms from which it was derived. An example of a visually identified MMN is shown in Figure 2. Area was measured by drawing a line between the onset and offset points, then calculating the enclosed area in msec $\times$ μV (Kraus et al, 1993a, c, d, 1995; Sharma et al, 1993; Tremblay et al, 1997). For this computation, waveforms were converted to ASCii format and exported to a spreadsheet for analysis.

Examiners conferred until agreement about the presence or absence of a MMN in each difference waveform had been reached. After decisions were recorded for every waveform, the stimulus condition in which each of the responses had been elicited was revealed.

Behavioral Performance

Listeners completed a traditional two-alternative, forced-choice, same/different discrimination task following MMN data recording.

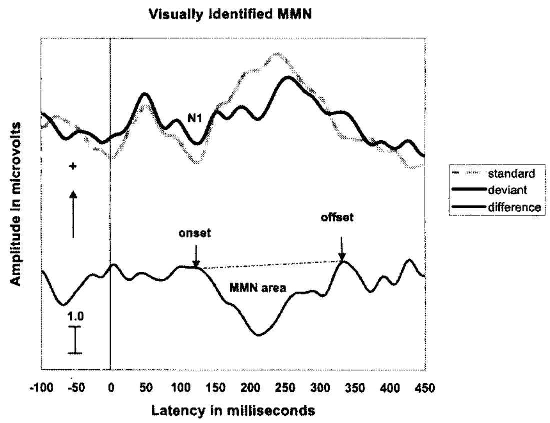

Figure 2 Example of a MMN response from an individual listener. The MMN is evident in the deviant and difference waveforms (onset latency < 235 msec; area > 190 msec × μV). In this and all subsequent figures, positive polarity is displayed as up-going.

The behavioral task was administered after MMN data collection in an effort to simulate anticipated clinical conditions, in which prior exposure to the stimulus contrasts would not occur. Presentation order was counterbalanced across listeners and conditions. Stimuli were presented in pairs and listeners were asked to decide if the tokens forming each pair were the same token presented twice or two different tokens. Listeners marked "same" or "different" on an answer sheet after listening to each pair. A total of 120 "different" pairs (i.e., 60 1–9 pairs and 60 3–7 pairs) and 120 "same" pairs (i.e., 60 9–9 pairs, 20 1–1 pairs, 20 3–3 pairs, and 20 7–7 pairs) was presented. Following data collection, hit rates and false alarm rates were calculated for each listener in each of the two contrast conditions, and a false alarm rate was calculated for the control condition.

RESULTS

Behavioral Results

Behavioral performance on a same/different discrimination task is best characterized by both hit rate (i.e., the percentage of trials in which a listener correctly indicates that a "different" pair is different, divided by the total number of different pairs) and false alarm rate (i.e., the percentage of trials in which a listener incorrectly indicates that a "same" pair is different, divided by the total number of same pairs). d' incorporates hit rate and false alarm rate into a single statistic that can be used to describe test performance (Swets, 1964). Behavioral performance in the "easy" contrast condition, the "difficult" contrast condition, and the control condition is characterized for the present study by hit rate, false alarm rate, and d' in Table 1. As expected, behavioral discrimination of the easy contrast was excellent (mean hit rate = 94%, mean false alarm rate = 3%, mean d' = 3.43) and discrimination of the difficult contrast was relatively poor (mean hit rate = 66%, mean false alarm rate = 7.5%, mean d' = 1.81). The false alarm rate in the control condition was low (mean = 3.5%).

Mismatch Negativity

MMN hit rate was defined as the percentage of presumably correct identifications of the MMN in each contrast condition, divided by the total number of observations in each of those conditions (n = 30). False alarm rate was defined as the percentage of incorrect identifications of the MMN in the control condition, divided by the total number of observations in that condition (n = 30). Hit rates and d' values for the two contrast conditions and the false alarm rate for the control condition are shown in Table 2. In the easy contrast condition, 12 MMNs were identified among 30 observations (MMN hit rate = 40%). In the difficult contrast condition, six MMNs were identified among 30 observations (MMN hit rate = 20%). In the control, six MMNs were identified among 30 observations (MMN false alarm rate = 20%). The hit rate for the easy contrast condition (40%) combined with the false alarm rate for the control condition (20%) to yield a d' value of 0.58. The hit rate for the difficult contrast condition (20%) combined with the false alarm rate (20%) to yield a d' value of 0.

The order in which stimulus conditions were presented was counterbalanced across listeners. The relationship between presentation order and MMN identification is summarized in Table 3. An MMN was identified seven times in the condition presented first to listeners, eight times in the condition presented second, and nine times in the condition presented last. Thus, it is unlikely that fatigue, habituation, or learning had an important effect on the rate of MMN identification.

An MMN was identified in response to both contrasts in only two listeners; in other words, listeners who demonstrated MMNs in the easy contrast condition were not necessarily the same as those who demonstrated MMNs in the difficult contrast condition, and vice versa. Some

Table 1 Behavioral Performance Characterized by Hit Rate (HT), False Alarm Rate (FA), and *d'* for the Two Contrast Conditions

	Stimulus Condition						
	Easy Contrast			*Difficult Contrast*			*Control*†
Listener	*HT (%)*	*FA (%)*	*d'*	*HT (%)*	*FA (%)*	*d'*	*FA (%)*
1	98	3	3.9	78	10	2.1	3
2	97	0	>4.2*	57	13	1.3	0
3	67	6	2.0	73	8	2.0	8
4	95	9	3.0	95	13	2.8	10
5	98	0	>4.4*	88	3	3.1	0
6	97	8	3.3	93	8	2.9	10
7	100	1	>4.6*	35	10	0.9	2
8	100	0	>4.6*	75	5	2.3	0
9	100	5	>4.0*	57	23	0.9	7
10	97	0	>4.2*	22	0	>1.5*	0
11	100	0	>4.6*	95	3	3.5	0
12	98	3	3.9	47	25	0.6	3
13	100	8	>3.7*	18	0	>1.4*	10
14	100	6	>3.9*	97	10	3.2	8
15	100	0	>4.6*	83	5	2.6	0
16	98	0	>4.4*	95	5	3.3	0
17	53	0	>2.4*	55	8	1.5	0
18	100	0	>4.6*	72	3	2.5	0
19	100	4	>4.1*	62	8	1.7	5
20	100	0	>4.6*	70	5	2.2	0
21	83	6	2.5	0	0	0	7
22	98	0	>4.4*	48	8	1.4	0
23	97	0	>4.2*	98	0	>4.4*	0
24	70	14	1.6	60	15	1.3	18
25	100	1	>4.6*	35	0	>1.9*	2
26	100	5	>4.0*	92	5	3.0	7
27	98	0	>4.4*	73	3	2.5	0
28	95	3	3.5	58	18	1.1	3
29	95	1	4.0	87	3	3.0	2
30	93	0	>3.8*	58	8	1.6	0
Range	53–100	0–14	1.6 > 4.6	0–98	0–25	0 > 4.4	0–18
Mean (SD)	94 (11)	3 (4)		66 (26)	7.5 (6)		3.5 (4.5)
d' based on mean HT and FA			3.43			1.81	

**d'* cannot be precisely determined when HT > 99% and/or FA < 1%.
†Performance in the control condition can be characterized by FA only.

listeners had identifiable MMNs in the difficult contrast condition but not in the easy contrast condition, although all had better behavioral performance in the latter. Difference waveforms (from the easy and difficult contrast conditions) for one such listener are shown in Figure 3. Figure 4 shows a set of difference waveforms from another listener in which an MMN was identified in the control condition (i.e., a false pos-

Table 2 Hit Rates (HT), False Alarm Rate (FA), and *d'* Values Associated with MMN Identification

Condition	*MMNs Identified*	*HT (%)*	*FA (%)*	*d'*
Easy contrast	12/30	40		0.58
Difficult contrast	6/30	20		0.00
Control	6/30		20	

Table 3 Relationship between Presentation Order of Stimulus Condition and MMN Identification

Presentation Order	*MMNs Identified*	*Rate of MMN Identification(%)*
First condition	7/30	23
Second condition	8/30	27
Third condition	9/30	30

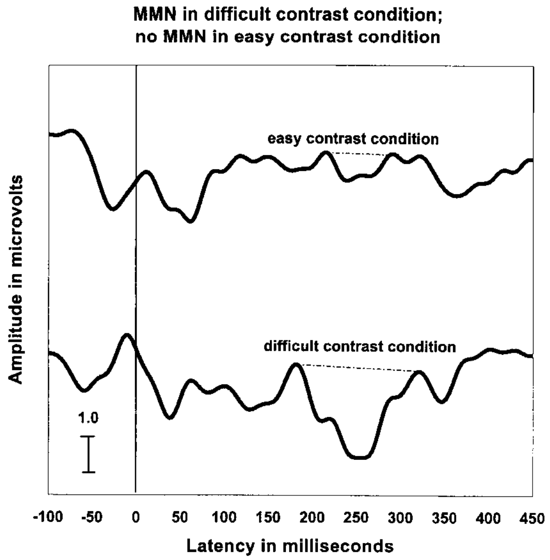

Figure 3 Difference waveforms for an individual listener recorded in the easy and difficult contrast conditions. An MMN was identified in the difficult contrast condition but not in the easy contrast condition. Behavioral discrimination performance: HT = 98%, FA = 0%, $d' > 4.37$ in the easy contrast condition; HT = 95%, FA = 5%, $d' = 3.28$ in the difficult contrast condition.

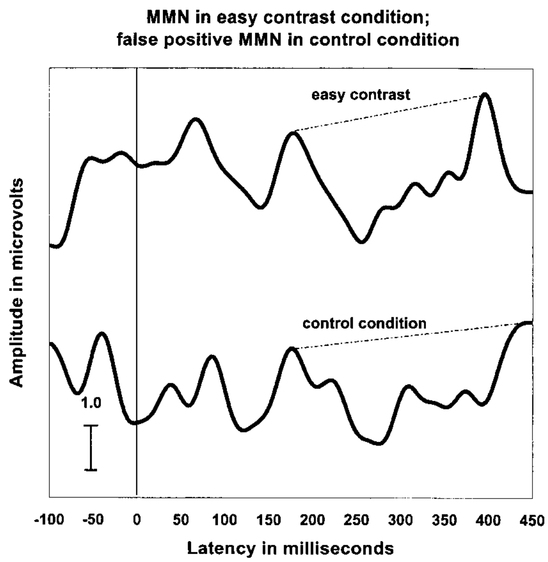

Figure 5 Difference waveforms for an individual listener recorded in the easy contrast and control conditions. The MMN identified in the control condition appears to replicate the MMN identified in the easy contrast condition. Behavioral discrimination performance: HT = 95%, FA = 9%, $d' = 2.98$ in the easy contrast condition; FA = 10% in the control condition.

itive response) but not in the easy contrast condition. Figure 5 shows a set of difference waveforms from yet another listener in which the "MMN" identified in the control condition deceptively appears to replicate the MMN identified in the easy contrast condition.

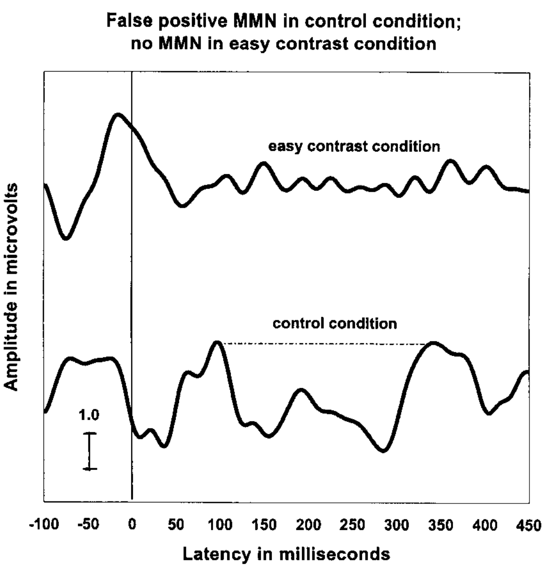

Figure 4 Difference waveforms for an individual listener recorded in the easy contrast and control conditions. An MMN was identified in the control condition but not in the easy contrast condition. Behavioral discrimination performance: HT = 100%, FA = 8%, $d > 3.72$ in the easy contrast condition; FA = 10% in the control condition.

Relationship between Behavioral Performance and Identification of the MMN

The relationship between MMN findings and behavioral discrimination performance is summarized in Table 4, in which behavioral hit rates are rank ordered from highest to lowest in each of the two contrast conditions. For this analysis, hit rates, rather than d' values, were used since the mismatch response reflects only the physiologic detection of acoustic differences among signals. False alarm responses presumably are dependent on cognition and attention and therefore were considered irrelevant in a comparison between behavioral discrimination ability and presence/absence of the MMN. Indeed, three of the six listeners with false positive MMNs in the control condition had behavioral false alarm rates of 0 percent.

In the easy contrast condition, 26 of 30 listeners had behavioral hit rates between 90 and 100 percent. Of those, nine listeners demonstrated MMN responses. However, the two listeners with the lowest behavioral hit rates (53%, 67%) also demonstrated negativities that met the MMN validation criteria imposed in this study.

Table 4 Relationship between Behavioral Performance and Identification of the MMN

Stimulus Condition			
Easy Contrast		*Difficult Contrast*	
HT (%)	*MMN*	*HT (%)*	*MMN*
100	+	98	
100	+	97	
100		95	+
100		95	
100		95	
100		93	
100		92	+
100		88	
100		87	
100		83	
100		78	
100		75	
98	+	73	
98	+	73	
98		72	
98		70	
98		62	
98		60	
97	+	58	+
97	+	58	
97		57	
97		57	
95	+	55	
95	+	48	+
95	+	47	
93		35	+
83	+	35	
70		22	
67	+	18	
53	+	0	
Mean = 94%	N = 12	Mean = 66%	N = 6
Median = 98%		Median = 71%	

In the difficult contrast condition, seven listeners had behavioral hit rates between 90 and 100 percent. Of those, two demonstrated MMNs. However, four listeners with poor behavioral hit rates (35%–58%) also demonstrated negativities that met all validation criteria.

Combining both contrast conditions resulted in a total of 33 observations in which behavioral hit rate exceeded 90 percent. An MMN was identified in 11 of those 33 observations. This implies an MMN hit rate of only 33 percent among observations in which behavioral discrimination scores were excellent. There were 13 observations in which behavioral hit rates were poor (0%–58%). MMNs were identified in five of those observations. If the MMN is viewed as an electrophysiologic correlate of behavioral discrimination ability, this suggests a false alarm rate of 38 percent among observations in which behavioral discrimination scores were poor. However, since behavioral responses are affected by nonauditory factors such as attention and cognition, the MMN may be present even when behavioral performance is poor. Moreover, it is possible that the MMN may reflect the detection of acoustic differences not consciously perceived by listeners in behavioral tasks (Dalebout and Stack, 1999).

DISCUSSION

Stimulus and recording conditions were more rigorously controlled in this study than would be typical of a clinical situation. Nonetheless, the accuracy with which the MMN could be identified cannot be considered different than chance. For the easy contrast condition, the d' value reflecting accuracy of MMN identification was 0.58. For the difficult contrast condition, $d' = 0$. Clearly, values such as these would preclude use of the MMN as a diagnostic tool for identifying patients with a disorder. Moreover, the lack of correspondence between behavioral discrimination scores and the presence/absence of the MMN was disappointing.

As shown in Table 5, hit rates from the present study are markedly different from those reported by McGee et al (1997). The fact that adults, rather than children, served as listeners in the present study may have contributed to this difference, since it has been reported that the MMN is of greater magnitude in children than adults (Kraus et al, 1992, 1993a). However, drawing the criterion values used for response validation in the present study from our data set should have minimized the effect of this difference. It also has been suggested that the MMN is more likely to be detected in the responses of children than in those of adults (Lang et al, 1995).

Another explanation for the poor accuracy of MMN identification in the present study could be an unfavorable SNR in the responses of some listeners. Data acquisition variables that have sometimes been linked to SNR include the total number of single trials recorded from a listener in each condition, the proportion of trials rejected due to artifact, and the number of responses to deviants included in a listener's averaged responses. In this study, data recording continued in each stimulus condition until no less than 1800 and no more than 1850 single trials uncontaminated by eye artifact had been collected for each listener. Thus, it is unlikely that

Table 5 Results from the Present Study and Results Reported by McGee et al (1997)

	HT (%)		*FA (%)*	*d′*	
	Easy	*Difficult*	*Control*	*Easy*	*Difficult*
Present study	40	20	20	0.58	0.00
McGee et al (1997)	70	63	16	1.56	1.33

this variable influenced the rate of MMN identification. However, more trials were rejected for some listeners than for others. Although not included in the averaged responses, the proportion of trials rejected is of some interest because it may reflect the overall activity level of a listener during data acquisition. That is, listeners who have more trials rejected may also have more noisy trials included in their averaged responses. In this study, there was no obvious relationship between the proportion of rejected trials and identification of the MMN. In other words, the responses in which MMNs were identified were not necessarily the responses in which a smaller (or larger) proportion of single trials had been rejected. Similarly, there appeared to be no relationship between the number of responses to deviant stimuli included in an averaged response and identification of an MMN, at least within the relatively narrow range found in this study (range of deviants included in averaged responses = 252–305). These findings were not unexpected, since none of these factors directly determines SNR or response quality (Elberling and Don, 1984; Turetsky et al, 1988).

More direct approaches to controlling response quality include the use of statistical techniques designed to quantify SNR and improve response identification (e.g., Elberling and Don, 1984; Raz et al, 1988; Turetsky et al, 1988; Ponton et al, 1997). When SNR can be quantified, it becomes possible to exclude from averaged responses those single trials in which the SNR is unacceptable or to exclude from grand averaged responses those subaverages in which the SNR is poor. The Fsp technique, for example, is a statistical approach for quantifying the SNR of the ABR developed by Elberling and Don (1984) and adapted for use with the MMN by Kurtzburg et al (1995). Unfortunately, Kurtzberg et al reported that the smaller number of single trials collected for the MMN (relative to the ABR) precludes computation of a satisfactory noise estimate based on this particular technique. A different quantitative approach was described by Ponton et al (1997), who developed a technique for statistical identification of the MMN in which a relatively noise-free representation of the response is derived. In this method, time-integrated responses evoked by standard and deviant stimuli are compared at a single time point. A variation of this method was included in the comparison of validation strategies reported by McGee et al (1997). However, due to a high false alarm rate (28.9%), the reported d' value was relatively low (1.18). Clearly, continued development and refinement of techniques for enhancing SNR and response identification remains a formidable challenge.

Other variables that contribute to differences in outcome among studies include the methods used to identify, measure, and validate MMN responses. For the purpose of this discussion, identification techniques are those used to detect the MMN in the difference waveform. Measurement techniques are used to quantify the MMN using indices such as onset and offset latency, peak latency, magnitude, amplitude, and duration. Validation techniques are used to ascertain whether a true response has been obtained (McGee et al, 1997). A review of the literature suggests that strategies for identifying, measuring, and validating the MMN have not been adequately described and certainly are not standardized. For example, reports from some laboratories describe techniques for identifying the MMN (e.g., visually identifying a negative deflection in the difference waveform based on an examination of the standard and deviant waveforms from which it was derived, using the method described by Ponton et al [1997] for statistical detection of the MMN, or applying another algorithm that can be justified). In place of identification strategies, reports from other laboratories describe measurement techniques in which mean amplitude within a specified time window (or within an interval surrounding the most negative peak occurring in a specified time window) is computed and used to make statistical comparisons of the "MMN" across listeners, experimental conditions, electrode sites, etc. An advantage of the latter method is that it is less subjective than visual detection of the MMN; however, it also seems likely to result in false positive identifications since the probability of mean voltage being negative within any given time frame is considerably greater than zero.

Another method for measuring the MMN that is frequently reported in the literature involves the visual identification of onset and offset points to represent the beginning and end of the MMN component, respectively. On occasion, onset and offset have been defined as the positive peaks preceding and following the visually identified MMN. From these points, onset latency, offset latency, duration, and area can be computed. However, even this technique lacks sufficient detail to allow results to be compared across investigations. Without a detailed set of rules governing the selection of onset and offset points, decisions about whether an MMN is "present" or "absent" in a given waveform are subjective. For example, it is likely that different decisions about the location of onset and offset points contributed to the differences in outcome observed between the present study and the one reported by McGee et al (1997). Figure 6 illustrates how the selection of different onset points can result in different outcomes relative to the presence or absence of an MMN, particularly when the difference waveform is analyzed in isolation (i.e., without comparing it to the standard and deviant waveforms from which it was derived).

Also lacking in the literature are descriptions of the mathematical techniques used to compute area. This is particularly important when the technique used to validate responses involves area computations, as was the case in the present study. It is difficult to compare the MMN across investigations when validation is based (in part) on area and the method for computing area is not described.

Finally, a review of the MMN literature reveals that, in many laboratories, the presence of a MMN is not validated with any technique. The paper by McGee et al (1997) addressed the need for validation, described a number of validation techniques, and demonstrated the relative performance of each. The validation strategy used in the present study was selected because it had been directly compared to a number of others and was shown to be superior (McGee et al). Nonetheless, this strategy is not compatible with many of the MMN measurement

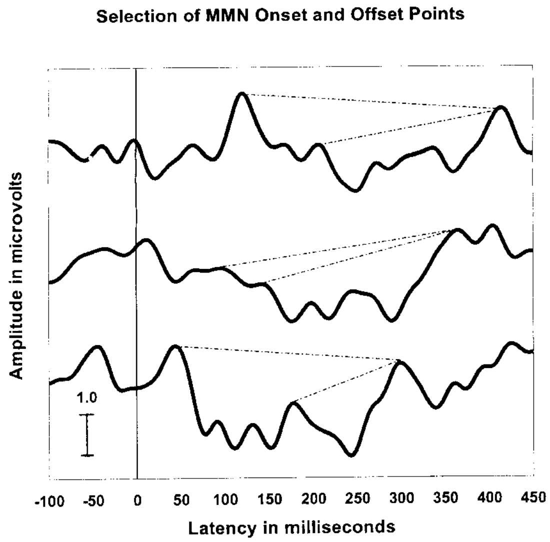

Figure 6 Illustration of how selection of the MMN onset point in the isolated difference waveform impacts MMN identification, measurement, and validation. In each of the three examples, the choice between the two onset points determines identification outcome.

techniques reported elsewhere in the literature (e.g., those based on a computation of mean amplitude within a specified time window), precluding a comparison of results from a variety of different laboratories.

In conclusion, it is essential that identification, measurement, and validation protocols be made explicit so they may be compared and evaluated by independent investigators. Clear and complete descriptions of such protocols will allow researchers to move forward based on collective experience. Only when the methods used for data analysis are adequately described can the viability of the MMN as a clinical tool be properly judged.

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