Quantification Technique for the Middle Latency Response

Herbert Jay Gould*,
Margie R. Crawford†
Maurice I. Mendel*
Scott L. Dodson†

Abstract
Few objective analysis techniques have been developed for, or applied to, the auditory evoked middle latency response (MLR). This report demonstrates the applicability of the Fsp statistical technique (Elberling and Don, 1984) to the MLR time domain. Subjects for this study were 10 normal hearing young adults. The stimuli were 60, 40, 20 dB nHL clicks and a NS control. Evoked responses were obtained as a series of 10,000 individual traces for each stimulus presentation and analyzed off line to determine the applicability of the Fsp technique. In addition, the effects of filtering and time window size were examined to determine the optimum collection characteristics for the Fsp analysis method. The results indicate that the Fsp technique is a viable tool for estimating signal-to-noise characteristics of the MLR. When using the Fsp technique with the MLR the high-pass filter should be set to 20 Hz so that a 50-msec time window can be used.

Key Words: Auditory middle latency response (MLR), Fsp

Few objective analysis techniques have been developed for, or applied to, the auditory evoked middle latency response (MLR). Mendel, Saraca, and Gerber (1984) examined interjudge validity and intrajudge reliability for identification of MLR peak latency and observed that intensity level was the only factor that had a significant effect on interjudge scoring validity. In 1988, McGee et al developed a strategy for analyzing the MLR waveform. They utilized area under the waveform peaks as an indication of total neural activity involved in peak generation. This technique provided a parametric description of the middle components but did not quantify the underlying signal-to-noise ratio (S/N).

Don and co-workers proposed a method that they labeled the Fsp technique (Don et al, 1984; Elberling and Don, 1984; Elberling and Don, 1987). This technique (see appendix) estimates and controls the final S/N in an averaged auditory brainstem response (ABR). Control of the final S/N in the ABR is established by setting a S/N as the criterion for stopping the averaging process rather than using an arbitrary number of stimulus presentations. They demonstrated that the background noise level in the ABR was constant across the time epoch. This meant that for any given latency in the response, the noise would vary about the deterministic signal (i.e., the evoked potential) and the variability would represent the background noise level. The ideal averaged evoked response assumes that the noise has been eliminated; therefore, the variance of the averaged response represents the variability within the signal across the time window. Using the two variances, an F ratio can be calculated that statistically describes the separation of the signal and noise levels (Elberling and Don, 1984).

A similar technique, using a multipoint estimate (Fmp) of background noise, has been applied to the late response (Gould et al, 1989;
Mendel et al, 1989). The multipoint estimate was required as the noise variance computed at different latencies in the late response time frame can be statistically different. In the Fmp technique the average of the variances at all sampled latencies is used as the measure of background noise. This technique although computationally more demanding is required because the noise level is not constant throughout the average. As two different techniques were required for the early and the late responses, we were interested in comparing the methods to determine which was most appropriate for the middle latency response. In addition, one of the major issues surrounding the middle components is the determination of appropriate filter settings for elicitation of the response. Inappropriate filter settings may be a source of variability in the middle component waveform. Previous investigations of filter settings examined the effects of analog and digital filtering on the waveform as well as attempted to determine the appropriate bandwidth of analysis (Lane et al, 1974; Scherg, 1982; Kavanagh et al, 1984; Musiek et al, 1984; Kavanagh and Domico, 1986, 1987; McGee et al, 1988). The present study was designed to compare the Fsp and Fmp statistics for determining the signal-to-noise ratio of the averaged middle latency responses. In addition, the effect of filter bandwidth on the resulting Fsp values was examined.

METHOD

Ten young adults with normal hearing were recruited as subjects for the study. Pure-tone thresholds were better than 15 dB (re: ANSI, 1989) for all audiometric frequencies. An interview indicated no history of head trauma, neurologic involvement, or recent middle ear disease. The ear tested was counterbalanced across subjects. Informed consent was obtained prior to testing.

The stimuli for the study were 100-μsec alternating polarity electrical square waves transduced through a 300-ohm Etymotic ER-3A insert receiver. The click rate was 7.7 per second. Four experimental conditions were utilized; 60, 40, 20 dB nHL stimulus presentation levels and a no-stimulus condition. The nHL level was determined from a set of 126 normal hearing adults seen in the Auditory Electrophysiology Laboratory at the Memphis Speech and Hearing Center. A signal of 60 dB nHL has a peak to peak deflection equivalent to an 85-dB 1000-Hz sine wave.

Auditory evoked responses were collected from the vertex referenced to the mastoid ipsilateral to the signal. The forehead served as ground. The response epoch was 100 msec sampled at 2500 samples per second. The electroencephalogram was band-pass filtered between 10 and 1000 Hz with a 6-dB per octave rolloff using the analog filter of the amplifier. A series of 10,000 epochs was collected and stored as individual traces on an 80386 based microcomputer for each experimental subject and condition. The traces were then transferred to a Vaxstation 3200 and stored off-line for analysis.

Statistical analysis was performed to compare Fsp or Fmp for estimating the presence of the MLR. A subsequent analysis was then undertaken to demonstrate effects of the epoch time window and filtering on the Fsp/signal-to-noise ratio estimate.

RESULTS AND DISCUSSION

Quantification Techniques

In order to perform either the Fsp or Fmp technique, the assumption is made that the signal is stationary in a gaussian distributed background noise. To test the assumption of a gaussian distributed noise, the Shapiro-Wilk statistic (SAS, 1990) was used to determine if the sample distribution was gaussian at a single latency within the response. Due to the size of the data set (400 megabytes), samples were randomly drawn across experimental conditions and subjects in blocks from successive epochs. Block sizes of 50, 100, 200, 300, 400, or 500 data points were used to determine if a minimum number of epochs was required to reach normality. The tested distributions did not differ from normal at the 0.05 probability level.

A second assumption is made when using the Fsp technique that is not necessary with the Fmp method. This assumption is that the variance at any latency is statistically the same as any other latency. In other words, the noise level is not significantly different for any given point across epochs. To test this assumption, the Fmax statistic was used (Kirk, 1968). No statistically significant difference was found in the variance between the time points in any experimental condition for any subject at the 0.05 probability level. This implies that the Fsp technique can be applied to the MLR and that the Fmp technique is not required.
As an additional method of confirming the similar outcomes of the two techniques, Fsp and Fmp statistics were performed on blocks of 200 epochs. The Fsp and Fmp distributions for the no-stimulus condition are shown in Figure 1. The distribution of values is similar for the two techniques. This supports the finding with the Fmax statistic that the variance computed at a single latency provides an adequate estimate of the noise level in the MLR average. Therefore, there is no advantage in using the Fmp.

The growth of the Fsp at various stimulus presentation levels was determined. As shown in Figure 2, the S/N grows at a faster rate with increasing stimulus intensity. This finding was expected as the amplitude of the MLR is directly related to the stimulus presentation level. In addition, the S/N of the averaged response improves by increasing the number of stimulus presentations. Again this is expected from sampling theory. It should be noted that there was a large difference between subjects in terms of S/N for any presentation level or number of stimulus presentations. Figure 3 demonstrates the mean and 99 percent confidence interval for all 10 subjects at a 60-dB nHL stimulus level.

The interesting point of Figure 3 is that the maximum Fsp value for the MLR, at 60 dB nHL, is well below that reported by Elberling and Don (1984) for a single subject during the ABR. When the accumulating averages were examined, a possible explanation for this discrepancy was found. As shown in Figure 4, the major peaks, Na, Pa, and Nb of the MLR occur in the first half of the 1.00-msec time window. This means that the second half of the window is approaching the variance of the noise with the accumulating average. Therefore, the second half of the time window is counterbalancing the first half, leading to an underestimation of the S/N in the response time region. Unfortunately, the Fsp and Fmp techniques are restricted by the interaction of the epoch duration and spectral content of the stimulus. If signals with periods longer than the time epoch are present, then the Fsp and Fmp values run the risk of being inflated. This occurs because the F test assumes gaussian distributed data sets that may no longer be present for the noise. Typically the noise variance will be underestimated when this problem occurs. Therefore, using a 10-Hz high-pass filter (100-msec time window) is detrimental to the estimation of the true S/N within the MLR region as it imposes a time window that is longer than the duration of the middle latency response (~ 50 msec).

![Figure 1](image1.png)

**Figure 1** Fsp and Fmp values for 500 blocks of 200 epochs each in a no-stimulus condition collected across all subjects. There is no advantage in using the Fmp technique as the functions overlay.

![Figure 2](image2.png)

**Figure 2** Mean Fsp values for all subjects in each experimental condition. The Fsp value was calculated at intervals of 500 epochs and averaged across subjects. The Fsp value is affected by stimulus presentation level and number of epochs obtained in an average.

![Figure 3](image3.png)

**Figure 3** The average Fsp value for all 10 subjects in a 60-dB nHL stimulus condition. The error bars reflect a 99 percent confidence interval.
Figure 4 Accumulating averaged MLR. Each trace represents an additional 500 epochs in the average. The first half of the time window (0-50 msec) shows an evoked response increasing in amplitude while the second half of the time window approaches the averaged noise background. This effect creates an underestimation of the actual signal-to-noise ratio in the response when using a 100-msec time window.

Filtering the MLR

The original time window, 100 msec, was selected to permit use of an open analog filter setting, 10 to 1000 Hz. To close the window, narrowing the analysis to the MLR region of 0 to 50 msec, a high-pass filter of 20 Hz was needed in order to meet the assumptions for Fsp. The majority of the MLR energy is between 20 and 60 Hz with an additional band of energy between 100 and 160 Hz (Suzuki et al, 1983). Therefore, a digital filter was used to do post-hoc filtering of the raw data. This permitted a shortening of the data collection window, which gave a closer approximation to the MLR response time. The filter was a digital implementation of a single pole, causal, Butterworth filter (Rabiner and Gold, 1975).

As shown in Figures 5 and 6, there is a trade-off between the effect of shortening the time window and raising the filter cutoff. As the filter cutoff is raised from 10 to 40 Hz, leaving the time window constant at 100 msec, the Fsp value falls. This decrease is due to a reduction in signal strength in the low frequency bands of the MLR. The decrease in the Fsp value after 10,000 epochs is approximately 1.6. However, maintaining a constant filter cutoff at 20 Hz and shortening the time window provides a significant increase in the Fsp value. The increase in Fsp after 10,000 epochs is approximately 9.2.

CONCLUSION

It appears that the Fsp technique is a viable method for estimating the S/N in the MLR and that the extra computation needed for calculation of the Fmp is not necessary. In addition, a higher filter cutoff, 20 Hz rather than 10 Hz, is required for an accurate estimate of the S/N in the MLR time window. Raising the cutoff frequency will be accompanied by phase shifting of peak latency values (Scherg, 1982; Kavanagh and Domico, 1987). This phase shifting may be of some significance in basic localization studies; however, with appropriately generated normative values it should present little problem in daily clinical use. A corollary to
using different filter settings is seen in the collection of the ABR where a lower frequency cutoff is often used for threshold detection than for evaluation of retrocochlear lesions. Finally the use of digital filters with 0 phase shift characteristics can totally alleviate this difficulty.

It is anticipated that being able to determine the S/N in the middle latency response will reduce the MLR variability seen within and between subjects, thus enhancing its use as a clinical tool in evaluating the auditory system. Part of the variability seen in the MLR has been attributed to effects of sleep state (Mendel and Goldstein, 1971). This study did not address the issue of subject state, other than using a standard clinical technique of having subjects in a relaxed setting. It is conceivable that as the subject passes through various states the S/N changes. In addition, as various sleep states are entered the frequency characteristics of the basic electroencephalic pattern changes. These changes may, and probably do, lead to changes in the degrees of freedom associated with assigning a response detection criterion. Further investigations are currently underway in this area by one of the authors (M.R.C.).

As shown in Figures 5 and 6, there is a trade-off of the estimated signal-to-noise ratio given the filter setting and the size of the response window. If not using a statistical test to estimate signal-to-noise ratio, or if a test can be devised that does not require a higher filter setting, it is clear that the 10-Hz high-pass filter provides the best signal-to-noise ratio. This suggests that if using a visual detection technique, as is the current clinical norm, the lower frequency is important. Conversely, the higher signal-to-noise ratios seen with the smaller windows is a reflection, not of improved signal-to-noise ratio in the response, but of better estimation by evaluating only the response window. If a statistical estimation of S/N is not used, the response window is less important, as the eye will pick the important peaks. This last point is the reason for using a statistical measure of response presence. If the S/N is low the probability increases that an error will be made in defining a random wave as a significant MLR peak. The estimation of S/N will reduce this probability.

Although this study was performed using click stimuli in order to enhance the MLR, the use of tone pip or other stimuli should not affect the basic technique. The technique is designed to measure the response of the brain to a stimulus over a set time window and should not be limited by the stimulus type.


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REFERENCES


APPENDIX

The following is a brief description of the calculations used for the Fsp and Fmp techniques. The reader is strongly urged to read Elberling and Don (1984) for a full discussion of the Fsp technique and theoretical limits. Fsp is an F test in which the noise level for the evoked response is computed at a single point (sp) in the response epoch. The Fmp also uses the F test but calculates the background noise from multiple points (mp) in the response epoch.

Table A1 represents a hypothetical evoked potential experiment. Each row signifies a successive epoch and each column represents a successive latency. The following formulas are based on Table A1.

In an evoked response recording the potential at any point in time can be designated as the sum of the neurologic signal, S, and the noise, N, in the system.

\[ P_{r,c} = S_{r,c} + N_{r,c} \]  

The assumption in signal averaging is that the signal, S, is constant and that the noise, N, varies in a gaussian manner around the signal. This means that over some period of time the noise will ideally average to 0, while the averaged signal at any point remains equal to the signal at that latency for any single trial.

\[ P_{a,c} = S_{a,c} = S_{r,c} \]  

This ideal is never fully met and therefore in reality the averaged response becomes

\[ P_{a,c} = S_{a,c} + N_{a,c} \]  

The signal-to-noise ratio, SNR, can be calculated as

\[ SNR^2 = \frac{\text{var}(S_{a,c})}{\text{var}(N_{a,c})} \]

A problem arises in estimation of the averaged noise variance,

\[ \text{var}(N_{a,c}) \]

One method to estimate the value of var(N_{a,c}) is to compute the variance, at a single latency, across epochs while collecting the averaged evoked response. This value represents the variance of the noise around the signal. Dividing the variance by the number of epochs collected approximates the average noise variance, \( \text{var}(N_{a,c}) \), value. This technique works provided that the noise maintains statistically equivalent variance across the epoch (i.e., there is no significant difference in the noise variance at any latency). The assumption of a nonvariant noise has been shown to be valid for the auditory brainstem response (Elberling and Don, 1984) and now for the middle latency response.

In the late response the noise level can vary across the response epoch; therefore, estimation of the noise level from a single latency is not valid (Gould et al, 1990). However, the overall noise level can be estimated as the average of the average noise variances at all latencies in the response epoch. To obtain this value the var\((N_{a,c})\) is calculated for each latency in the epoch in the same manner as for Fsp. The mean \( \text{var}(N_{a,c}) \) value is then computed and used in the Fmp calculation.

\[ SNR^2 = \frac{\text{var}(S_{a,c})}{\text{var}(N_{a,c})} \]