Improving the Reliability of the Auditory Middle Latency Response by Monitoring EEG Delta Activity

Therese McGee, Nina Kraus, Mead Killion, Richard Rosenberg, Cynthia King

ABSTRACT

The auditory middle latency response (MLR), a useful tool in the assessment of low-frequency auditory sensitivity, can be consistently recorded in young children during wakefulness, stages 1 and 2, and REM sleep. Responses are often absent or questionable during stage 4. An on-line measure indicating favorable periods for recording MLR during sleep is important for interpretation of absent potentials. Here, for children 5 to 7 years old, the reliability and detectability of MLR was compared to sleep state and the dominance of delta activity (0–3 Hz) in the EEG frequency spectrum. Dominance of delta activity, a characteristic of stage 4, was expressed in a "delta ratio," a measure of relative EEG energy in the 0 to 3 Hz frequency spectrum. A fixed delta ratio (DR=9) allowed the differentiation of periods favorable for MLR. MLR wave Pa amplitude and latency also varied with delta ratio. Results indicate that on-line monitoring of the delta ratio will allow reliable testing of MLR in clinical situations.

By definition, the auditory middle latency response (MLR) consists of the series of auditory evoked potentials that occur between 10 and 80 msec after the onset of an acoustic stimulus. Clinical uses of the MLR include the electrophysiological determination of low-frequency hearing thresholds, the assessment of cochlear implant function, the assessment of auditory pathway function, and the localization of auditory pathway lesions.

Of these, the most widespread application is the assessment of low-frequency hearing thresholds for patients too young to be tested behaviorally. For assessing higher frequency sensitivity, the ABR is the test of choice when behavioral methods cannot be used. However, because the ABR is highly dependent on neural synchrony, lower frequency stimuli (500–1000 Hz), with their slower onset, elicit a small, poorly defined ABR that may be undetectable in clinical situations. The MLR is less dependent on neural synchrony, produces a robust response to low-frequency stimuli (Vivion, Hirsch, Frye-Osier, & Goldstein, 1980), and in adults accurately reflects low-frequency hearing thresholds (Brown, 1971; Kileny & Shea, 1986; Musiek & Geurnink, 1981; Scherg & Volk, 1983; Zerlin & Naunton, 1974).

The MLR in children is of chief interest, because an accurate electrophysiological measure of low-frequency hearing thresholds is essential to the appropriate management of hearing loss in children too young to be tested by behavioral audiometric methods. Testing such young children requires that the response be reliable during sleep. However, various investigators have reported that the MLR is only intermittently obtained in sleeping children (Engel, 1971; Hirabayashi, 1979; Kileny, 1983; Kraus, Smith, McGee, Stein, & Cartee, 1987b; Kraus, Smith, Reed, Stein, & Cartee, 1985; Okitzu, 1984; Skinner & Glattke, 1977; Stapells, Galambos, Costello, & Makeig, 1988; Suzuki, Hirabayashi, & Kobayashi, 1983a; Suzuki, Kobayashi, & Hirabayashi, 1983b). When the MLR is present, it provides information about low-frequency hearing sensitivity, but the reported variability of the response even in normal children is such that the absence of a response cannot be interpreted as an indication of hearing loss. This difficulty has been the major factor limiting the clinical usefulness of the MLR with children.

From infancy to adolescence, the detectability of MLR waves recorded during sleep increases monotonically, from 20% in infancy (1–6 mo) to 90% at 12 yr of age (Kraus et al, 1985). In adults, Pa amplitude is largest during REM sleep and smallest during sleep stages 3 and 4 (Okitzu, 1984; Osterhammel, Shallop, & Terkildsen, 1985). There is, however, general agreement that sleep does not impede the detectability of MLR waves in adults, as it does in children. The trend of increased detectability with age exists regardless of whether the child is developing normally or has any of a wide range of neurological, cognitive, or speech and language disorders. A trend of increased MLR detectability with age has also been observed in the

Auditory Evoked Potentials Laboratory, Northwestern University, Illinois (T.M., N.K., C.K.); Etymotic Research, Elk Grove Village, Illinois (M.K.); and Sleep Disorders Center, Evanston Hospital, Evanston, Illinois (R.R.)

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more controlled context of an animal model (Kraus, Smith, & McGee, 1987a; Kraus et al, 1987b; Kraus, Smith, & McGee, 1988). Thus, both human and animal data indicate that a systematic process underlies the maturational changes in the detectability of MLR waves. The MLR has been shown to have multiple generators, reflecting both primary and nonprimary auditory pathways (McGee, Kraus, Comperatore, & Nicol, 1991; McGee, Kraus, Littman, & Nicol, 1992). The changes in detectability may be related to different developmental time courses for the multiple generators of the MLR (Kraus et al, 1988).

Collet, Duclaux, Challamel, and Revol (1988) demonstrated that MLRs in 6 to 7 week old infants are evident during wakefulness and during active or REM sleep. In awake 10 week old infants, Rotteveel, Stegeman, de Graf, Colon, and Visco (1987) reported an MLR detectability of 80%, but detectability varied greatly during sleep. Findings from our laboratory indicate that MLRs in children are consistently present during certain stages of sleep, undetectable during other stages of sleep, and that detectability during unfavorable stages improves with age. Stage 4 sleep is a particularly unfavorable time period for recording MLR, whereas MLRs are easily recorded during stages 1, 2, and REM (Kraus, McGee, & Comperatore, 1989).

Newborns (1–15 days) spend up to 50% of total sleep time in REM sleep (Roffwarg, 1966). Thus, the MLR is likely to be obtainable in this population, even without sleep stage monitoring. By 6 to 12 mo of age, stage 4 sleep has developed and the proportion of time spent in REM has dropped to 30%. By 2 yr old, 46% of total sleep time is spent in stage 4, whereas total time in REM remains at 25% (Kahn et al, 1973; Roffwarg, Muzio, & Dement, 1966). Thus, results from sleep studies indicate that unfavorable sleep stages for MLR would affect the clinical situation for children ages 6 to 24 mo, the time period when electrophysiological assessment of low-frequency hearing is most likely to be an issue.

Changes in response filtering can affect the detectability of MLR during development (Kraus et al, 1987a; Suzuki et al, 1983a,b), leading to speculation that EEG spectral characteristics can mask the MLR in young children. However, even when the recommended setting of 10 or 20 Hz is used, MLR is absent in stage 4 (Kraus et al, 1989). An alternative hypothesis holds that the MLR has multiple generators, one of which develops early, but is sleep state dependent. Over the first 10 to 12 yr of life, other sleep state-resistant generators develop. These late-developing generators dominate the adult response, which then shows only minimal changes with sleep state (Kraus & McGee, 1992). Important for clinical applications is the possibility that if sleep stage can be tracked on-line during a test session, and MLR is recorded during favorable periods, then the MLR may be a reliable measure for clinical use in young children.

To completely classify EEG epochs by sleep stage is complex and requires considerable judgment and expertise. Stage 4 sleep is characterized by the presence of high-amplitude (>75 μV), low-frequency (<3 Hz) activity (Rechtschaffen & Kales, 1968). The marked contrast between this activity and the low-amplitude, fast activity which characterizes stage 1 and REM offers hope that distinguishing favorable from unfavorable periods may be possible by monitoring specific aspects of EEG. Possibly, the differences could be distinguished by a computer algorithm or a hard-wired circuit.

Computer-aided determination of sleep stage is an issue which has received considerable attention (Gaillard & Tissot, 1973; Hasan, 1985; Johnson, 1977). Ways to detect sleep stages have been proposed (Church, March, Hibi, Benzon, Caveness, & Feinberg, 1975; Okuma, Fukuma, & Hata, 1970), typically based on analysis of frequency spectrum, periodicity of the waveform, and the relative amplitude of activity in several channels. The detection of stage 4 typically focuses on the predominance of slow waves, or delta waves (Coble, Reynolds, Kupfer, & Houck, 1987; Goeller & Sinton, 1989; Ray, Lee, Morgan, & Airth-Kindree, 1986). To measure delta activity, Long, Shah, Loughlin, Spydell, and Bedford (1989) utilized a "delta ratio," calculating the ratio of power in the 8 to 20 Hz spectral range to power in the 1 to 4 Hz range. Similarly, Labar, Fisch, Pedley, Fink, and Soloman (1991) utilized the ratio of power in the 1 to 3 Hz spectral range to power in the 1 to 30 Hz range. An advantage of a power ratio approach is the quantification of EEG in an continuous monitoring mode.

Computer analysis of sleep EEG has been directed toward specifically delineating sleep stages. It is likely that formal sleep staging is not necessary for clinical application of the MLR in young children. This article focuses on aspects of the EEG that characterize those epochs where MLR is present versus those epochs where MLR is absent. That is, could a specific aspect of sleep (such as a particular frequency spectrum or relative amplitude pattern) sufficiently delineate those periods in which MLR is likely to be present?

In the current study, EEG and MLRs were simultaneously recorded from young children. The predominance of delta waves, as reflected in the relative amplitude of energy in the 0 to 3 Hz range, was compared during periods in which MLRs were present and periods in which MLR was absent. It is our hypothesis that the detectability and robustness of MLR will be directly proportional to the predominance of delta activity in the EEG.

Methods

Recording Procedure

Six children, two males and four females, 5 to 7 yr of age, served as subjects. All had normal hearing (thresholds better than 10 dB HL from 500 to 8000 Hz), uneventful medical histories, and no developmental abnormalities. Subjects were given a period of familiarization with the laboratory. Then electrodes were applied and subjects were instructed to lie on a bed and to sleep. No sedation was used.

Two data acquisition systems were used to acquire auditory evoked potentials (Biologic Navigator) and spontaneous EEG (Biologic Sleepscan). Before testing, the clocks of the two systems were synchronized. Within the software, each EEG epoch and each MLR was marked with an associated system clock time. Initial synchronization of the two computer clocks allowed the time of each MLR recording to be correlated with the time of the EEG recording.

Simultaneous ABR and MLR activity were obtained in response to monaural 50 dB nHL clicks delivered at a rate of 11.1/sec, through insert (Etymotic) earphones, from an electrode placed at Cz with the reference at the ipsilateral earlobe. Responses were digitized at a sampling rate of 6400 points/sec and filtered with a band pass of 10 to 3000 Hz (12 dB/octave roll-off). Eighty msec of poststimulus time was averaged. Averaged responses (each consisting of 1024 stimulus presentations) were recorded continuously for the entire recording session. The amplitude and latency of the ABR was monitored continuously to ensure against displacement of the earphones. Averaged responses were stored for subsequent analysis.

Ongoing EEG records were obtained from locations C3-A2, Cz-A2, and Oz-A2. Bipolar recordings of muscle (chin-A2) and eye activity (right outer canthus-A1 and left outer canthus-A2) were also monitored. EEG, EMG, and EOG activity were recorded with a bandwidth of 0.3 to 30 Hz. The activity was digitized at a sampling rate of 100 Hz and stored on disk.

Data Analysis

MLR. The presence or absence of waves Na and Pa of the MLR was scored without knowledge of the subjects' sleep stage. The presence of a response was judged on the basis of the characteristic appearance of adult MLR: a broad negative trough (Na) beyond the ABR, followed by a vertex-positive response (Pa). This type of visual scoring is the manner in which evoked potentials are typically identified clinically. This scoring method has been shown to be reliable (Mendel, Saraca, & Gerber, 1984) and has yielded similar wave identification as observed by another, more objective method (Kraus et al, 1985). Responses with atypical morphology were classified as questionable, but were scored. Amplitude was measured from the Na trough to the Pa peak. For present responses, Pa peak latency was scored. Typically, Pa occurs within a poststimulus latency range of 25 to 40 msec (McGee et al, 1988; Özdamar & Kraus, 1983). In consideration of subject age and possible variation due to sleep state, we extended this and scored positivities in the latency range of 25 to 60 msec.

Sleep Stages. Sleep stages were determined by a diplomat of the American Board of Sleep Medicine (RR) for 30 sec epochs using standard polysomnographic criteria (Rechtschaffen & Kales, 1968). Stage 1 sleep is characterized by the absence of alpha (8–12 Hz) activity in the occipital EEG derivation and the presence of synchronized theta (3–7 Hz) activity in the central EEG recording. Vertex sharp waves and slow eye movements are frequently seen in stage 1 sleep. Stage 2 is characterized by the presence of sleep spindles (12–15 Hz). Stages 3 and 4 are characterized by the presence of delta activity, defined as high-amplitude (>75 μV), low-frequency (<3 Hz) activity from the central EEG derivation. Stage 3 contains 20 to 50% delta waves, whereas stage 4 is scored when more than 50% of the epoch consists of delta waves. REM sleep is characterized by "sawtooth" theta band EEG activity, REM in the EOG, and suppression of tonic EMG activity from the chin derivation.

Delta Ratio. EEG delta activity is typically recorded from the C3-A2 leads (Rechtschaffen & Kales, 1968). Activity from that channel associated with MLR recordings was segmented into 10.24 sec epochs (1024 digitized points). Each epoch was digitally filtered (Blackman filter) in two ways, at 3 Hz low pass and 10 Hz high pass, producing two filtered waveforms. The RMS values of the two waveforms were computed. The ratio of the 3 Hz RMS value to the 10 Hz RMS was computed, yielding the delta ratio.

Computation of Delta Ratio:

$$\text{EEG from C3-A2} \rightarrow \begin{cases} \text{low-pass filter (<3 Hz)} \rightarrow \text{RMS}_3 \\ \text{high-pass filter (>10 Hz)} \rightarrow \text{RMS}_{10} \end{cases} \rightarrow \frac{\text{RMS}_3}{\text{RMS}_{10}} = \text{delta ratio}$$

This algorithm for delta ratio was developed with an eye toward clinical implementation of the measure. It is a measure that is convenient to instrument electronically or program in software. The low-pass filtered RMS indicates the level of delta activity (0–3 Hz). The 10 Hz high-pass RMS gives an indication of the general voltage level and, during stage 2, would give some indication of the level of spindle activity (12–15 Hz). A predominance of low-frequency activity (delta waves), as seen in stage 4, resulted in a high delta ratio.

Data Set

Each MLR required approximately 90 sec to record. Thus, each MLR comprised three 30 sec sleep stage epochs and three associated sleep stage scores. An average of the sleep scores was calculated for that MLR. It happened that in no case did a child experience REM sleep during the click stimulation. Thus, only stages 1 to 4 were at issue, and there was no need to assign a numeric value to REM epochs. "Awake" was assigned a numeric value of zero. A review of the raw data showed no instances where the subjects jumped two stages within an evoked response. Thus, averages of the stage levels included sequential stages, such as 4-3-4, and not, for example, 4-1-4. Epochs of EEG with excessive sweat or movement artifact were excluded from the analysis.

In addition, each MLR comprised at least eight 10.24 sec EEG epochs and eight delta ratio values. For each MLR, an average delta ratio was computed. Thus, a data set consisted of

1. the MLR (detectability, amplitude, and latency),
2. mean sleep stage (mean of three values), and
3. mean EEG delta ratio (mean of eight values).

A regression correlation was performed between sleep stage and delta ratio. MLR amplitudes and latencies were compared across delta ratio. These data were subjected to a signal detection theory (SDT) analysis (Green & Swets, 1974) in order to determine what delta ratio is the optimum criterion, providing the best separation of favorable and unfavorable stages. Two analyses were performed: one regarding the detection of stage 4 by monitoring delta ratio and the other regarding the prediction of MLR occurrence by monitoring delta ratio. These analyses yielded an optimum delta ratio criterion for separating favorable from unfavorable periods for the current data set. *t*-Tests were used to compare Pa amplitude and latency in favorable and unfavorable periods.

Results

The average test time was 97 min per child. Five subjects slept for more than 80 min, and one child slept for only 28 min. A total of 145 MLRs were elicited by the clicks during those sessions.

Kraus et al (1989) have previously published a series of examples of MLRs recorded from young sleeping children during favorable and unfavorable periods. Figure 1 shows such an example from one of the current subjects, a 6 yr old child in stage 2 sleep and in stage 4 sleep. Note the large response in stage 2, but the absence of Pa in stage 4. Four children showed a period of absent MLRs during stage 4. For two children, both 7 yr old females, MLR morphology changed and latencies became variable or delayed during stage 4, although a scorable positivity still occurred in a 20 to 60 msec latency range.

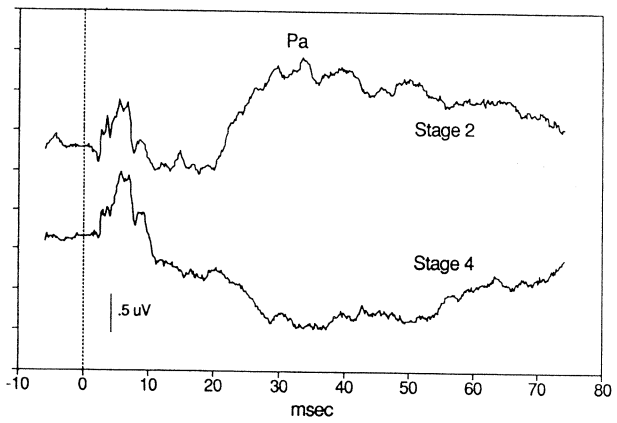

FIGURE 1. Representative MLRs from a 6 yr old child in stage 2 and in stage 4. Wave Pa is present during stage 2, but absent during stage 4.

Two 10 sec epochs of EEG from a 5 yr old child (Fig. 2) illustrate the differences in the EEG when the MLR was easily detectable versus when no MLR could be obtained. EEG in unfavorable periods (poor MLR) clearly shows high-amplitude, low-frequency (delta) activity. Figure 3 shows the average frequency spectra

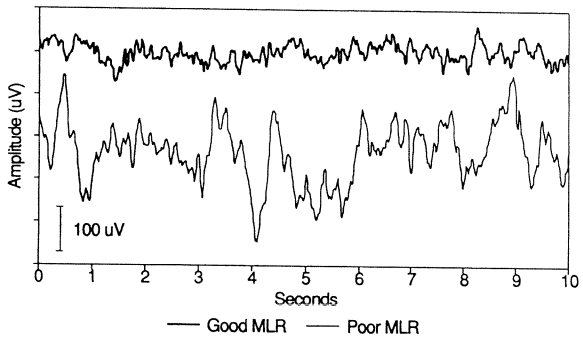

FIGURE 2. EEG activity recorded from C3-A2 during a period favorable for MLR (good MLR, top) and during an unfavorable period (poor MLR, bottom). "Poor MLR" activity is associated with high-amplitude, low-frequency components.

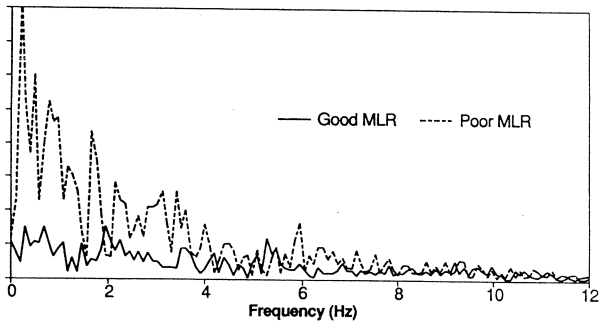

FIGURE 3. Frequency spectrum of EEG activity from C3-A2 during a period favorable for MLR and during an unfavorable period. Each spectrum is an average of the spectra of eight 10 sec epochs.

of eight 10 sec epochs of "good MLR" EEG versus eight 10 sec epochs of "poor MLR" EEG. The predominance of high-amplitude, low-frequency components is obvious in the poor MLR activity.

Recordings from C3-A2 and Cz-A2 produced very similar, although not identical waveforms. A point to point correlation performed on the simultaneously recorded activity from C3-A2 and Cz-A2 shown in Figure 4 showed a high correlation ($r = 0.86$). Generally, the Cz-A2 recordings showed lower amplitude delta activity. Electrical noise interfered more on the Cz-A2 channel, probably due to the electrode pair being connected to both data collection systems. For the purposes of this study, EEG activity from the C3-A2 channel was analyzed, but it appeared that analysis of the Cz-A2 channel could yield equivalent information if the electrical interference was resolved.

Delta ratios showed good correspondence to sleep stage for individual children, as shown in Figure 5 for a 7 yr old child. Group data (Fig. 6) showed a regression

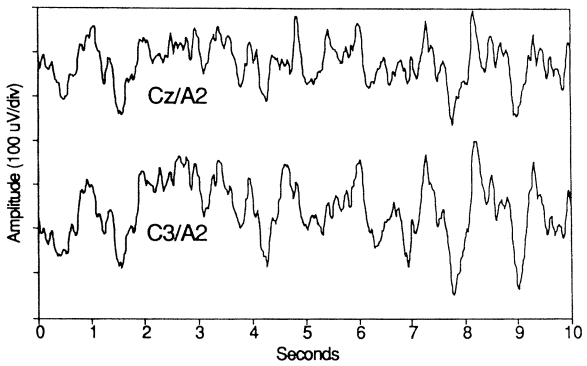

FIGURE 4. EEG activity recorded simultaneously from C3-A2 and Cz-A2. Note the similarity except for some amplitude reduction on the Cz channel.

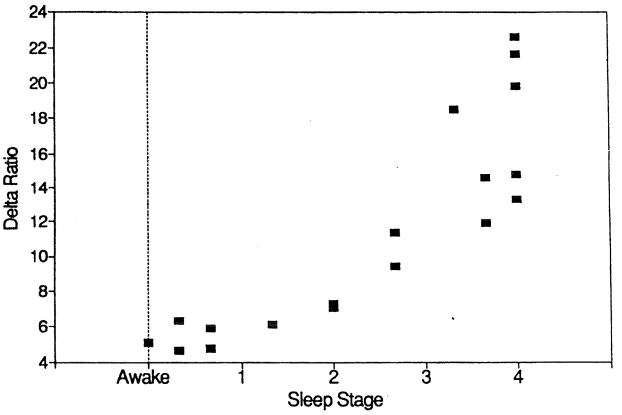

FIGURE 5. Correspondence of sleep stage with delta ratio for EEG activity recorded during MLR testing. Data for one child (7 yr old male) is shown).

correlation of 0.71 of sleep stage versus delta ratio, with higher delta ratios being associated with stage 4. Interestingly, in this data set, the relationship between delta ratio and sleep stage appeared not to be linear, but was best fit with an exponential function of $y = e^{0.67x-0.56} + 5.65$, where x = sleep stage and y = delta ratio.

For clinical purposes, it would be convenient to have an estimate of delta ratio "cutoff" for time periods unfavorable to the MLR. When delta ratio rises above this cutoff, then the clinician would know that this is an inadvantageous time to record MLR. Is the relationship between unfavorable periods and delta ratio sufficiently systematic that such a procedure is feasible?

The stage by delta ratio data fit well into a framework of SDT. SDT analysis considers the ability of an observer to separate a signal from a concurrent noise background. The noise is assumed to be variable and normally distributed. Addition of the signal to the noise

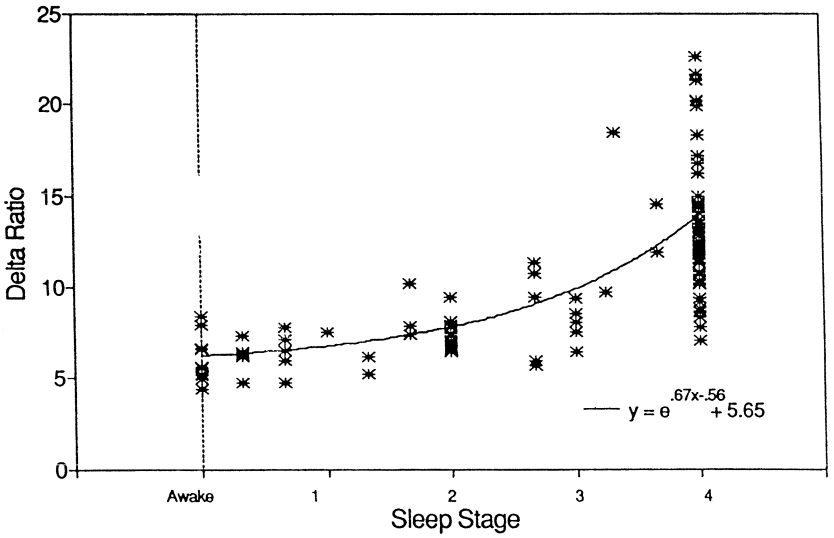

FIGURE 6. Correspondence of sleep stage with delta ratio for all six subjects for EEG activity recorded during MLR testing. Solid line indicates line of best fit, $y = e^{0.67x+0.56} + 5.65$, where x is the sleep stage and y is the delta ratio.

(N) increases the energy, but the signal+noise (S+N) remains normally distributed. The underlying distributions of N and S+N can overlap, resulting in some uncertainty as to the detection of the signal (Green & Swets, 1974). Applying this to the current data set, stage 4 is considered to be the "signal." When the delta ratio is above some criterion level, then we judge that the "signal is present" (subject is in stage 4). Of course, this may or may not be true, leading us to have either made a correct judgment (a hit) or a false judgment (a false alarm). According to SDT, the relative percentages of hits and false alarms allow the determination of the detectability of the signal; in this case, how well one can detect stage 4 by attending to the delta ratio.

In Figure 7 is plotted the receiver operating characteristic (ROC) curve for the detection of stage 4. This is a plot of the hit rate versus the false alarm rates, as the delta ratio criterion varies from 4 to 18. The criterion corresponding to each is indicated by the data labels. If the predictive value of the delta ratio was at chance, the points would fall along the diagonal line from (0,0) to (100,100). The greater the deviation from this line, the greater the predictive value. According to SDT, the deviation from chance is proportional to d', which is a measure of the difference between the means of the underlying N and S+N probability distributions. For the current data set, d' = 2.53.

As indicated in Figure 7, a line from (50,50) to (0,100) bisects the data at the cutoff value of the ideal observer,

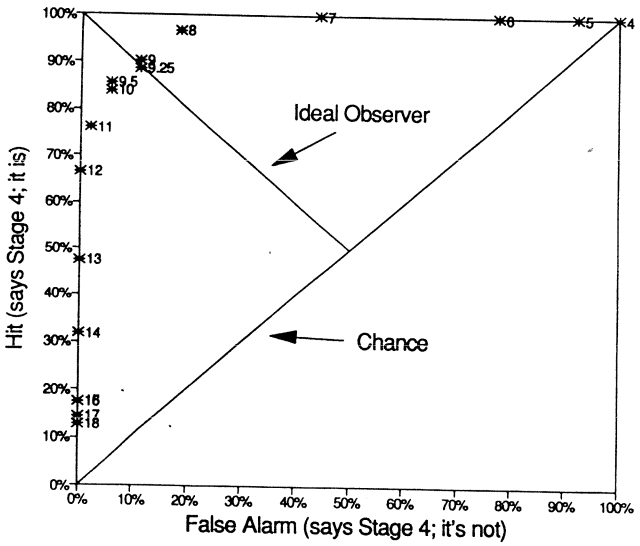

FIGURE 7. ROC curve of the detection of stage 4 by the delta ratio. The data labels next to each point indicate the corresponding delta ratio criterion used to compute the hit and false alarm rates. The diagonal from (0%,0%) to (100%,100%) indicates where the data would lie if detection were at chance. Deviation from this line toward the upper left corner corresponds to better discrimination of the signal. The line from (50%,50%) to (0%,100%) crosses the data at the point of the optimum criterion.

that is, the cutoff value for delta ratio which best separates stage 4 and nonstage 4 epochs. Closest to this line is a delta ratio criterion of 9 to 9.25. Mathematically, the optimum criterion can be precisely determined by calculating β, which equals the ratio relative height of the S+N:N distributions (P_{SN}/P_N). As β approaches 1 (the distributions are equal in height), the hit rate is maximized and the false alarm rate is minimized. When the delta ratio = 9, $\beta = 0.9$. Intuitively, it can be seen that this is a reasonable cutoff. In sleep stages 1 to 3, 88.9% of epochs showed a delta ratio of less than 9, whereas 90.5% of epochs consisting of stage 4 or a mixture of stages 3 and 4 showed a delta ratio greater than 9.

The critical issue is not, however, whether sleep stage corresponds to the delta ratio, but whether the robustness of the MLR corresponds to the delta ratio. The correspondence of MLR and delta ratio can also be fit into the framework of SDT, in the sense that one can consider what delta ratio criterion is optimum. However, the question of interest here is slightly different from that of the previous analysis. If the delta ratio can accurately predict an unfavorable period, then, given that the delta ratio is below a certain criterion, the clinician can proceed with confidence. Of concern is whether the delta ratio criterion would indicate that an MLR should occur, when in fact it does not (causing the clinician to have false confidence in the testing). This would happen if the delta ratio criterion was set too high. Conversely, setting the criterion too low would result in a very limited testing time, and the test could not be accomplished.

This dilemma can be addressed by analyzing the correct rejection rate (CR), the rate at which, given no signal, the observer correctly says that no signal occurred. More specifically, given that the MLR is not robust, will the delta ratio indicate that this is an unfavorable time to record MLR?

For each delta ratio criterion, CR rates were calculated for both MLR "reliability" and "detectability." Reliability was defined as the percent of MLRs with normal morphology; that is, "questionable" responses were not included. Detectability was defined as the percent of MLRs that could possibly be considered present; that is, questionable responses were included.

In Figure 8a are plotted the CR rates for MLR reliability and detectability for delta ratio criteria from 5 to 15. Delta ratios of less than 9 were associated with reliability and detectability CR rates of better than 90%, whereas delta ratios greater than 9 showed decreasing CR rates, indicating that the higher delta ratios would not adequately signal unfavorable periods. The lower bar graph (b) indicates the number of recordings obtained when the delta ratio was less than the criterion value. Lower delta ratios showed a very limited number

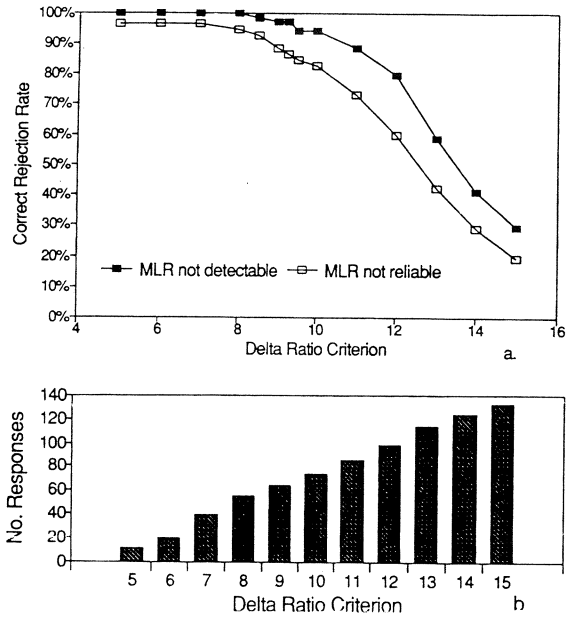

FIGURE 8. (a) The rate at which poor MLRs would be correctly rejected, given the delta ratio criterion. (b) The number of responses obtained with the delta ratio less than the criterion value. The optimum criterion is one that has a high correct rejection rate, but includes the maximum number of responses.

of recordings. The optimum criterion would be one that maximized the number of recordings without sacrificing the correct rejection of unfavorable periods. Interestingly, as with the separation of stages, the optimum criterion was approximately 9.

Lower delta ratios corresponded to higher Pa amplitude. Figure 9 shows the correspondence between Pa amplitude and delta ratio for one child. Figure 10 shows group mean Pa amplitude by delta ratio. Pa amplitude was significantly larger in periods with a delta ratio less than 9 compared to those greater than 9 (5.78; $p < 0.001$). Pa latency was significantly earlier when the delta ratio was less than 9 ($t = 4.94$; $p < 0.001$). If questionable and absent MLRs were not included in the analysis, Pa amplitude was still significantly larger when the delta ratio was less than 9 ($t = 3.94$; $p < 0.001$), and Pa latency was still significantly earlier ($t = 3.26$; $p < 0.01$). Thus, even when Pa was clearly present, amplitude and latency varied with sleep state.

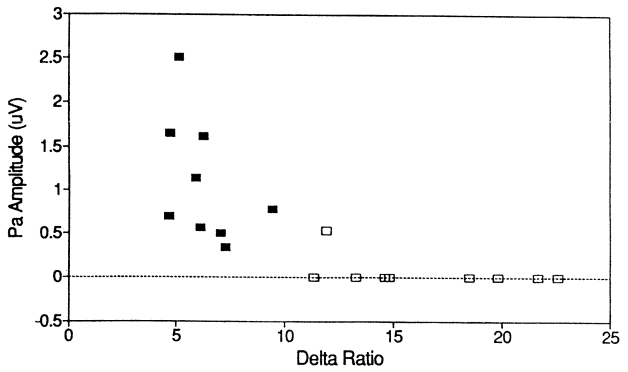

FIGURE 9. Pa amplitude as a function of delta ratio for one subject (7 yr old male). □, Questionable responses and no response; ■, Pa.

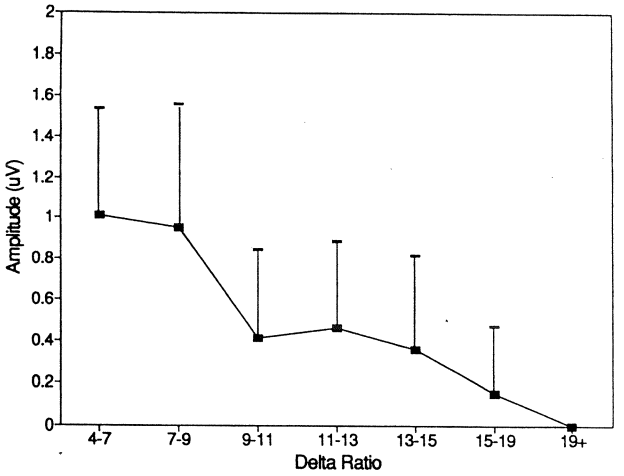

FIGURE 10. Mean Pa amplitude as a function of delta ratio. Vertical bars indicate a range of the mean + 1 SD.

Discussion

The results indicate that the delta ratio shows an excellent correspondence to stage 4, an unfavorable period for the occurrence of MLR. The sensitivity of the delta ratio to MLR occurrence in this data set is an indication that it is possible to reliably record MLR from young patients in clinical settings provided delta activity is monitored. The correspondence between delta ratio and MLR occurrence was evident not only for pooled data, but also for individual subjects, indicating that the relationship is strong enough for clinical application. The determination of an optimal delta ratio must consider the balance between how well the delta ratio criterion rejects unfavorable periods versus the limitation of testing time.

Pa amplitude and latency varied with delta ratio, even when questionable responses were excluded from the analysis. Thus, sleep state affects not only detectability of MLR, but also these other attributes of Pa.

The delineation of favorable versus unfavorable periods can be determined on-line by an experienced observer simply by monitoring EEG while testing a child. This is the current procedure in our laboratory. However, on-line, visual analysis of the EEG requires considerable training and costly additional equipment. This complicates the testing situation to the point that many clinicians may be reluctant to incorporate the technique into routine testing. An excellent corre-

spondence of stage 4 and delta ratio was indicated by the high d' in the SDT analysis of those data. This is evidence that determining favorable periods for MLR need not be complicated. The simplicity of the delta ratio calculation offers promise that it could be incorporated in commercial software or a hard-wired circuit, allowing on-line monitoring of favorable and unfavorable periods. The improvement in MLR detectability is likely to be equivalent to that obtained with formal sleep staging.

The current study included a small subject population in a limited age range. The population of interest for clinical application of delta ratio monitoring extends to younger ages than those of the current subjects. Further study is needed to acertain whether these results will be valid with larger populations. Questions remain as to whether similar associations between delta ratio and MLR reliability will exist for younger children. The amplitude of delta activity develops between 6 and 12 mo of age and continues to change through adolescence (Anders, Carskadon, & Dement, 1980). After 6 yr of age, the proportion of delta activity slowly declines (Coble et al, 1987). Added to this is the developmental progression of MLR reliability. Thus, optimal delta ratio may vary with age. Fortuitously, infants demonstrate a much higher proportion of REM sleep during the sleep cycle (Anders et al, 1980; Roffwarg, Muzio, & Dement, 1966). Because REM is a favorable stage for MLR, the higher proportion of REM in infants bodes well for reliable clinical MLR testing of infants. The duration of favorable periods may be longer in infancy, extending available testing time.

Here it was our intent to elicit the best possible MLR given the sleep state. Thus, moderate intensity (70 dB nHL) click stimuli were used. The issue of the interaction between low-frequency MLR and sleep state is more pertinent for clinical applications, and is a topic for further investigation.

Conclusions

The MLR Pa wave is sleep state dependent in young children. In the current study, for subjects ages 5 to 7, it was shown that the predominance of delta (0–3 Hz) activity in the EEG indicates a period that is unfavorable for the elicitation of Pa. A measure of the predominance of delta activity is the delta ratio, a ratio of the relative amplitude of 0 to 3 and 10 to 30 Hz activity. Pa reliability and detectability varied inversely with the delta ratio. Even when Pa was reliably present, Pa amplitude and latency varied with delta ratio. Results indicate that formal sleep staging is likely not to be necessary in determining favorable periods for recording MLR.

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Address reprint requests to Therese McGee, Ph.D., Evoked Potentials Laboratory, Northwestern University 2299 N. Campus Drive, Evanston, IL 60208.

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