Abstract

Objective: To study the variability of auditory brainstem response (ABR) and middle latency response (MLR) over a long term period.

Methods: 50 normal hearing subjects participated in the study. All the subjects were tested at 3 months, 6 months and 12 months of the initial testing. The absolute latencies and interpeak latencies of ABR waves and amplitudes & latencies of waves Na and Pa of MLR were measured.

Results: The Repeated measure ANOVA did not reveal any statistically significant difference (p>0.05) between interpeak latencies of wave I-III, III-V and I-V across the four visits. The amplitude of MLR wave Pa showed no significant difference across four visits. However significant difference (p<0.05) across visits was observed for latency of wave Na.

Conclusions: The absolute latencies of wave III & V and the interpeak latencies of waves I-III, III-V and I-V have good test-retest reliability. Reliability of wave I however has not been established. Amplitude of wave Pa has good test-retest reliability.

Significance: The ABR and MLR can be used as monitoring tools in a number of cases like neurodegenerative disorders, progressive disorders of the central nervous system.

Keywords: Auditory Brainstem Response; Middle Latency Response; Test-retest Reliability

Introduction

The most widely used auditory evoked potential measurements are ABR and MLR that have a widespread application. ABR audiometry refers to an evoked potential generated by a brief click or tone pip transmitted from an acoustic transducer in the form of an insert earphone or headphone. The elicited waveform response is measured by surface electrodes typically placed at the vertex of the scalp and ear lobes. The amplitude (micro voltage) of the signal is averaged and charted against the time (millisecond), much like an EEG. The waveform peaks are labelled I-VII. These waveforms normally occur within a 10-millisecond time period after a click stimulus presented at high intensities (70-90 dB normal hearing level [nHL]).

The most widely used measure is the latency of a component peak and the interpeak latencies (IPL). The latency of a component peak is simply the time after stimulus onset that a given peak occurs. As described by several researchers the clinical advantages of AEP lie in the fact that these are accurate and objective tests, independent from an individual’s subjective response, and it may be very useful in the evaluation of children with language disorders and also in monitoring therapeutic process because of the very plasticity of the nervous system. Moreover, it has been stressed that it bears high correlation to physiological changes in the auditory pathway and is efficient in distinguishing lesions from functional alterations in the Central Nervous System (CNS) (Sininger and Wesson, [1,2]).
Several responses can be evoked from the auditory cortex. The most useful component of the auditory evoked response in the diagnosis of auditory cortical abnormalities is the middle-latitude auditory evoked response (MLR). The MLR can be elicited by frequency-specific signals at relatively low intensities (Neves et al. [3]). This potential occurs between 10 and 80 milliseconds (ms) after the acoustic stimulus onset, and seems to have multiple generators, with a greater contribution of the thalamus cortical pathways, and less contribution from the inferior colliculus and the reticular formation.

The morphology of such potentials is clinically important, and one should confirm the presence of a long negative peak (Na), followed by a positive peak (Pa), between 15 and 30 ms, besides wave reproducibility. Although the Pa wave is the dominant component, its morphology may vary substantially from individual to individual and also between the ears and electrodes in the same individual.

As in any other auditory evoked potential (AEP), response analysis criteria are in function of the latency (milliseconds - ms) and amplitude (microvolt - µv) values, and an intensity reduction causes an increase in latency values and reduction in amplitude values. Studies suggest that CNS alterations would affect more the amplitude than the latency values. Amplitude also seems to be the best indicator of functional alterations, since latency values bear large variations even among normal individuals. In general, the measured amplitude is generated between peaks Na and Pa, since it is the most robust. Using the Pa-Nb amplitude value may be one option if it is not possible to attain the Na-Pa amplitude value.

MLR is one of the most promising procedures for the identification of alterations in the central nervous system. Nonetheless, its little clinical use is due to the fact that there may be a great variability in latency and amplitude values among subjects, and this makes it difficult to establish values of normality, thus making it necessary to research this.

Test retest is a method of estimating test reliability in which a test developer or researcher gives the same test to the same group of research participants on two occasions. The results from the two tests are then compared to produce a stability coefficient. Studying the coefficients for a particular test allows the assessor to see how stable the test is over time. Thus, studies aiming at studying the long term variability and the test retest reliability become extremely valuable to expand the clinical use of both ABR and MLR.

Need for the Study

Since ABR and MLR enjoy a widespread clinical application in a number of cases like neurodegenerative disorders, progressive disorders of the central nervous system, it is empirical to study the variability of these measures over a long term period. On extensive review of literature there was a paucity of data on the long term variability of these measures; hence this study.

Methodology

50 normal hearing subjects participated in the study. All the subjects were tested at 3 months, 6 months and 12 months of the initial testing. At the second follow-up i.e. after 6 months of initial testing 2 subjects dropped out of the study while 4 subjects dropped out on the third follow up.

Auditory Brainstem Evoked Response (ABR) measurement and MLR measurements were carried out on the evoked potential system developed by Intelligent Hearing System, USA.

The test was conducted in a sound treated room with minimal electrical and mechanical interference. Silver-silver chloride button electrodes were used. The non-inverting electrode was placed on Cz position (vertex), inverting electrode was placed on M1 and M2 position (mastoid), and the ground electrode was placed on Fz position (forehead) after applying conduction gel. The skin electrode surface impedance for all electrodes was first measured before starting the recording. The impedance was always adjusted and kept below 5KΩ to facilitate proper recording.

The following parameters were selected for recording ABR. All the subjects were recorded at 70 dB nHL and 90 dB nHL intensity level in both ears separately. The bandwidth of filters was adjusted between 100 Hz to 3,000 Hz. Rate of stimulus used was 19.3/sec. Duration of stimulus was 100 µsec/click. Minimum of 1024 clicks were given at a time of each recording. The responses were repeated at each intensity level to ensure reproducibility. During ABR recording the absolute latencies of wave I, III and V and the interpeak latencies of Wave I-III, III-V and I-V were studied.

MLRs were measured along with ABRs using same instrumentation and electrode configuration. All the subjects were recorded at 70 dB nHL intensity level in both ears separately. The bandwidth of filters was adjusted between 10 Hz to 300 Hz. Rate of stimulus used was 5.1/sec. and the duration of stimulus was 100 µsec/click. Number of stimuli presented were 1000. Peaks that were picked was Na, Pa and Nb. Latency measures were made from the centre point of the peak. The amplitude of Na and Pa waves were measured. Wave Na to Wave Pa was taken as the amplitude of Na and Wave Pa to Wave Nb was taken as the amplitude of Pa. The mean values and standard deviations were calculated for all the measures. Statistical analysis was done using repeated measure ANOVA. The informed consent was taken from all the subjects and the study was approved by the institutes’ ethical committee.

Results

To find out the test re-test reliability of ABR and MLR, the repeated measure analysis of variance (ANOVA) was applied across all the visits.

Table 1 shows the comparison of mean and SD values for the various ABR parameters of the four visits. Statistical significant
difference ($p<0.05$) in the mean values of four visits was found for the absolute latency of wave I in right ear revealing poor test retest reliability. However, in left ear, no significant difference was observed between the mean latency values of wave I across four visits depicting good test re-test reliability. Similarly, difference in the mean values of four visits for the other ABR parameters viz. absolute latency of wave III, V and interpeak latencies of wave I-III, III-V & I-V were statistically non-significant implying good test re-test reliability. Hence, it can be inferred that ABR has good long-term test retest reliability for majority of the parameters studied.

**Table 1:** Comparison of four visits on Auditory Brainstem Response (ABR).

| ABR parameter       | Ear   | First visit | Second visit | Third visit | Fourth visit | F-value |
|---------------------|-------|-------------|--------------|-------------|--------------|---------|
|                     | Mean  | S.D.        | Mean         | S.D.        | Mean         | S.D.    |       |
| Latency of wave I (ms) | Right | 1.55        | 0.06         | 1.54        | 0.05         | 1.53    | 0.05  | 1.52 | 0.04 | 7.65*** |
|                     | Left  | 1.53        | 0.06         | 1.53        | 0.04         | 1.53    | 0.04  | 1.51 | 0.03 | 2.01   |
| Latency of wave III (ms) | Right | 3.69        | 0.14         | 3.68        | 0.12         | 3.65    | 0.13  | 3.64 | 0.10 | 1.16   |
|                     | Left  | 3.67        | 0.14         | 3.64        | 0.13         | 3.66    | 0.11  | 3.63 | 0.11 | 1.52   |
| Latency of wave V (ms) | Right | 5.53        | 0.13         | 5.51        | 0.12         | 5.53    | 0.12  | 5.51 | 0.11 | 0.87   |
|                     | Left  | 5.54        | 0.16         | 5.54        | 0.13         | 5.55    | 0.11  | 5.52 | 0.10 | 2.09   |
| Interpeak latency I-III (ms) | Right | 2.14        | 0.14         | 2.14        | 0.10         | 2.12    | 0.10  | 2.13 | 0.09 | 0.32   |
|                     | Left  | 2.13        | 0.13         | 2.11        | 0.13         | 2.13    | 0.10  | 2.12 | 0.10 | 0.90   |
| Interpeak latency III-V (ms) | Right | 1.85        | 0.16         | 1.84        | 0.13         | 1.88    | 0.09  | 1.87 | 0.11 | 1.21   |
|                     | Left  | 1.87        | 0.12         | 1.90        | 0.12         | 1.88    | 0.10  | 1.88 | 0.10 | 0.97   |
| Interpeak latency I-V (ms) | Right | 3.99        | 0.12         | 3.98        | 0.12         | 4.00    | 0.10  | 4.00 | 0.10 | 0.60   |
|                     | Left  | 4.00        | 0.15         | 4.02        | 0.13         | 4.02    | 0.11  | 4.01 | 0.10 | 0.55   |

**Table 2:** Comparison of four visits on Middle Latency Response (MLR).

| MLR parameter       | Ear   | First visit | Second visit | Third visit | Fourth visit | F-value |
|---------------------|-------|-------------|--------------|-------------|--------------|---------|
|                     | Mean  | S.D.        | Mean         | S.D.        | Mean         | S.D.    |       |
| Latency of wave Na (ms) | Right | 18.21       | 3.24         | 19.14       | 1.77         | 19.30   | 1.82  | 19.62 | 1.69  | 3.04*   |
|                     | Left  | 18.59       | 2.35         | 19.51       | 2.18         | 19.94   | 1.99  | 20.13 | 2.17  | 8.64*** |
| Amplitude of wave Na (µA) | Right | 1.49        | 0.52         | 1.40        | 0.45         | 1.32    | 0.41  | 1.36  | 0.40  | 8.33*** |
|                     | Left  | 1.34        | 0.45         | 1.34        | 0.38         | 1.31    | 0.36  | 1.30  | 0.33  | 1.17   |
| Latency of wave Pa (ms) | Right | 30.32       | 2.69         | 30.21       | 2.13         | 30.53   | 2.15  | 30.50 | 2.91  | 0.74    |
|                     | Left  | 30.36       | 2.89         | 30.21       | 1.53         | 30.75   | 1.87  | 31.10 | 1.91  | 7.76*** |
| Amplitude of wave Pa (µA) | Right | 1.25        | 0.43         | 1.20        | 0.34         | 1.20    | 0.28  | 1.21  | 0.26  | 1.16   |
|                     | Left  | 1.20        | 0.35         | 1.23        | 0.38         | 1.22    | 0.32  | 1.22  | 0.32  | 0.33   |

**Table 2:** Comparison of four visits on Middle Latency Response (MLR).

| MLR parameter       | Ear   | First visit | Second visit | Third visit | Fourth visit | F-value |
|---------------------|-------|-------------|--------------|-------------|--------------|---------|
|                     | Mean  | S.D.        | Mean         | S.D.        | Mean         | S.D.    |       |
| Latency of wave Na (ms) | Right | 18.21       | 3.24         | 19.14       | 1.77         | 19.30   | 1.82  | 19.62 | 1.69  | 3.04*   |
|                     | Left  | 18.59       | 2.35         | 19.51       | 2.18         | 19.94   | 1.99  | 20.13 | 2.17  | 8.64*** |
| Amplitude of wave Na (µA) | Right | 1.49        | 0.52         | 1.40        | 0.45         | 1.32    | 0.41  | 1.36  | 0.40  | 8.33*** |
|                     | Left  | 1.34        | 0.45         | 1.34        | 0.38         | 1.31    | 0.36  | 1.30  | 0.33  | 1.17   |
| Latency of wave Pa (ms) | Right | 30.32       | 2.69         | 30.21       | 2.13         | 30.53   | 2.15  | 30.50 | 2.91  | 0.74    |
|                     | Left  | 30.36       | 2.89         | 30.21       | 1.53         | 30.75   | 1.87  | 31.10 | 1.91  | 7.76*** |
| Amplitude of wave Pa (µA) | Right | 1.25        | 0.43         | 1.20        | 0.34         | 1.20    | 0.28  | 1.21  | 0.26  | 1.16   |
|                     | Left  | 1.20        | 0.35         | 1.23        | 0.38         | 1.22    | 0.32  | 1.22  | 0.32  | 0.33   |

*P<0.05, ***P<0.001
Hence it is revealed that among the various parameters of MLR, amplitude of Pa has the best test retest reliability.

**Discussion**

The results show that the F value reached a significant level (p<0.05) only for latency of wave I in the right ear. The F values for all the other measures tested did not reach a level of significance (p>0.05) indicating little or no variability in these measures over a long term follow up. Thus these findings suggests that the ABR latency of wave III and V have good test – retest reliability over a long duration of time. Our present findings however indicate variability in the absolute latency of wave I. This is in agreement with the study of Lauter and Karzon [4] who reported low level of consistency across subjects for peak I of ABR. Peripheral hearing status and other testing parameters like ambient noise, minimal wax in the external auditory meatus and transient middle ear pathology has been known to affect the latency of wave I in ABR (Sininger and Wesson [1,2]). This finding must be examined cautiously further and requires attention during measure of latency of ABR waves on a long term basis.

The interpeak latencies of wave I-III, III-V and I-V did not show any variability over a period of one year of the study. These values remained stable as indicated by non significant F-values (p > 0.05). Thus the authors emphasize the value of this measure in any long term follow up as in cases of demyelinating diseases, degenerative neurological disorders. Bergamaschi et al. [5] also reported good test-retest reliability of ABR components over one week period and recommended it as a good useful monitoring tool in longitudinal studies.

The MLR measure i.e. amplitude of wave Pa showed no variability over time and remained stable as denoted by non – significant p values (p>0.05). This measurement remains relatively stable over time and thereby has good test retest reliability. Thus this measure can be utilized to determine hearing thresholds at all frequencies in patients with abnormal ABR due to neurologic damage to the brainstem and in the pre and post operative management of patients with cochlear implants. These measures can be used in the localization of auditory pathway lesions, the diagnosis of syndromes that compromise MLR generating system. While ABR provides information unto the level of brainstem the MLR extends assessment of auditory system beyond the brainstem to the thalamocortical pathway. The latency values of Na wave in our study did show variability with time as the p values obtained were significant (p<0.05). This is in correlation to the previous findings of Kavanagh et al. [6] who also established the fact that the MLR measures often fluctuate over time.

**Conclusion**

The absolute and interpeak latency measures of ABR waves III and V remain stable over a long period of time. However some variability in latency of wave I have been observed. The latency of wave Na and Pa in MLR also shows variability over an extended period although amplitude of wave Pa remains relatively stable.

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