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# A Doctor's Dilemma: To Sedate or Not Sedate Subjects Undergoing ABR Measurements

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***Abstract:*** **Auditory Brainstem Response (ABR) is a widely used screening method, mainly for determining the hearing threshold, as well as neurological assessment of the elements of hearing. A key requirement for a successful ABR test is that the subject should be idle, in order to minimize the background signals that lower the signal/noise ratio. A sedative, such as chloral hydrate, is employed as a mode of sedation especially in children, who are difficult to be kept idle throughout the test (especially so, if there are developmental defects, common among the subjects with neurological defects of hearing conduction). However, the need of sedatives in the test has been debated, given that intolerance or side-effects of the sedatives may outweigh the benefits of use, especially in children. It has been suggested that simple sleep deprivation on the prior night of the test might be sufficient to induce sleep among the child subjects during the test. The current study was aimed at comparing the ABR protocols among children with or without sedation at 60dBnHL for both left and right ears. The major factors being compared included the time consumed for each test and also the latency, intensity levels and overall morphology of wave V of ABR. Additionally, the hearing threshold was also determined. The study was conducted among 27 children between the age group of 6 months to 24 months. The two protocols were performed exclusively at two different time points. The results indicate that the assessment in the absence of sedation was as good as the similar results obtained in the presence of sedation, with respect to hearing threshold determination. Similarly there was no significant difference with respect to the wave V output parameters among the two conditions. However, the time consumed for each test was significantly more in the absence of sedation. Though the current study indicates that ABR may also be conducted in absence of sedation, further studies to evaluate the same may be necessary, given the low sample size and absence of a case-control study.**

***Keywords:*** **ABR, Sedation, wave V, latency.**

## 1. INTRODUCTION

Auditory Brainstem Response (ABR) is a routinely used screening test for the auditory response to a controlled artificial stimulus (Hood, 1998). Though there are many modes of stimuli and ABR protocol, the simplest form, known as click stimuli is among the most common (Ferm, Lightfoot & Stevens, 2013). The test, performed and interpreted by audiologist, is commonly suggested when other methods of auditory response are not practical, as in case of infants.

**Overview of the technique:**

ABR audiometry measures the evoked potential (auditory stem evoked potential) generated in response to a stimuli (a brief click, tone burst or beep) from an acoustic transducer (in the form of insert earphone or patched headphone). The response waveform is measured using surface electrode attached at different montages on head. Similar to an EEG, a chart is generated with amplitude (μV) and time (milliseconds) on the two axes (Montaguti, Bergaozoni, Zanetti & Rinaldi, 2007). The various peaks of the waveform are labeled as wave I-VII (described in **table 1**). At high intensities (60-90 dBnHl), the waveforms appear within 10 milliseconds after the stimulus.

**Physiological and clinical significance of the ABR waveforms:**

The response towards an ABR stimulus is generated in the basilar regions of cochlea, which further travels proximally along the auditory path from nuclear complex of cochlea to the inferior colliculus. The signal travels along the auditory pathway from the cochlear nuclear complex proximally to the inferior colliculus.

The first two peaks in the waveform (waves I & II) represents the true action potentials, and are used to normalize the data in certain extrapolations of ABR test. Subsequent waves (wave III-VII) are thought to represent postsynaptic activity at the brainstem auditory centers which are reflected as waveform crests (peaks) and troughs (Henry, 2015). The afferent (and possibly efferent) activity of the axonal pathways in the auditory brain stem is reflected as the positive peaks (crests) of the waveforms. Although accurate identification of the origin of the various peaks has not been yet possible, and are debated, evidences indicate each of the wave's origin (Satheesh et al., 2012). Hence by identifying the wave peaks, the latency at which each of the wave appears after the stimulus, and the overall morphology of individual peaks, it is possible to identify the presence of defects in each of the anatomical locations in the auditory path from cochlear nucleus (**table 1**).

Two main applications of ABR include threshold search and assessment of neurologic activity of the auditory response (Yao et al., 2013) ('Short Latency Auditory Evoked Potentials', 1987). The threshold search estimates the hearing sensitivity in infants (especially in subjects below 2 years of age, at which point of time auditory neural developments are completed and become 'adult like'), in response to a stimuli (tone or click) with air/bone conduction. In threshold search, the presence or absence of hearing loss is assessed and the degree and type of the defect is also estimated. The structure of the hearing deficit is typed as, 'sloping', 'flat', 'rising', etc., based on the test.

The neurological assessment using ABR is performed typically on adults, to test the integrity of auditory system. In the latter form, peak latencies are measured, in what is termed as a rate study. This format can also be used to detect auditory neuropathy spectrum disorders.

**Table 1: The major component peaks observed in an ABR, with possible origin and description**

| Wave | Origin | Remarks |
|---|---|---|
| I | First-order neurons of the CN VIII fibers, as they leave cochlea and enter the internal auditory canal | Far-field representation of the compound auditory nerve action potential of CN VIII |
| II | Proximal VIII nerve as it enters brain stem | |
| III | Second-order neurons (beyond CN VIII) in or near cochlear nucleus. Caudal portion of the auditory pons. | Cochlear nucleus contains approximately 100,000 neurons, most of which are innervated by CN VIII nerve fibers |
| IV | Mainly from pontine third-order neurons near superior olivary complex; additional contributions from cochlear nucleus and nucleus of lateral lemniscus | Often shares same peak as with wave V |
| V | Widely believed to originate from the vicinity of Inferior colliculus*; additional contribution from second-order neurons | Clinical application of ABR, reflects activity of multiple anatomic auditory structures |
| VI and VII | Actual origin uncertain, but thought to originate from the medial geniculate body of thalamus | |

***Note:** The inferior colliculus is a complex structure, with more than 99% of the axons from lower auditory brainstem regions going through the lateral lemniscus to the inferior colliculus.

**Role of sedation in ABR protocols; to sedate or not?**

There has been considerable debate on the need of sedation in ABR procedure. Though the procedure could be performed on pediatric subjects in a natural sleep state without the need for sedation, considerable variation in ABR procedure exists, with some of the audiology clinics preferring sedation during the test period ('Short Latency Auditory Evoked Potentials', 1987)..

The proponents of mitigating sedation are of the view that unnecessary sedation in infants should be avoided wherever possible, given that infants are at an increased risk to develop adverse effects to sedation, which includes hypoxia, air

passage obstruction, allergic responses and even could be fatal ('Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update', 2007). They also point out that the concerns of parents regarding sedation are often dismissed and are assured of the safety. However, it is well reported that sedation is often applied without standard procedures, with wide variations existing in sedation procedure. As observed at a summit on pediatric sedation,

*"Most of the anesthesiologists that regularly use these drugs did not consider the average sedation case to be technically challenging. These observations beg the question, 'Why is pediatric sedation commonly provided with relatively unpredictable, low potency, long acting drugs like oral chloral hydrate by non-airway experts in a suboptimal monitoring environment?'"* (Heistein, 2006)

The panelists of the forum noted that a few limiting aspects such as (regulatory, economic and political) were barriers in adopting uniformly acceptable good practices in sedation of infants.

On the other hand, there is a differing view among a few audiologists, who feel that ABR is better performed when infants are sedated, especially helping to minimize the background noise from any voluntary body activity which might reduce the signal to noise ratio and hence the sensitivity (Speech-language-pathology-audiology.advanceweb.com, 2015). A less serious argument is that sedation aids in pacifying the infants for a fixed period of time, unlike natural sleep state which is unpredictable, and this helps in administrative scheduling of audiology practices. Another argument in favor of sedation includes reduction in the time required for performing and individual case compared to a subject in normal sleep. This argument is quite important, especially when ABR is used as a screening program for infants in populated low income countries, even though the time saved in presence of absence of sedation may not vary significantly.

Given the importance of the issue of sedation, which is still inadequately addressed, evidenced practices in ABR are necessary (Janssen, Usher & Stapells, 2010). There are no standards or guidelines yet, on whether or when infant subjects are to be sedated during the procedure.

The current study is aimed at evaluating the ABR output from two test conditions, conducted at two different time periods, either in presence or in the absence of sedation. Major parameters such as, time conducted for each test, threshold hearing and wave V morphology, amplitude and latency were compared among the two test conditions (Abramovich., 2013).

## 2. MATERIALS AND METHODS

**Clinical subjects:**

The study included 27 children between the age group of 6-24 months (median-15 months), recruited from the Security Forces Hospital, [place], as outpatients in Audiology clinic, [over a period of [period]. Medical notes were reviewed to identify subjects who met the inclusion criteria. Parents of the infant subjects who met the inclusion criteria were contacted; study was explained to them, subsequent to which their permission was sought for inclusion of the subjects to the study.

**Inclusion criteria:**

The subjects were included only if, a) they were between 6-24 months, b) free from neurological disorders and c) free from ear problems (such as middle ear effusion, middle ear surgery etc., to rule out conductive elements of hearing loss). Both male and female subjects were included

**ABR test conditions:**

**Test environment**: Threshold ABR diagnostic/biologic test was performed in a sound-proofed room; any unnecessary electronic devices, such as computer monitors and cellular phones, in the test room were turned off. In addition, fluorescent lights were turned off. All test set up such as electrodes were kept as much hygienically as possible including covers for electrodes, to prevent cross-infection. All tests were performed with the supervision of a qualified audiologist.

**Choice of electrodes and application:** The skin was gently and carefully abraded using NuPrep (a gel with fine pumice granules) to help exfoliate the skin with clean gauze. In addition, ten-20 was used as an electrode paste for non-disposable cup electrodes.

**Electrode location (montage) – AC**: As per recommendation for AC-ABR (AudiologyOnline, 2015), a single channel recording was performed. The electrodes were placed at montages as per general recommendations for ABR. The positive electrode was placed at high forehead, as much as possible closer to Cz (the point along the midline of scalp half way between the bridge of the nose and the start of the skull at the rear of the head) and midline. The negative electrode was placed at ipsilateral mastoid and the common electrode at contralateral mastoid.

**Electrode impedance:** Since the artefact size from induced electrical interference is proportional to the difference in the electrode impedances, low impedances for all electrodes were ensured. The impedances, as measured between each electrode pair were kept under 5000 Ω and similar across electrodes,

**Stimulus and transducer:** click stimuli, a broadband stimulus comprised frequencies range between (1000 – 4000 Hz), over 100μs, was used. The clicks were provided using foam insert earphones.

**ABR Protocol Setup:** ABR was set up as per the settings listed in **table 2**.

**Table 2: The equipment settings used in the ABR procedure**

| | |
|---|---|
| AEP. ABR (1 channel) window | 10.66 ms |
| Sampling rate (#points) | 256 |
| Maximum number of sweeps | 1000 |
| Polarity | Rarefraction |
| Stimulus rate (per second) | 13.30 |
| Amplification gain | 100K |
| Artifact reject (uV) | 23.80 |
| Low filter (Hz) | 100 |
| High filter (Hz) | 1500 |

**Middle Ear Analyzer:** Tympanometry GSI, was used to analyze middle ear for perfusions.

**Procedure:**

Each patient was seen twice at the audiology clinic; ABR measurements were taken in two of the test conditions, *viz.* either in the presence or absence of the sedation. Each of the test condition was performed at different time periods.

**a) First visit: ABR with Sedation:**

Pre sedation Instructions were informed prior the appointment day which includes the following: depriving food for the child subject 4-6 hours prior to appointment, partial deprivation of the child subject on the prior night of the test.

Additional information regarding medication allergy, seizure disorder, etc., was sought from the parents (by the audiologist in-charge). Similarly, information pertaining to general health such as, fever, flue or antibiotic course on the day of test was also sought.

Oral Chloral hydrate 50mg/kg was given as the general sedative. Otoscopic examination of the external and middle ear appearance was performed, subsequent to which the diagnostic ABR test was performed to determine the wave V threshold. Tympanometric measurement was also conducted to rule out hearing loss due to conductive elements of hearing.

**b) Second visit: ABR WITHOUT sedation (Normal sleep)**

After conducting the first test, second appointment was scheduled (at a different time point) in order to complete the objective of the study.

Instructions were given to parents of the subjects prior the appointment day. As with the first test, the parents were advised to avoid feeding the subject until prior to the test, who at which point of time, were fed full stomach to help induction of sleep. The parents were also instructed to deprive their child of sleep on the night prior to the test, to induce sleep during the entire procedure.

Otoscopic examination of the external and middle ear appearance was performed, subsequent to which the diagnostic ABR test was performed to determine the wave V threshold. Similar to the first test, a tympanometric measurement was also conducted to rule out hearing loss due to conductive elements of hearing.

## 3. DATA ANALYSIS

The ABR test was used for both threshold searches as well as for neurologic assessment using wave V characteristics (Online.uncg.edu, 2015). The sweep threshold search was conducted from a high intensity (80 dBnHL) towards lower intensities and observing the ABR response waves. A subject was ruled as normal with respect to hearing threshold if a discernable wave V response could be identified at 20 dBnHL (behavioral threshold).

For the neurological assessment, the morphology, latency (milliseconds) and amplitude (microvolts) of wave V, generated at 60 dBnHL, was assessed, for individual ear (both left and right for all subjects). The wave V was determined on the basis of a discernable wave IV, and where ever wave IV could be separately identified, wave V latency was taken as the time point corresponding to the highest point of wave V peak. For a complex wave IV and Wave V, the wave V was calculated as the farthest point of the combined peak, before the onset of the drop of the peak.

Data interpretation was performed in Microsoft Excel, with statistical significance calculated using Student t test. A 'p' value less than 0.05 was considered as significant.

## 4. RESULTS AND DISCUSSION

The subjects (median age – 13 months) included an equal number, 13 each, of males (median age – 20 months) and females (median age – 11 months).

There was significant difference in the time consumed for each test between the two conditions; in presence of sedation the time taken for a test was lower (median-26 minutes) compared to the test in its absence (median–36 minutes); **table 3**.

Though savings of a mere 10 minutes in an ABR test by using sedation may not appear appealing, in clinics, which utilizes ABR as a means of screening hearing sensitivity (especially in low income countries, with poor healthcare resources and large populations), this might be seen as an impediment. Similarly, close to $1/3^{rd}$ reduction in the time period of a test may also reflect in the reduction of subscription fee for the consumers, and in the profitable running of diagnostic/screening audio clinics (due to administrative scheduling). However, sedation and anesthesia are relatively more costly and necessitate dedicated trained staff in anesthesia, both of which may outweigh the benefits of time saved. A previous study (Janssen, R., Usher, L., & Stapells, D. 2010) indicated that the time savings using sedation is not of practical significance to ABR clinics; our results were in concurrence with their overall findings even though in the current study, irrespective of sedation status, we could perform the ABR test a third shorter than reported in their paper. Institutional and procedural variations might explain the difference in timings.

The threshold search using ABR in either of the test settings (sedated and non- sedated ABR) yielded concurring results. All the infant subjects screened elicited response at the minimal 20 dBnHL intensity, in either condition.

There was no difference in the wave V morphology among either of the groups, with a clear discernable peak obtained in all the cases, irrespective of the presence or absence of sedation (data not shown). Additionally, the hearing threshold in all the subjects in either of the test conditions were similar and within limits, with a detectable signal at 20 dBnHL intensity, well within the standards (data not shown).

When evaluating the wave V, charecteristics, *viz.* latency and amplitude, among the two test conditions, no significant difference was observed in either of the parameters (**table 3**). Similarly good correlation (~0.9) was observed among the latency and amplitude values from the two test conditions.

A previous case-control study (Norrix, 2012), comparing the sedated and non-sedated groups, identified that the absolute wave V latencies are significantly depressed in general anesthesia and attributed these findings to general alterations in the body homeostasis (such as body temperature) due to the sedatives. However, the current study did not identify any such significance. A possible reason could be that the control group in that particular study included older children when compared to the test cohort, who were significantly younger. It is known that the ABR results would be more adult like after 2 years of development (Salamy, 1984). Another plausible reason could be the use of general anesthesia in that study, which could potentially alter ABR output. Similarly, infants are prone to loss of body heat due to vasodilation in response to anesthetics, due to higher body mass/surface area ratio; the difference in body temperature could reflect in altered ABR results.

In an apparent discrepancy, we found differences in the tympanometric measurements among the two conditions, with 7 subjects in the non-sedated test being found with 'As' tympanogram in either ears(corresponding to inner ear stiffening),

compared to 4 subjects in the sedated category. A plausible explanation for the same would be the presence of middle ear effusions or 'otitis media'.

Though our study yielded no significant difference between ABR-output in sedated and non-sedated conditions, there still could be a case for the use of sedatives, especially when the subjects who undergo the test are simultaneously exhibiting developmental defects. In many of the cases the neurological aspects of hearing defects are likely to be developmental defects (François, Teissier, Barthod & Nasra, 2012). It may then be necessary to have the test performed under sedation or anesthesia.

**Table 3: ABR output parameters compared between subjects in two conditions (sedation and without sedation).**

| Parameter | Latency (ms) | | | | Amplitude (μV) | | | | Time (min) | |
|---|---|---|---|---|---|---|---|---|---|---|
| Condition | Without Sedation | | With Sedation | | Without Sedation | | With Sedation | | Without Sedation | With Sedation |
| Ear | Left_ear | Right_ear | Left_ear | Right_ear | Left_ear | Right_ear | Left_ear | Right_ear | | |
| Mean | 6.064 | 6.012 | 6.073 | 6.000 | 0.107 | 0.104 | 0.106 | 0.104 | 36.04 | 26.62 |
| Std. Error of Mean | 0.054 | 0.071 | 0.053 | 0.063 | 0.010 | 0.009 | 0.010 | 0.010 | 0.680 | 0.503 |
| Median | 6.100 | 6.100 | 6.050 | 6.100 | 0.095 | 0.090 | 0.100 | 0.100 | 36.00 | 26.00 |
| Std. Deviation | 0.276 | 0.364 | 0.272 | 0.320 | 0.049 | 0.046 | 0.049 | 0.049 | 3.470 | 2.562 |
| P value* | 0.607 | 0.722 | | | 0.942 | 0.923 | | | 2.57E-12 | |

The p-value indicates the statistical significance of the comparison of each ear compared to its counterpart in the two conditions (except for time). * p-value indicates the result of paired t test.

## 5. CONCLUSIONS

Given the serious side-effects and associated cost, it is of extreme importance to formulate novel procedures associated with ABR-tests. However, at the same time, it is also important to get quality output from ABR test, a supporting case for sedation, especially since it is used both as diagnostic and screening tool in audiometry. Our results, though from a limited sample size supports the idea that sedation may indeed not be necessary, especially since we got concurring data in both the sedated and non-sedated conditions. Recent studies indicate that sedatives could be replaced with melatonin, which improves the sleep quality, thereby enhancing the ABR output and at the same time does not have the side effects of common sedatives ((Shangase & Mavrokordatos, 2013) & (Schmidt, Knief, Deuster, Matulat & am Zehnhoff-Dinnesen, 2007)). A point to note is that our results were from same patients at two different time points undergoing ABR in two different procedures. Hence it is likely that interpersonal variations in assessment are mitigated, though temporal variations still could be present. However, our study was limited to small sample size and to limited objectives; detailed studies on large sample population are essential to conclusively formulate new guidelines in ABR.

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