Journal of Pharmaceutical and Scientific Innovation
www.jpsionline.com
Research Article

THE USE OF MELATONIN FOR SEDATION DURING AUDITORY BRAINSTEM RESPONSE TESTING: AN ALTERNATIVE TO SEDATION IN NON-MEDICAL SETTINGS?

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DOI: 10.7897/2277-4572.02579
Published by Moksha Publishing House. Website www.mokshaph.com

Received on: 24/07/13 Revised on: 28/09/13 Accepted on: 16 /10/13

ABSTRACT
The audiological use of the auditory brainstem response (ABR) to obtain diagnostic audiological information can be challenging in the "difficult-to-test" populations where sedation is required. This challenge becomes more pronounced in non-medical settings where medical personnel who can provide drug administration as well as monitor the patient while under sedation are not readily available. The non-medical setting comprises a big portion of audiology practices and clinics; hence the importance of exploring sedation protocols that can be used in this setting. The current study explored the use of melatonin as a "sedative" during ABR testing. Within a prospective pretest - posttest design, 27 adults with normal hearing comprised the study sample. All participants underwent basic audiologic testing comprising of otoscopy, tympanometry, and pure tone audiometry followed by an ABR which was conducted pre and post melatonin administration. The initial recording was conducted prior to the administration of melatonin with the second recording performed 40 minutes following the participants' intake of 3 milligrams of melatonin. Data was analysed using both qualitative and quantitative statistical measures. Findings indicated that melatonin can be successfully utilised as a "sedative" during ABR testing as it allowed for statistically significant reduction in muscle artifacts, did not present negative impact on morphology, repeatability, amplitude and latency of the recordings; and also did not induce any obvious and/or reported negative effects for the participants. These findings have important clinical and training implications, particularly in resource-constrained contexts and in contexts where audiologists function within non-medical facilities.
Keywords: auditory brainstem response, difficult-to-test, melatonin, muscle artifacts, non-medical, sedation

INTRODUCTION

The auditory brainstem response (ABR) is an evoked electrophysiological response to auditory stimuli generated by anatomical sites of the auditory pathway. This recording allows for effective and objective clinical assessment of the auditory system as well as establishment of the neural integrity and hearing sensitivity of the auditory pathway.[1] It comprises of seven positive peaks which represent the neural activity of anatomical sites of the auditory pathway.[1] Analysis of these peaks allows for differential diagnosis and confirmation of the degree of hearing loss[2] and this is influenced by the type of stimuli and recording parameters adopted. The objective nature of the ABR causes it to be a crucial measure in the audiologist's test battery as it accommodates testing of the "difficult-to-test" populations such as neonates and infants, cognitively impaired individuals, as well as other populations where an active response from the patient would not be reliably obtained. The ABR measure is not affected by the physiological state of the individual being tested[2] but is however extremely sensitive to patient mobility (muscle artifacts) during recordings.[3,4] Uncontrolled artifacts can cause significant distortion of the averaged ABR waveform.[5] This muscle artefact influence is observed similarly in the paediatric as well as adult populations and it has significantly negative influences on the ABR results. Although, noise resulting from patient mobility can be reduced by filtering, signal averaging and artifact rejection[6] excessive levels of this noise can be detrimental to the measure even in the presence of noise reduction strategies.[7] Evidence exists which indicates that under ideal situations, with patients relaxed and/or immobile during the testing procedure, artifact rejection is a successful means of noise reduction. However, when patients are active, which is often the case with children and difficult-to-test populations, artifact rejection precludes measurement of reliable recordings.[7] When conducting an ABR, one aims to reject artifacts such that they remain at levels below 10 % of the sweeps during the recording.[5] Sedation is therefore usually required for those patients who are restless during ABR testing to ensure control over artifacts.[8] It allows for the reduction of noise during ABR measurements, in order for reliable recordings to be obtained.[4] Evidence has shown that sedation does not affect the ABR;[2] and that most drugs and pharmacological agents have no negative influence on the ABR waveform, allowing for them to be utilised as sedatives during testing.[3,9,6] Some anticonvulsants, lidocaine and phenytoin, however, have been shown to affect the ABR waveform[9] and could result in false negatives or false positive findings. One of the most widely used forms of sedation for ABR testing; probably because it is one of the first forms of sedation to be used during ABR testing, is chloral hydrate.[10] Chloral hydrate's use however requires a medical setting with the presence of a nurse and a physician on standby as a requirement. In addition, the vital signs of the patient are to be monitored throughout the sedation period as there are documented medical contraindications to the use of this drug. These contraindications include vomiting, and central nervous system side effects such as dizziness and disorientation.[3] More recently, other forms of sedation such as propofol have been utilised. Similarly, the use of propofol has been compared to that of propofol-ketamine combination for sedating patients undergoing an ABR.[11] These drugs have been documented as sedatives that are introduced intravenously, but also require a medical setting as they affect

respiration, and can also cause cardiovascular depression and other medical factors such as nausea or hallucinations.[11] At an audiology training clinic, or a setting where doctors and nurses are unavailable to provide patients with sedatives or general anaesthetic, and where monitoring of the patients' medical progress while under sedation is not possible, sedating restless patients for an ABR is a challenging task for audiologists and student audiologists. Furthermore, there is limited published research focussing on the use of sedatives which do not require the presence of a medical professional. Most audiology training institutions do not routinely have medical professionals on site, and anaesthetists are not readily available to provide sedation services during ABR testing of the clients who require sedation. This lacuna in clinical training set-ups of audiologists presents implications for training of students as well as audiology service provision in independent practices which are not situated within medical facilities (as is the case with most audiology practices in South Africa). The challenge for clinical training in the area of ABR testing means that all ABR training involving sedation can only be conducted within hospital based training; and for practicing audiologists, additional cost implications have to be incurred by the patient who then has to consult medical practitioners and be admitted to hospital for what is an out-patient procedure. These factors highlight the importance of conducting research into the use of different sedatives, such as melatonin, which might have positive implications for both clinical assessment and clinical training, hence the current study. Melatonin is an endogenous hormone which is naturally produced by the pineal gland.[12,13] Its major function is to control the sleep-wake cycle.[14] However, an exogenous version is available for individuals with sleep disorders and sleep-related medical requirements,[14,13] as well as to ease jetlag.[12] It has been reported that exogenous melatonin (in the form of a hormonal supplement)[13] treats reduced sleep onset latency, increases sleep efficiency as well as sleep duration in humans.[12] Melatonin is easily accessible and cost-effective. The current study aimed to determine if melatonin could be utilised successfully as a "sedative" during ABR recordings, in order to induce sleep or a relaxed state, and reduce and/or eliminate muscle artifacts which preclude efficient recording of the ABR. Melatonin requires 20 – 120 minutes to take-effect and is reported to be non-toxic and does not normally cause negative side effects in healthy individuals[15] and children.[8] Moreover, clear contraindications for the use of the drug have been documented;[16] and additionally, medical monitoring is not required.[8] Long term use of melatonin has also not shown major side-effects.[17,18] The most frequently reported side effects of melatonin are "hangover effects",[13] drowsiness, dizziness, nausea, and headaches,[19] fatigue,[20] and decreased concentration.[21] Similarly, research has indicated that exogenous melatonin is safe for individuals to use on a short-term basis (over a period of days or weeks).[19-21] However, literature does caution that individuals using the drug should be cautious whilst driving or using heavy machinery.[20,21] Those that overdose on the drug could experience difficulties with balance and walking.[20] In addition, it has been reported that individuals could experience altered sleep patterns and impaired cognitive functioning following the intake of melatonin.[13] Melatonin has also been reported to be healthy as it stimulates immune function and contains anti-oxidants.[16] It is for these apparent benefits of melatonin that it was considered a possible solution for "sedation" during ABR testing in non-medical settings; laying foundation for the current study which aimed at determining the effectiveness of using melatonin as a "sedative" when recording ABRs in adults with normal hearing sensitivity. Melatonin has previously been successfully utilised as an alternative to sedation in children undergoing magnetic resonance imaging examinations (MRI), as conventional sedation methods and/or general anaesthetic propose high failure rates as well as risk factors for this population.[22,15] The results of this study indicated that 65 % of the children who received melatonin fell asleep within 35 minutes of receiving the drug; and findings of this study also highlighted the positive outcomes of using melatonin, in terms of cost, age, patient safety and resuscitation facilities and equipment; which are factors associated with conventional sedation methods and/or general anaesthetic.[22] Some studies have reported the use of melatonin in combination with sedatives when sedating children undergoing MRI examinations.[23] Depending on their weight, the children were either provided with 3 or 6 mg of melatonin ten minutes prior to sedation.[23] On the contrary to the successful use of melatonin, dentists attempted to utilise melatonin as a form of premedication in anxious children whilst under sedation; however findings indicated that melatonin was not successful as a pre medicant, and did not improve the sedation for dental treatments; but improved the sleep of the participants following sixty minutes of oral intake of melatonin.[24] Audiologically, the use of melatonin was explored in 250 children with suspected hearing loss in Germany.[8] In that study, findings indicated that melatonin-induced sleep is appropriate for the completion of ABR recordings in the paediatric population; whilst simultaneously eliminating the medical risks of conventional sedatives. The current study aimed to explore this and examine possible effects on the ABR response as well.

MATERIALS AND METHODS

Aims

The primary aim of the current study was to determine the success of using melatonin as a "sedative" during ABR recordings of adults with normal hearing sensitivity. This was determined by comparing the pre and post-melatonin ABR results for the following factors:

- Waveform morphology
- Waveform repeatability
- Waveform amplitude
- Absolute wave latencies of waves I, III and V.
- Inter wave latencies of I-III, III–V and I–V.
- Absolute inter-aural latency difference of wave V.
- Muscle artifacts during the recordings.

Participants

Sample and sampling procedure

The sample size initially comprised 30 participants, but three were excluded due to failure in meeting the inclusion criteria, with the consequent sample size being 27 adults with normal hearing sensitivity on basic audiometric testing as indicated by pure tone average mean of 4.31 dBHL in the right ear and 4.11 dBHL in the left ear. All participants were recruited by personal invitations and/or emails to the researcher's peers and acquaintances, and by approaching students in lecture theatres at the university campus. The age of the participants was a mean of 21.8 years (standard deviation = 2.4 years). Of the 27 participants in the study, 10 were male and 17 were

female. Quota sampling was adopted in the current study as a sampling strategy as specific target features and requirements had to be met in order for participants to form part of the study.[25] Inclusion criteria included the following:

- Participants were required to be between 18 and 50 years of age to ensure that presbycutic hearing loss was eliminated as a confounding variable;[26] and also to make sure that participants were of the age where they could provide informed consent to reliably participate in such a study.
- Participants were required to present with normal hearing sensitivity (as determined by normal otoscopic and tympanometric findings, as well as normal pure tone air conduction);[26] as these would have presented confounding variables for ABR testing for the purposes of the current study.
- Participants had to not present with the documented medical contraindications of melatonin.[16,15,20,21]
- Participants were required to have transport arrangements to ensure their safety from driving following assessment, should they have experienced any side-effects from melatonin which could affect their ability to drive.[20,21]

Design

The current study adopted a prospective pretest-posttest design.[27] This was deemed an appropriate design as it measured the change in ABR recordings following the administration of melatonin and comparing this to the pretest condition findings. It is acknowledged that the fact that the study was not blinded could have had an influence on findings due to possible bias.

Test Protocol

Data collection was conducted at the Hearing Clinic observing all standard audiology testing conditions including the use of calibrated equipment, testing in sound-proof booths, with strict adherence to infection control guidelines. The equipment and associated accessories used included a Heine Mini otoscope for otoscopic examination, a Grason Stadler, Incorporated 38 Version 4 tympanometer for tympanometry measures, a GSI or AC40 audiometer for basic audiometry testing, a Biologic Navigator Pro or GSI Audera Auditory Evoked Potential equipment with insert earphones for ABR testing.

Testing Procedure

Basic Audiological Testing

All standard otologic, audiologic and medical case history data was obtained from each participant in an interview which was conducted in a quiet private room where there were no interruptions. Over and above the standard case history questions, enquiry was made with each participant specific to the melatonin, specifically regarding medical contraindications of melatonin as well as history of known side effects of melatonin. Basic audiologic assessment then commenced with otoscopic examination, followed by tympanometry utilizing the standard 226 Hz probe tone, followed by pure tone audiometry.[26] These assessment measures determined each participant's hearing sensitivity and thus their ability to continue participation in the study. At this stage, all participants who presented with abnormal hearing sensitivity were referred appropriated referred on for intervention, but did not continue being part of the current study. For participants to be able to continue in the current study, Table 1 below depicts criteria that needed to be present.

Table 1: Audiological criteria adhered to for participants to be able to advance to the ABR testing phase of the study

Factor	Inclusion findings
Otoscopy	Clear external auditory canals and intact tympanic membranes with cone of light[28]
Tympanomery	Type A tympanograms where middle ear pressure was between +50 and – 150 daPa; static compliance was between 0.27 and 2.8 cc ^{3}; and ear canal volume was 0.4 to 1.5cc ^{3,29}
Pure tone audiometry	Hearing thresholds at frequencies between 250 Hz and 8000 Hz needed to fall within normal limits (between – 10 and 25 dB HL) ^{30}

At this stage, three participants were excluded from continuing with the study as they did not meet the set criteria, leaving the total sample size at 27.

ABR testing (pre and post-melatonin)

All 27 participants then underwent ABR testing without melatonin; and then a repeat ABR after taking melatonin orally. For both the pre and post-melatonin ABR testing, the neuro-diagnostic test protocol was used where the repetition rate was set to 11.1 clicks/second, total number of sweeps was 1150, intensity was at 90 dBHL and both ipsilateral and contra lateral recordings were obtained.[6] Although testing was conducted in normal ears, contra lateral masking was presented at 50 at a standard 50 dBHL because stimuli were presented at levels above 70dBHL. For each recording, each participant was requested to "lie-down and relax" for the duration of the data collection. Each wave recording was repeated twice to establish repeatability of absolute wave latencies as a reliability measure.[6] Once the pre-melatonin ABR assessment was concluded, each participant received two 1.5 mg capsules of "Biogen Platinum Series Melatonin" and was requested to "lie-down and relax" in a darkened test room for a duration of 40 minutes prior to the post-melatonin ABR testing. Melatonin has been reported to require 20 – 120 minutes to take-effect[15] and so 40 minutes was thought to be sufficient time for the purposes of the current study. Wave form analysis following Hall's[6] protocol, as detailed in Table 2, was conducted and data captured on an excel spread sheet for ease of data analysis. Each ABR waveform was analyzed by looking at waveform morphology, repeatability, amplitude, absolute wave latencies of waves I, III and V; inter wave latencies of waves I – III, III – V and I – V; and inter aural latency difference of wave V.[6] For the purposes of the current study, close monitoring of the muscle artifacts during the recordings was also conducted pre-and post-melatonin:

Table 2: ABR factors and parameters observed in the current study

Factor	Norm
Morphology	Well-defined peaks and the presence of at least Waves I, III and V for each ear
Repeatability	Waveforms of each ipsilateral recording were morphologically repeatable to the repeated tracing, and absolute latencies were within 0.2 ms of each other
Amplitude	Comparison of the amplitudes of wave I and wave V: wave I was to be less than half as large as wave V
Absolute latencies of waves I, III and V	Wave I = 1.65 ms (SD = 0.14 ms) Wave III = 3.80 ms (SD = 0.18 ms) Wave V = 5.64 ms (SD = 0.23 ms)
Inter wave latencies of I–III, III–V and I–V	I–III=2.15 ms (SD = 0.14 ms) III–V=1.84 ms (SD = 0.14 ms) I–V=3.99 ms (SD = 0.20 ms)
Absolute inter aural latency difference of wave V	0.0 ms with a standard deviation of plus or minus 0.11 ms
Muscle artifacts during the recordings	A maximum of 10 % of artifacts to the sweeps during recording was considered to be normal with those above this regarded as not within normal limits

Following the ABR testing, it was ensured that each participant was feeling physically stable before they left the testing facility.

Data analysis and statistical procedures

Both descriptive and inferential statistics were utilized to analyze the data.[31] Basic audiological test findings were all analyzed through descriptive statistical analysis procedures. In addition, descriptive statistics were employed to compare the morphology, repeatability, amplitudes, and artifacts of pre and post-melatonin ABR recordings. Inferential statistics in the form of Matched pairs t-Tests and Cohen's kappa were utilized to analyze the data.[32] Cohen's kappa (used to establish reliability of the pre and post-melatonin ABR recordings in terms of the morphology, repeatability and the amplitude of the ABR waveform. Cohen's kappa (was therefore used to determine inter-judge agreement of data and determine the reliability of ratings.[27,33] Matched pairs t-Tests were thus used to compare the pre and post-melatonin ABR results in terms of absolute wave latencies of waves I, III and V; inter wave latencies of waves I–III, III–V and I–V; absolute interaural latency difference of wave V; and muscle artifacts during the recordings.

Reliability and Validity

Reliability was determined by ensuring that all audiological equipment was calibrated, and that sound-treated booths were utilized during testing. The cross-check principle was applied in all testing to ensure that there was good agreement between all test measures. Validity was assured by employing inclusion criteria that would eliminate confounding variables, although this was restricted, thereby reducing generalize ability of findings to a larger population; particularly pediatric populations, difficult-to-test populations, or populations which present with hearing loss.

Ethical considerations

Ethical clearance was obtained (Protocol Number: M10259) prior to the study being conducted. As part of ethical considerations in the current study, written informed consent was obtained from each participant and participants were assured of confidentiality and anonymity as research codes were used instead of identifying information. Additional ethical principles observed in the current study included:

- Autonomy: participants were respected and had freedom of choice in accepting the invitation to participate in the study and to withdraw from the study at any stage without any negative consequences.
- Beneficence and non-maleficence: positive steps were taken to reduce and prevent participant harm, by clarifying and adhering to the inclusion criteria, and ensuring that participants were completely aware of the side-effects of the melatonin. It was ensured that the
- participants benefited from the participation, by receiving a comprehensive hearing assessment.[34]

It was only once ethical clearance was obtained and permission obtained from all relevant authorities, that data collection was conducted in the sequence described above.

RESULTS AND DISCUSSION

The results of the current study are described and discussed in accordance with its aims.

Results of Basic Audiological Tests

Of the total sample of 27 participants, 26 participants presented with normal basic audiologic findings including clear otoscopic findings, normal tympanometric findings, and pure tone audiometry findings consistent with normal hearing sensitivity bilaterally. The mean pure tone average (PTA) was 4.31 dBHL in the right ear (SD = 3.93 dBHL), and 4.08 dBHL in the left ear (SD = 3.5 dBHL). These findings ensured that participants could undergo the ABR testing phase of the study.

Results of the ABR testing

Morphology, Repeatability, and Amplitude of the ABR waveform

Analysis of these factors pre and post-melatonin use revealed findings that were normal and consistent with normal hearing function. Normal and repeatable morphology with distinct and clear peaks with clinically significant peaks present at expected amplitudes was found during both testing conditions. This indicated that reliable and valid ABR could be recorded under both test conditions; which was a positive finding in the current study indicating that melatonin did not induce negative effects on morphology, repeatability and amplitudes of ABR in compliant adults with normal hearing. These findings exclude melatonin from pharmacological agents which are reported to affect the ABR[9] and support findings by Schmidt *et al.*[8] which show that melatonin does not negatively affect the ABR waveform. To ensure reliability of these findings, a randomized double blind analysis strategy was adopted; and an independent rater was also utilized to establish Cohen's kappa (inter-rater

agreement).[27,35] The inter-rater agreement was good as depicted in Table 3.

Table 3: Measures of agreement: Morphology, Amplitude and Repeatability of the ABR waveform. (N=108 recordings)

Factor	Percentage of agreement	value
Morphology of pre-melatonin recordings.	92 %	0.45
Morphology of post-melatonin recordings.	96 %	0.48
Repeatability of pre-melatonin recordings.	94 %	0.37
Repeatability of post-melatonin recordings.	90 %	0.49
Wave V: Wave I amplitude comparison of pre-melatonin recordings.	90 %	0.78
Wave V: Wave I amplitude comparison of post-melatonin recordings.	81 %	0.53

Absolute wave latencies, inter wave latencies, and absolute inter-aural latency difference of wave V

On the analysis of the absolute wave latencies, inter wave latencies, and absolute inter-aural wave latency difference of wave V, current findings are depicted in Table 4.

Table 4: Mean values and standard deviations of absolute wave latencies; inter wave latencies, and absolute latency difference of wave V of pre and post-melatonin ABR recordings. (N = 108 recordings)

Factor	Pre-melatonin ABR	Post-melatonin ABR
R AWL I	M: 1.44 ms SD: 0.11 ms	M: 1.43 ms SD: 0.05 ms
L AWL I	M: 1.42 ms SD: 0. 85 ms	M: 1.43 ms SD: 0.10 ms
R AWL III	M: 3.60 ms SD: 0.13 ms	M: 3.72 ms SD: 0.80 ms
L AWL III	M: 3. 62 ms SD: 0.13 ms	M: 3.61 ms SD: 0.14 ms
R AWL V	M: 5.45 ms SD: 0.18 ms	M: 5.39 ms SD: 0. 26 ms
L AWL V	M: 5.41 ms SD: 0.19 ms	M: 5.39 ms SD: 0.12 ms
R IWL I – III	M: 2.16 ms SD: 0.14 ms	M: 2.17 ms SD: 0.14 ms
L IWL I – III	M: 2.20 ms SD: 0.15 ms	M: 2.18 ms SD: 0.17 ms
R IWL III – V	M: 1.83 ms SD: 0.11 ms	M: 1.82 ms SD: 0.16 ms
L IWL III – V	M: 1.77 ms SD: 0.17 ms	M: 1.77 ms SD: 0.17 ms
R IWL I – V	M:3.99 ms SD: 0.17 ms	M: 3.96 ms SD: 0.21 ms
L IWL I – V	M: 3.98 ms SD: 0.21 ms	M: 3.96 SD: 0.14
ALD V	M:0.11 ms SD: 0.13 ms	M: 0.12 ms SD: 0.11 ms

R = right; L = left; AWL = absolute wave latency; IWL = inter wave latency; M = mean; SD = standard deviation; ALD = absolute latency difference; ms = milliseconds

Table 4 indicates mean results within normal limits for all tracings recorded under both test conditions. The mean absolute wave latencies of wave V are within normal limits for the pre-melatonin recordings, but are slightly earlier (0.02 ms) for the post-melatonin recordings. This earlier occurrence of the ABR waveforms post-melatonin was the general finding found in the current study in terms of absolute latencies, inter wave latencies, and absolute latency difference of wave V; although descriptively these differences were small. These differences were found to be statistically non-significant ($p > 0.05$) on the matched pairs t-Tests where comparisons of the absolute wave latencies, inter wave latencies, and absolute latency difference of wave V of the pre and post-melatonin ABR recordings were made (Table 5). These findings confirmed that melatonin did not lead to statistically significantly changes in the ABR results, a positive finding for the current study.

Table 5: Two-tailed p values (p = 0.05) of absolute wave latencies, inter wave latencies, and absolute latency difference of wave V of pre and post-melatonin ABR recordings. (N = 13 ABR analysis criteria)

Factor	t value	p value
R AWL I	0.532	0.599
L AWL I	-0.458	0.651
R AWL III	-0.804	0.429
L AWL III	0.424	0.675
R AWL V	1.086	0.296
L AWL V	0.635	0.531
R IWL I – III	-0.642	0.526
L IWL I – III	0.695	0.493
R IWL III – V	0.543	0.592
L IWL III – V	0.050	0.961
R IWL I – V	0.859	0.398
L IWL I – V	0.390	0.700
ALD V	-0.102	0.919

R = right; L = left; AWL = absolute wave latency; IWL = inter wave latency; ALD = absolute latency difference. $P < 0.05$ indicates significant findings

The fact that absolute wave latencies, inter wave latencies and absolute inter-aural latency difference of V were the same under both conditions is also a positive finding in that it indicates that melatonin did not impact on the reliability of the ABR as a measure in the current sample, a finding supportive of Schmidt *et al.*'s report on melatonin. [8]

Muscle artifacts of the ABR recordings

Although muscle artifacts were not exceedingly high pre-melatonin as none exceeded the 10 % cut-off when compared to the number of sweeps (a fact attributed to the fact that the sample comprised of adults who were cooperative during the testing, and did not present mobility that generated high artifacts), findings for comparison of muscle artifact pre and post melatonin still yielded positive results as depicted in Table 6.

Table 6: Summary of mean number of artifacts for pre and post-melatonin recordings

Factor	Pre-melatonin	Post-melatonin
Right	5.81 (SD = 10.619)	0.89 (SD = 2.044)
Left	11.78 (SD = 20.215)	2.85 (SD = 8.175)

The comparison of individual sets of pre and post-melatonin recordings indicates a significant decrease in muscle artifacts in post-melatonin recordings. The artifacts were significantly reduced during the melatonin state in 78 % of the recordings, and these changes were statistically significant ($p < 0.05$). The statistically significant reduction in muscle artifacts in the current sample has significant clinical implications as high artifacts are known to have a severe negative influence on the ABR recording. In the current study, a recommended dosage of 3 mg was used, which confirms the positive effect of this dosage in adults when recording is conducted even prior to the participants falling asleep; a factor different to previous studies. For example, in a similar study, children with suspected hearing loss were provided with between 5 mg and 20 mg of melatonin; depending on their age, and the testing began once each child had begun sleeping.[8] In another

study also on children 10 mg of melatonin was administered 30 minutes prior to the initiation of the testing procedure[22] granted that these were for different procedures. Although it has been reported that adults can be safely provided with 50 mg of melatonin[13] the current study indicated that 3 mg 40 minutes prior to the ABR testing can be just as effective. Current findings are thought to possibly be due to the fact that most drugs are reported to affect cortical functioning rather than brainstem functioning[6] an area that the ABR focuses on; and so there's an indicating from the current study that melatonin does not influence brainstem function, and also efficiently facilitates relaxation that is required during ABR to eliminate the noise that precludes ABR recording. The authors however believe that certain test conditions might need adherence to for these positive benefits to be achieved. Firstly, sufficient dosage of melatonin as well as adequate time period between the administration of melatonin and the initiation of the post-melatonin ABR can have an influence on the findings; and so need to be closely monitored. Secondly, the actions of the participants during the 40 minute waiting period, such as walking around and/or remaining active in a brightly lit room might also affect the results. Moving about might affect and/or delay the body's reaction to the melatonin. Lastly, as the current study was on adults who could voluntarily lie still and so did not need to be asleep for the test, a different protocol might need to be adopted for children where the requirement might be that they must fall asleep before testing can commence.

Additional analysis

Due to the nature of the current study, analysis of the effects of melatonin as a drug was thought to be crucial. No negative side effects were reported by any of the participants after an hour following testing. Participants reported a feeling of being well-rested; but were however normally functioning with no obvious and/or reported negative side effects.

CONCLUSIONS AND RECOMMENDATIONS

The current study which investigated the use of melatonin as a "sedative" during ABR testing in non-medical settings yielded positive results indicating that indicated that melatonin has a positive influence on ABR recording as it significantly reduced artifacts which are the main negative effect precluding ABR recording. Secondly, findings further indicated that melatonin does not negatively affect the ABR recording in terms of morphology, repeatability, and latencies; highlighting that the validity and reliability of the ABR as a measure is not compromised by melatonin as it can be by some pharmacological agents. It should be noted that this may only be true in the current sample which comprised of compliant normally hearing adults; and could vary significantly in other populations – an important implication for future studies. Current findings mean that melatonin does not appear to influence the ABR in a manner that might cause false positive or false negative findings, thereby impacting diagnosis. These findings may have significant implications for the audiologist in private practice as well as clinical facilities where medical personnel are not available to administer conventional sedation and medically monitor patients during testing. Arguably, since the current sample did not include pediatric populations; who form the majority of the "difficult-to-test" populations (and did not also include adults with functional hearing loss who present with their own testing complexities); it is impossible to automatically generalize current findings to these populations. Nonetheless, the current authors are of the view that an extension of the findings to the pediatric population can possibly be supported by earlier reports on successful use of Melatonin as an alternative to sedation in children undergoing MRI.[15,22] The consequent benefits for patients, particularly from contexts where resources are limited, are significant. Patients would not need to be admitted as inpatients and pay for additional resources just to undergo an audiologic evaluation. Current findings must however be interpreted within the scope of the current study which only focused on adults with normal hearing who were not "difficult-to-test", although it is not anticipated that these would be much different in other populations if factors mentioned above (dosage and duration of waiting time prior to ABR recording) have been taken into account. Current findings raise implications for future research such as replication of the study in larger sample sizes, in the pediatric population, in populations with suspected hearing loss, and with the inclusion of a control/placebo group.

REFERENCES

1. Hood LJ. Clinical applications of the auditory brainstem response. New York: Thomson Delmar Learning; 1998.
2. Johnson A, Yonovitz A. Habituation of auditory evoked potentials: the dynamics of waveform morphology. Aust NZ J Audiol 2007; 29(2): 77-88. http://dx.doi.org/10.1375/audi.29.2.77
3. Baranak CC, Marsh RR, Potsic WP. Sedation in brainstem response audiometry. Int J Pediatr Otorhi 1984; 8: 55-59. http://dx.doi.org/10.1016/S0165-5876(84)80025-7
4. Pillion JP, Bibat G, Naidu S. Effects of sedation on auditory brainstem response in Rett Syndrome. Paediatr Neurol 2010; 42 (5): 331-334. http://dx.doi.org/10.1016/j.pediatrneurol.2010.01.003 PMid:20399386 PMCid:PMC2858058
5. Roger A, Thornton D. Instrumentation and Recording Parameters. In, Burkard RF, Don M, Eggermont JJ (eds). Auditory Evoked Potentials: Basic Principles and Clinical Application. Baltimore: Lippincott Williams and Wilkins; 2007. p. 73-101.
6. Hall J. New handbook of auditory evoked responses. Boston: Pearson Education, Inc; 2007.
7. Sanchez JT, Gans D. Effects of artifact rejection and bayesain weighting on the auditory brainstem response during quiet and active behavioral conditions. Am J Audiol 2006; 15: 154-163. http://dx.doi.org/10.1044/1059-0889(2006/019)
8. Schmidt CM, Knief A, Deuster D, Matulat P, Zehnhoff Dinnesen AG. Melatonin is a useful alternative to sedation in children undergoing brainstem audiometry with an age dependent success rate - a field report of 250 investigations. Neuropediatric 2007; 38(1): 2-4. http://dx.doi.org/10.1055/s-2007-981467 PMid:17607596
9. Arnold SA. The auditory brainstem response. In, Roeser RJ, Valente M, Hosford Dunn H (eds.), Audiology: Diagnosis. 2nd ed., New York: Thieme Medical Publishers; 2007. p. 426-477. PMid:17387466
10. Reich DS, Wiatrak BJ. Methods of sedation for auditory brainstem response testing. Int J Pediatr Otorhi 1996; 38: 131-141. http://dx.doi.org/10.1016/S0165-5876(96)01432-2
11. Akin A, Esmaoglu A, Tosun Z, Gulcu N, Aydogan H, Boyaci A. Comparison of propofol with propofol-ketamine combination in pediatric patients undergoing auditory brainstem response testing. Int J Pediatr Otorhi 2005; 69: 1541-1545. http://dx.doi.org/10.1016/j.ijporl.2005.04.011 PMid:15936092
12. Naguib M, Gottumukkala V, Goldstein PA. Melatonin and anesthesia: a clinical perspective. J Pineal Res 2007; 42(1): 12-21. http://dx.doi.org/10.1111/j.1600-079X.2006.00384.x PMid:17198534
13. Mac Mahon K, Broomfield N, Espie C. A systematic review of the effectiveness of oral melatonin for adults (18 to 65 years) with delayed sleep phase syndrome and adults (18 to 65 years) with primary insomnia. Curr Psych Rev 2005; 1: 103-113. http://dx.doi.org/10.2174/1573400052953556
14. Mahlberg R, Kunz D. Melatonin excretion levels and polysomnographic sleep parametersin healthy subjects and patients with sleep-related disturbances. Sleep Med 2007; 8: 512–516. http://dx.doi.org/10.1016/j.sleep.2006.11.001 PMid:17581781
15. Ashrafi MR, Mohammadi M, Tafarroji J, Shabanian PS, Zamani GR. Melatonin versus chloral hydrate for recording sleep EEG. Eur J Pediatr

Neurol 2010; 14: 235–238. http://dx.doi.org/10.1016/j.ejpn.2009.06.010 PMid:19616978
16. Biogen. Melatonin. Retrieved from http://www.biogen.co.za/products/melatonin.asp; 2009.
17. Dodge NN, Wilson GA. Melatonin for treatment of sleep disorders in children with developmental disabilities. J Child Neurol 2001; 16(8): 581-4. http://dx.doi.org/10.2310/7010.2001.16810
18. Luboshitzky R, Shen Orr Z, Ishai A, Lavie P. Melatonin hyper secretion in male patients with adult-onset idiopathic hypogonadotropic hypogonadism. Exp Clin Endocr Diab 2000; 108(2): 142-5. http://dx.doi.org/10.1055/s-2000-5809 PMid:10826523
19. Buscemi N, Vandermeer B, Pandya R, Hooton N, Tjosvold L, Hartling L, Baker G, Vohra S, Klassen T. Melatonin for treatment of sleep disorders. Agency Healthcare Res Qual 2004; 108: 1- 8.
20. Natural Standard Research Collaboration. Melatonin. Retrieved from http://www.nlm.nih.gov/medlineplus/druginfo/natural/patient-melatonin.html; 2010.
21. World Wide Labs. Melatonin.com. Retrieved from http://www.melatonin.com/melatonin-cautions.php; 2010.
22. Johnson K, Page A, Williams H, Wassemer E, Whitehouse W. The Use of Melatonin as an Alternative to Sedation in Uncooperative Children Undergoing an MRI Examination. Clin Radiol 2002; 57: 502-506. http://dx.doi.org/10.1053/crad.2001.0923 PMid:12069468
23. Sury MRJ, Fairweather K. The effect of melatonin on sedation of children undergoing magnetic resonance imaging. Brit J Anaesth 2006; 97(2): 220-225. http://dx.doi.org/10.1093/bja/ael144 PMid:16782974
24. Isik B, Baygin Ö, Bodur H. Premedication with melatonin vs midazolam in anxious children. Paediatr Anaesth 2008; 18: 635-641. http://dx.doi.org/10.1111/j.1460-9592.2008.02608.x PMid:18616492
25. Sturgis P. Surveys and sampling. In, Breakwell G, Hammond S, Fife Schaw C (eds.), Research Methods in Psychology. 3rd ed., Sage Publications: London; 2006. p. 104-122.
26. Roeser R, Valente M, Hosford Dunn H. Diagnostic procedures in audiology. In, Roeser R, Valente M, Hosford Dunn H (eds.), Audiology: Diagnosis. 2nd ed., New York: Thieme Medical Publishers; 2007. p. 1-16.
27. Maxwell DL, Satake E. Research and statistical methods in communication sciences and disorders. New York: Thomson Delmar Learning; 2006.
28. Rappaport J, Provencal C. Neuro-otology for Audiologists. In, Katz J (Ed.), Handbook of Clinical Audiology. 5th ed., Baltimore: Lippincott Williams and Wilkins; 2002. p. 9-32.
29. Clark J, Roeser R, Mendrygal M. Middle Ear Measures. In, Roeser R, Valente M, Hosford Dunn H (eds.), Audiology: Diagnosis. 2nd ed., New York: Thieme Medical Publishers; 2007. p. 238-260.
30. Bess FH, Humes LE. Audiology: The fundamentals (4thed). Philadelphia: Lippincott Williams and Wilkins; 2008.
31. Meline T. Research in Communication Sciences and Disorders: Methods-Applications-Evaluations. New Jersey: Pearson Education, Inc; 2006. PMid:16427169
32. Fife Schaw C. Principles of statistical inference tests. In, Breakwell G, Hammond S, Fife Schaw C, Smith J (eds.), Research methods in psychology. 3rd ed., London: Sage Publications; 2006. p. 388-413.
33. Howell DC. Statistical methods for psychology (4thed). Belmont: Wadsworth Publishing Company; 1997. p. 659-689.
34. Robertson M, Ryan C, Walter G. Overview of psychiatric ethics III: principles-based ethics. Aust Psych 2007; 15(4): 281-286. http://dx.doi.org/10.1080/10398560701390231 PMid:17612879
35. Sardanelli F, Leo G. Biostatistics for radiologists: planning, performing, and writing a radiologic study. Milan: Springer; 2009. p. 125-140. http://dx.doi.org/10.1007/978-88-470-1133-5

Source of support: Nil, Conflict of interest: None Declared

QUICK RESPONSE CODE	ISSN (Online) : 2277 –4572
	Website http://www.jpsionline.com

How to cite this article:
Katijah Khoza-Shangase, Marika Mavrokordatos. The use of melatonin for sedation during auditory brainstem response testing: An alternative to sedation in non-medical settings? *J Pharm Sci Innov*. 2013; 2(5): 60-66.