Perspective Article

Cortical Auditory Evoked Potentials: Evidence for use in Clinical Practice

JAIISH(2016)
Vol 35, pp. 1-8

C. S. Vanaja

Affiliations

School of Audiology and Speech Language Pathology, Bharati Vidyapeeth Deemed University, Pune, Maharashtra, India

Corresponding Author

C. S. Vanaja
Professor, Bharati Vidyapeeth Deemed University, School of Audiology and Speech Language Pathology, Pune Satara Road, Pune - 411043, Maharashtra, India
Email: csvanaja@gmail.com

Key Words

Long latency response
N1-P2 complex
Aided cortical responses
CAEP protocol

Abstract

Electrophysiological measures are used during clinical evaluation to supplement and/or compliment the results of behavioural measures. Cortical auditory evoked potentials (CAEPs) have many clinical applications but are not widely used during clinical evaluation. However, considerable evidence exists in literature recommending the use of CAEPs in clinical practice. This article summarises these evidences highlighting its strengths and limitations. The protocol recommended for recording CAEPs in clinical practice is also briefly discussed.

Background

Cortical Auditory Evoked Potentials (CAEPs), initially referred to as slow vertex responses, were the first auditory evoked potentials to be recorded from the human brain. Davis initially recorded cortical responses to auditory stimuli in 1939 (reported in Picton, 2010). These responses reflect synchronous neural activation of structures in the thalamic-cortical segment of the central auditory system (Souza & Tremblay, 2006). The exogenous, obligatory CAEPs recorded from an adult with normal hearing typically consists of P1-N1-P2 complex (Figure1) occurring in the latency range of 60 to 300 ms after the onset of a stimulus.

CAEPs can be recorded from newborn babies and the responses undergo changes through childhood (Sharma & Cardon, 2015; Wunderlich, Cone-Wesson, & Shepherd, 2006). CAEPs recorded from newborn babies and infants typically consists of a large positive-negative complex that starts to differentiate into P1, N1, P2, N2 as the child grows (Cone & Whitaker, 2013; Gilley, Sharma, Dorman, & Martin, 2005; Sharma, Kraus, McGee, & Nicol, 1997).

Although CAEPs were the first auditory evoked potentials to be discovered and the first potentials to be used for objective assessment of hearing, they are under-utilised in today's clinics. The clinical applications of CAEPs include estimating threshold in difficult-to-test population, assessing auditory neuropathy spectrum disorders, measuring outcome with hearing devices (hearing aids/cochlear implants), assessing central auditory processing, monitoring improvement/changes in auditory processing with use of hearing devices and/or auditory training.

CAEPs in estimation of hearing thresholds

CAEP threshold, the lowest intensity at which a replicable response is obtained, can be used to predict behavioural threshold. It has been reported that CAEP threshold is generally 5 to 10 dB higher than the behavioural threshold (Lightfoot & Kennedy, 2006). Picton (1991) suggested that a physiological test that is most appropriate for assessing behavioural thresholds should satisfy five important criteria. It should assess hearing threshold accurately; it should be possible to record the responses from persons of all age groups; it should be easily recorded during different sleep and wakefulness; it should be recordable for stimuli representing different frequencies of the conventional audiogram and it should assess thresholds specific to different frequencies. The major limitation of CAEPs is that the responses are affected by sleep

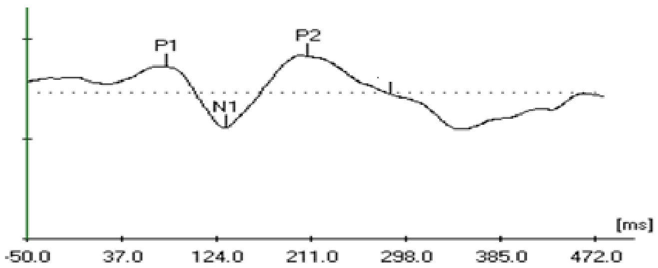

Figure 1: CAEP recorded from an adult with normal hearing .

and alertness (Rapin, Schimmel, & Cohen, 1972). CAEPs satisfy the other four criteria and the efficiency of CAEPs in estimating frequency specific hearing thresholds is well documented. Another challenge is difficulty in obtaining replicable artefact free responses. Interpretation of the waveforms becomes difficult when the waveforms are noisy. Recent studies emphasise the usefulness of CAEPs in threshold estimation using automatic detection software. Lightfoot and Kennedy (2006) have developed an automatic software that can estimate hearing thresholds for three frequencies in both ears in 20.6 minutes. Van Dun, Dillon, and Seeto (2015) reported that behavioural thresholds can be accurately predicted based on CAEPs using appropriate statistical response detection algorithm in combination with a decision tree to adjust the presentation level. Considering the accuracy with which CAEPs can predict frequency specific thresholds, it is a good choice of test for assessing or crosschecking hearing thresholds in older children and adults who can be tested while they are awake. However, audiologists often use physiological tests to estimate threshold in infants or young babies who are difficult-to-test while they are awake. Hence, auditory brainstem response is preferred to CAEPs for estimating hearing thresholds.

CAEPs in measuring outcome with hearing aids

Attempts to record CAEPs in persons wearing hearing aid started 50 years ago (Rapin & Graziani, 1967). Controversy has prevailed over the years regarding its usefulness as a clinical measure in measuring outcome with hearing aid/s. The vast majority of evidence suggests that CAEPs demonstrate whether a person is hearing with a hearing aid (Korczak, Kurtzberg, & Stapells, 2005; Koul & Vanaja, 2010) but CAEPs do not reflect the hearing aid gain. Tremblay, Kalstein, Billings, and Souza (2006) observed very subtle enhancement in amplitude of CAEPs when the hearing aid provides mild high frequency gain. Similarly, Billings, Tremblay, Souza, and Binns (2007) reported no significant difference in latency and amplitude of CAEPs when the hearing aid gain was changed by 20 dB. However, evidence suggests that CAEPs can indicate whether the signal is audible and this can help in validating benefit from hearing aid/s. While validating benefit from hearing aids, a clinician is interested in knowing whether a person can understand normal conversation with the hearing aid and audibility is a prerequisite for this. This can be evaluated by recording CAEPs at 65 dB SPL.

Korczak and Stapells (2010) reported that the use of personal hearing aid substantially improved the detectability of CAEPs and a majority of individuals with hearing impairment showed reduced latency, increased amplitude and improved morphology when tested with their hearing aids. The improvement in detectability was especially observed in individuals with higher degree of hearing impairment. Vanaja and Khandelwal (2016) also observed that the detectability of CAEPs to speech stimuli presented at 65 dB SPL increased with the use of personal hearing aids especially in persons with moderately-severe to severe hearing loss. Figure 2 shows a CAEP waveform recorded at 65 dB SPL from a person with severe hearing loss who benefits from hearing aids while Figure 3 shows aided CAEPs which did not show any improvement when compared to unaided responses. The results of a majority of the studies (Billings, Tremblay & Souza, & Binns; Tremblay, Kalstein, Billings & Souza, 2006) also suggest that latency and amplitude of aided CAEPs may not be good parameters to measure the benefit from hearing aid/s. Rather, detectability of a response is a better indicator of hearing aid benefit in a clinical setting.

A few investigations indicate that N1-P2 complex can be an index of performance with hearing aids. Koul and Vanaja (2010) observed significant correlation between morphology of CAEPs and functional gain of hearing aids. Hemanth (2015) reported that the cortical representation of signals as reflected by CAEPs was better in hearing aid users whose acceptable noise levels was higher.

Researchers have investigated the usefulness of CAEPs in assessing benefit from hearing aids in different frequency regions. Considerable work has been carried out in the National Acoustic Laboratory by Dillon and his co-workers using speech stimuli /m/, /g/ and /t/ to assess hearing across the speech spectrum (Chang, Dillon, Carter, Van Dun, & Young, 2012; Golding et al., 2007; Munro, Purdy, Ahmed, Begum, & Dillon, 2011). Overall, the results of these investigations suggest that CAEPs can be a promising tool. Additionally, a few studies have shown that the benefit of activation of frequency compression can be documented using CAEPs (Billings, Papesh, Penman, Baltzell, & Gallun, 2012; Ching, Zhang, Hou, & Van Buynder, 2016; Glista, Easwar, Purcell, & Scollie, 2012).

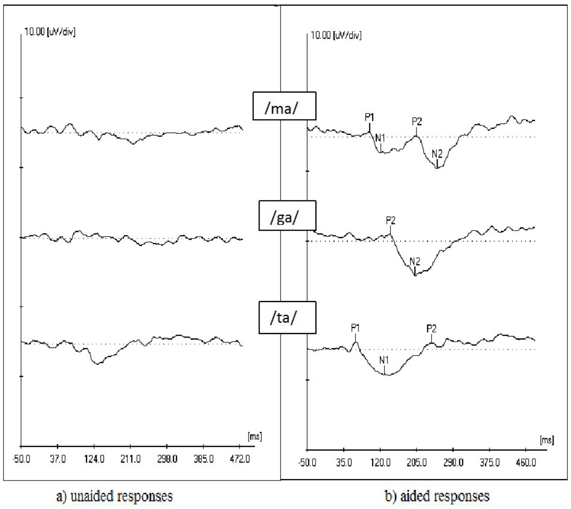

Figure 2: CAEPs from a person with hearing loss who showed benefit with hearing aids.

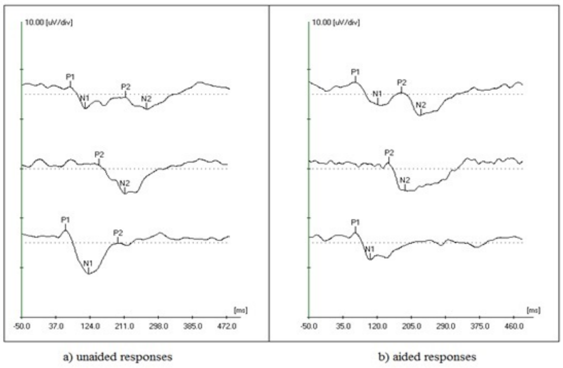

Figure 3: CAEPs showing no improvement with use of hearing aids.

Overall, there is evidence in literature suggesting that CAEPs can be recorded reliably from persons using hearing aids, but there is variability in the results observed in different studies. This variability may be due to the differences in the test protocol and the amplification devices used. It has been well established that both stimulus related and acquisition related factors can affect CAEPs. In addition, hearing aid related variables can influence aided cortical potentials and the nature of these effects is yet to be completely explored. It has been reported that hearing aid processing alters the acoustic properties of the signal used for eliciting CAEPs and the aided CAEPs may not accurately reflect the signal amplified from a hearing (Jenstad, Marynewich, & Stapells, 2012; Marynewich, Jenstad, & Stapells, 2012). Also, CAEPs may not reliably reflect hearing aid gain, as amplification alters the signal to noise ratio, which in turn can affect the CAEPs (Billings, Tremblay, & Miller, 2011). An investigation by Billings and Grush (2016) also documented that the latency of CAEPs are affected by signal-to-noise ratio and there is an interaction between the effects of signal type and signal-to-noise ratio. Van Dun, Kania, and Dillon (2016) observed a significant increase in CAEP amplitude with increase in gain of a hearing aid in persons with hearing impairment, but such an effect was not observed in persons with normal hearing. They hypothesised that hearing aid increased audibility in persons with hearing impairment whereas in persons with normal hearing, where the signals were already audible, the internal noise of the hearing aid reduced the signal-to-noise ratio.

Further, the effect of amplification on hearing aid output is complicated as it depends on the amplification device or the hearing aids used. Easwar, Purcell, and Scollie (2012) compared hearing aid processing of phonemes in running speech and phonemes used for recording CAEPs. There was a difference in processing of the two signals by hearing aids. In addition, they observed that the output from the hearing aid varied depending on the hearing aid used.

Thus, the present level of evidence suggests that the presence of CAEPs in persons using hearing aid indicates whether a signal is audible but it cannot be used to assess aided threshold. Also, aided CAEPs may not reflect the gain of the hearing aid. Further, the absence of CAEPs must be interpreted with caution as many factors unrelated to hearing loss may also lead to absence of CAEPs.

CAEPs in persons with cochlear implants

Evidence from literature indicates that CAEPs help in deciding candidacy for cochlear implantation. Absence of CAEPs with hearing aids (aided CAEPs) in children with normal radiological findings suggests that hearing aids may not be providing sufficient gain to enable them to hear. Cochlear implantation may be a choice of rehabilitation in such children. Punch, Van Dun, King, Carter, and Pearce (2016) have described the CAEP protocol followed in clinics of Australian Hearing for infant hearing aid evaluation. The protocol includes recording CAEPs for /m/, /t/ and /g/ at 55 dB SPL, 65 dB SPL and 75 dB SPL. Based on a survey of audiologists working for Australian Hearing Clinic, they report that it is feasible to include CAEPs in infant hearing aid evaluation protocol. There is a need to investigate whether the use of CAEPs has increased the number of children being referred for cochlear implantation at a younger age. Recording of CAEPs may also help in predicting usefulness of cochlear implants in children with cochlear nerve deficiency. Roland, Henion, Booth, Campbell, and Sharma (2012) explain with case examples the possible usefulness of P1 biomarker in determining cochlear implant candidacy in children with cochlear nerve deficiency. Follow-up studies are required on children who are recommended cochlear implantation based on the results of CAEPs.

Reliable CAEPs can be recorded from children using cochlear implants. Figure 4 shows CAEPs recorded using Biologic Navigator Pro from a child using cochlear implants. A series of studies by Sharma and her colleagues (Sharma, Dorman, & Spahr, 2002; Sharma et al., 2005; Sharma, Martin, Roland, Bauer, Sweeney, Gilley & Dorman, 2005 ; Sharma, Glick, Deeves & Duncan, 2015) have indicated that the latency of P1 can be used as a biomarker of development of central auditory pathway in children with hearing loss using cochlear implants. The results indicate that latency and amplitude of P1 depends on the age of implantation as well as implant age. A recent investigation by Sharma, Campbell, and Cardon (2015) suggests that N1 can also be used in conjunction with P1 to assess maturation of the cortical pathway.

CAEPs in persons with Auditory Neuropathy Spectrum Disorders

Auditory neuropathy spectrum disorder (ANSD) is a disorder characterized by dyssynchrnous nerve firings. Auditory brainstem response (ABR), which requires highly synchronous firing, is absent or abnormal in persons with ANSD. CAEPs may be present in many persons with ANSD, as it require less synchronous firing when compared to ABR (Kraus et al., 2000; Kumar & Jayaram, 2005; Narne & Vanaja, 2008; Singh & Barman, 2010; Vanaja & Manjula, 2004; Yuvaraj & Mannarukrishnaiah, 2015). The presence or absence of CAEPs may be taken as an indicator of severity of ANSD. Absence of CAEPs in a person with ANSD indicates more problem in understanding speech when compared to a person with ANSD who has recordable CAEPs. Rance, Cone-Wesson, Wunderlich, and Dowell (2002) reported that in children with ANSD, the presence of CAEPs with normal latency and amplitude was consistent with reasonable speech perception ability. Narne and Vanaja (2008) observed that the amplitude of N1-P2 complex correlates with word recognition scores in persons with ANSD, suggesting that CAEPs may help in predicting perceptual skills in persons with ANSD. This is in consensus with the reports of Vanaja and Manjula (2004) who reported that persons with ANSD in whom CAEPs could be recorded showed greater benefit with hearing aid when compared to those with absence of CAEPs. Narne, Barman, and Sinha (2011) reported that prolongation in latency and reduction in amplitude of N1 observed in persons with ANSD correlate with word recognition score and gap detection threshold but not with audibility.

Sharma, Glick, Deeves, and Duncan (2015) suggested that children with ANSD can be classified as having mild, moderate or high level of dyssynchrony based on P1 response. A child with normal P1 is said to have mild dyssyncnrony while a child with delayed and low amplitude P1 has moderate dyssynchrony. They further suggested that absent P1 in a child with ANSD indicates high level of dyssynchrony. Evidence in literature indicates that CAEPs, when used in conjunction with other measures, help in diagnosis and thus help in early management of children with ANSD (Gardner-Berry, Purdy, Ching, & Dillon, 2015; Pearce, Golding, & Dillon, 2007). It is also useful in monitoring progress with the hearing devices (Cardon & Sharma, 2013).

CAEPs in persons with Central Auditory Processing Disorders

CAEPs reflect cortical functioning and hence they can be expected to be deviant or abnormal in persons with central auditory processing disorder. Although a few studies report of abnormal or absent CAEPs in persons with central auditory processing disorder (Jirsa & Clontz, 1990; Tomlin & Rance, 2016), there is lack of evidence demonstrating CAEPs as a good measure of assessing central auditory processing disorder. A few studies on children with learning problem/dyslexia have reported abnormal CAEPs indicating deviant auditory processing. Some of the studies indicate that CAEPs recorded in presence of noise may be more sensitive in identifying auditory processing problem when compared to CAEPs in quiet (Cunningham, Nicol, Zecker, Bradlow, & Kraus, 2001; Wible, Nicol, & Kraus, 2002). Attempts have been made to use CAEPs to assess gap detection ability (Harris, Wilson, Eckert, & Dubno, 2012), temporal integration ability (Srividya & Vanaja, 2003), but there is dearth of evidence demonstrating their usefulness during clinical assessment.

At present, CAEPs may be a choice of tests in assessment of persons with CAPD only when behavioural measures cannot be administered. In such cases, absence of CAEPs may be taken as an indication of CAPD. Presence of CAEPs does not rule out CAPD, as it merely indicates that the signal has reached the cortex but does not provide any information regarding processing of the signal. CAEPs are useful in demonstrating auditory plasticity, changes in organisation of central auditory system that has occurred with rehabilitation, either through use of hearing devices (Purdy & Kelly, 2016) or with auditory training (Tremblay & Kraus, 2002; Tremblay, Shahin, Pic-

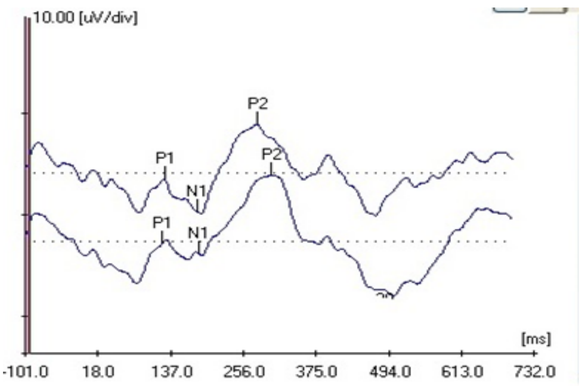

Figure 4: CAEPs recorded from a child using cochlear implant.

ton, & Ross, 2009; Vaidyanathan, 2015; Vanaja & Maruthy, 2004).

Protocol for recording CAEPs

It is crucial that appropriate test protocol be used for recording CAEPs, as the response latency, amplitude and morphology depends on factors related to the stimuli and acquisition parameters . The protocol used for recording CAEPs varies across studies in terms of stimuli, acquisition and waveform analysis. Further research is needed to standardise a uniform protocol for recording CAEPs during clinical evaluation. Some of the important factors that need to be considered while recording CAEPs are discussed briefly here.

Stimuli: CAEPs can be recorded using a variety of stimuli including clicks, tone burst and speech. If CAEPs are used for threshold estimation, then tone burst is the choice of stimuli. A variety of stimuli has been used for recording CAEPs to assess benefit from hearing aids or cochlear implants. However, the influence of signals processed through hearing aids or cochlear implants on these stimuli is yet to be understood completely. The advantage of CAEPs over auditory brainstem response in measuring hearing aid benefit is the possibility of recording good responses using long duration stimuli. Only a few investigators have recorded CAEPs using tone bursts in persons with hearing aids (Billings et al., 2012; Glista et al., 2012; Marynewich et al., 2012). The majority of these investigators have used speech syllables. The choice of speech syllables has varied among the researchers. Syllable /ba/ is used by Sharma and colleagues while Dillon and co-workers recommend the use of syllables /m/, /t/, /g/ and /s/. Other phonemes, /a/, /i/. /u/, and /sh/ have been used less frequently (Easwar et al., 2012; Koul & Vanaja, 2010). Tone bursts are not the choice of stimuli for evaluating benefit of hearing aids, unless the usefulness of frequency compression hearing aids is being evaluated. Getting information about audibility of specific frequencies may throw more light on the effectiveness of frequency compression. Otherwise, syllables with acoustic energy concentration at high frequencies should be used to evaluate the usefulness of frequency compression hearing aids. An investigation by Ching et al. (2016), using speech syllables /g/, /t/ and /s/, demonstrated that CAEPs to /s/ was effective in detecting the activation of nonlinear frequency compression circuit of hearing aids. HEARLab^{TM} is an instrument that has been fabricated specifically for recording aided cortical responses, with inputs from National Acoustic Laboratory, Australia. This instrument has facility to present four syllables, /m/, /t/, /g/ and /s/. Since many audiologists use this instrument during clinical evaluation and many investigators carryout research using this instrument, these syllables may soon become standard stimuli for recording aided CAEPs.

The stimuli for recording CAEPs can be presented through supra-aural earphones or insert earphones while assessing hearing sensitivity. A bone vibrator may be used when required. Sound-field speakers are recommended for recording CAEPs in persons wearing hearing aids/cochlear implants. The intensity chosen for presentation of stimuli varies depending on the purpose of evaluation. Threshold estimation involves recoding CAEPs for stimuli presented at different intensities, whereas fixed intensity/intensities (supra threshold) may be used while checking benefit from hearing aids/cochlear implants (e.g., 65 dB SPL). The clinical protocol used in Australian Hearing aid for hearing aid evaluation of infants includes recording of CAEPs at 55 dB SPL, 65 dB SPL and 75 dB SPL for /m/. /t/ and /g/ (Punch et al., 2016).

Recording of waveforms: CAEPs have been recorded through single channel as well as multichannels. The number of electrodes used for recording generally varies from 3 to 64, with a few investigators having used as many as 256 channels. Multichannel recording with topographical analysis is useful for understanding neurophysiology. Of course, it has the additional advantage of improving signal-to-noise ratio. However, when a clinician is only interested in the presence or absence of a response, the use of just a few electrodes which gives a clear responses, is preferred. Therefore, a single channel recording is sufficient and may be practical if CAEPs are recorded in clinical practice for assessing hearing or benefit from hearing devices. Sharma and colleagues in Northwestern University suggest that single channel recording with non-inverting electrode on Cz and inverting electrode on mastoid (either test ear or contralateral mastoid) can be used for recording CAEPs with hearing aids during clinical evaluation. However, they recommend monitoring of ocular artefacts using additional 2 electrodes while recording CAEPs in persons using cochlear implants. Dillon and co-workers use single channel recording while testing persons using hearing aids and do not monitor ocular artefacts. Lightfoot (2016) opines that recording of ocular artefacts is not essential during clinical evaluation, though research studies show that removing ocular artefacts and carrying out independent component analysis using multichannel recording will significantly improve signal to noise ratio.

The responses picked-up are amplified by a factor of 30,000 and passed through a band-pass filter with high-pass cut-off of 1 Hz and a low-pass cut-off of 30 Hz or 100 Hz. If a clinician is interested in only N1-P2 complex, a much narrower filter range of 1 Hz to 15 Hz can be used to improve signal-to-noise ratio as the spectral content of N1-P2 complex is 2 to 5 Hz (Lightfoot, 2016). The analysis window should be at least 500 ms. It is important to include a pre-stimulus window of 100 ms to 200 ms to get a baseline recording. With this time window, inter-stimulus interval should be at least 600 ms to 700 ms, so a repetition rate of 1.1 per second is recommended for adults. A repetition rate of 0.5 per second (1 stimulus in every 2 seconds) or lesser is recommended for infants and children. A minimum of 2 averages (each for 50 stimuli) is required to check replicability, especially when automatic detection of waveforms is not used. A grand average may be taken after checking for replicability to improve signal-to-noise ratio.

Waveform analysis: One of the challenges in using CAEPs for clinical evaluation is the waveform analysis. As in all evoked potential testing, replication of responses is the golden rule followed in ensuring correct detection of response. However, obtaining a response with a good signal to noise ratio is difficult especially during single channel recording without rejection of ocular artefacts. HEARLab^{TM} incorporates an automatic statistical detection method based on Hotelling's T2 to identify the presence of a response. Hence, it overcomes the challenges posed to a beginner in interpreting CAEPs.

Thus, the present level of evidence is encouraging for use of CAEPs during clinical evaluation of persons with hearing aids or cochlear implants. It gives information regarding benefit from hearing aids or cochlear implants and helps in planning further rehabilitative measures in difficult-to-test population. Aided CAEPs are not a good measure of aided thresholds, they merely indicate if the sounds/speech is audible at a given intensity, e.g., at 65 dB SPL which is the normal conversational level. The presence of CAEPs reflect neural processing of the signal but does not indicate that the brain has interpreted the stimulus heard. The absence of CAEPs does not always mean that there is a problem in processing of the signal, as many factors related to the stimuli, recording and hearing aids/cochlear implant processor can affect the responses.

Acknowledgments

Author wishes to thank the editorial committee of JAIISH for the invitation to write an article. Author wishes to acknowledge Ms. Nimisha Khandelwal for assisting in collecting CAEP waveforms while studying at Bharati Vidyapeeth Univeristy School of Audiology and Speech Language Pathology, Pune.

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