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Acoustic Change Complex as a Neurophysiological Tool to Assess Auditory Discrimination Skill: A Review

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Abstract

Introduction Acoustic change complex (ACC) is a type of event-related potential evoked in response to subtle change(s) in the continuing stimuli. In the presence of a growing number of investigations on ACC, there is a need to review the various methodologies, findings, clinical utilities, and conclusions of different studies by authors who have studied ACC.

Objective The present review article is focused on the literature related to the utility of ACC as a tool to assess the auditory discrimination skill in different populations.

Data Synthesis Various database providers, such as Medline, Pubmed, Google, and Google Scholar, were searched for any ACC-related reference. A total of 102 research papers were initially obtained using descriptors such as *acoustic change complex*, *clinical utility of ACC*, *ACC in children*, *ACC in cochlear implant users*, and *ACC in hearing loss*. The titles, authors, and year of publication were examined, and the duplicates were eliminated. A total of 31 research papers were found on ACC and were incorporated in the present review. The findings of these 31 articles were reviewed and have been reported in the present article.

Conclusion The present review showed the utility of ACC as an objective tool to support various subjective tests in audiology.

Keywords
- auditory discrimination
- review
- acoustics

Introduction

Auditory evoked potentials (AEPs) are defined as small changing voltages that are elicited using auditory stimuli.[1] These potentials are divided into various categories based on the latency, amplitude, and origin of the potentials. Cortical event-related potentials (ERPs) are slow and late potentials that occur at least 50 milliseconds following the stimulus onset, recorded in response to the auditory stimuli.[1,2] These responses are mainly used for studying the maturation[2,3] and aging processes.[4,5] Cortical auditory evoked potentials (CAEPs) are also used to assess the auditory system in specific clinical populations, such as patients with cochlear hearing loss[6,7] and cochlear implants recipients.[8,9] The acoustic change complex (ACC) is a type of ERP recorded in response to the change(s) in the continuing stimuli in terms of frequency, intensity, and duration. As a waveform reflects the acoustic change contained in the stimuli, it was termed

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ACC by Martin and Boothroyd.[10] The ACC shows the auditory discrimination skill at the higher auditory level, that is, the auditory cortex, and it provides information about the brain's capacity to process the acoustic features of speech.[11] As reported by various studies, ACC is used in various populations, such as in children,[12] adults,[13,14] individuals with auditory neural spectrum disorders,[15] as well as hearing aid[12] and cochlear implant users.[16] Various researchers also suggested that ACC may be a useful tool in the assessment of the auditory perception capacity.[17] As compared with other potentials, such as P300 and mismatch negativity (MMN), which is used to investigate the auditory discrimination skill, ACC elicits responses with larger amplitudes and better signal-to-noise ratios, thus requiring less time and fewer stimuli presentations for recording.[10] In view of the growing number of research articles on ACC, there is a need to summarize its clinical utility and its role as a potential tool to investigate the auditory discrimination skill in the clinical population. The present study aimed to review research articles on the clinical implications of ACC.

Review of Literature

Several search engines, like Google Scholar, Pubmed, SciELO, Biblioteca Cochrane, PsycInfo, Web of Science, and Index Copernicus, were explored. The search terms used were: *acoustic change complex*, *clinical utility of ACC*, *ACC in children*, *ACC in cochlear implant users*, and *ACC in hearing loss*. Research papers published between 1980 to 2020 were shortlisted for review. A total of 102 articles were initially obtained using the above-mentioned search terms. The titles, authors, and date of publication were compared, and the duplicates were excluded. This resulted in the retention of 56 articles. In the second stage, the articles found on other auditory evoked potentials, such as CAEP , P300, MMN, and mid latency response (MLR), were excluded from the present review, and the articles on the ACC's core area were retained. This resulted in the exclusion of 25 articles, which led to only 31 articles being included in the review. The outcomes and clinical implications from these 31 articles were reviewed and have been reported in the present article. The Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines were used for the present review. ►**Fig. 1** displays the flowchart showing the various stages of the selection process of the articles reviewed in the present study.

The Effect of Aging, Gender, and Hearing Loss on Auditory Discrimination

The ACC has been studied to investigate the effect of aging on the auditory discrimination skill.[18] Harris et al., in 2007, investigated behavioral and electrophysiological intensity discrimination performance in 20 subjects, 10 young and

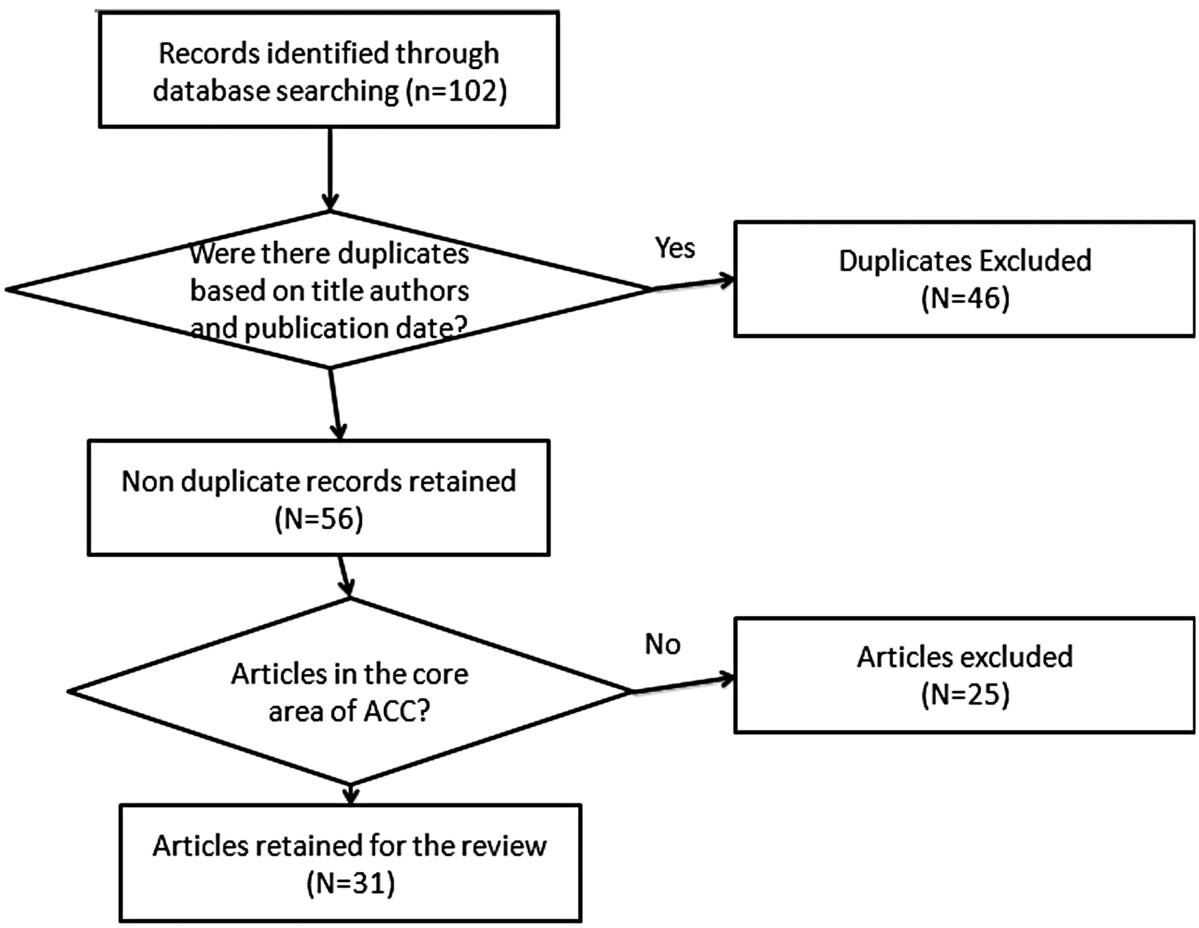

Fig. 1 Flowchart showing the various stages for selecting the final articles for the present review study.

10 older.[18] The behavioral measure showed that normal hearing older adults have poor intensity discrimination skill compared with younger ones, which may be due to poor temporal processing caused by aging. In this study, they also investigated the age-related effects on intensity discrimination with ACC. The intensity increments ranged from 0 to 5 dB in single dB steps. The N1–P2 was evoked by intensity increase in an otherwise continuous pure tone delivered at 70 dB SPL. The threshold for intensity discrimination was considered as the minutest change in intensity to evoke N1–P2 responses. Similar to what happened in the case of behavioral responses, the N1–P2 (ACC) responses for older adults were significantly delayed when compared with those of younger adults. The concordance in intensity discrimination thresholds for behavioral measures and evoked potentials (ACC) supports the possibility that the N1–P2 measures (ACC) shows the physiological detection of intensity change, which, in turn, relates to intensity discrimination. From the above-mentioned study, it can be inferred that ACC can act as an objective tool to assess age-related changes in the brain's capacity to process changes in acoustic features.

Shetty and Manjula, in 2012, investigated the relationship between gender and ACC using the /sa/ and /si/ stimuli.[14] The result showed that the mean latencies of N1–P2 and 2N1–2P2 were shorter in female when compared with male participants. They also reported that there was a significant main effect on the latency of 2N1 alone between male and female participants. In terms of amplitude, it was observed by researchers that female subjects had larger amplitude compared with male subjects in all components of ACC. The results also revealed that there was a significant main effect in the amplitude of N1 and 2P2 between male and female participants. The reason could be the head circumference size, which is relatively smaller in females, so the stimulus takes less time, and volume is better conducted.

Trembley et al., in 2006, did a study on aided ACC to know more about the combined effect of amplification and hearing loss on the cortical neural representation of consonant-vowel (CV) transition (/si/ and /ʃi/).[19] Seven subject aged 50 to 76 years with bilateral mild-to-severe cochlear hearing loss were considered for the investigation. They found that the group's mean waveforms from all electrode sites demonstrated distinct responses to /si/ and /ʃi/. The results revealed that amplification did not significantly alter the onset of /s/ and /ʃ/, because they did not find any latency and amplitude difference in the first negative peak of /si/ and /ʃi/. The above-mentioned literature showed that acoustic changes within a syllable are normally represented in the auditory cortex in subjects with sensorineural hearing loss. Mathew et al., in 2016, investigated behavioral sensitivity to pitch cues using ACC among individuals with cochlear hearing loss.[20] They found that the ACC amplitudes were reduced for the group with cochlear hearing loss compared with controls. From the outcome of the study, the authors concluded that they would recommend the use of ACC to evaluate the processing of complex acoustic cues in individuals with cochlear hearing loss. The authors concluded that ACC can be a potential clinical tool in the evaluation of benefit from auditory training and hearing instrument digital signal processing strategies. Cowan et al. reported that ACC might be preferred over visual reinforcement infant speech discrimination for auditory discrimination evaluation in infants, which shows the utility of ACC in a difficult-to-test population.[21]

Neural Representation of Subtle Changes in a Continuous Stimulus

Martin and Boothroyd reported that ACC is a CAEP (P1–N1–P2) evoked by an alteration within a continuous stimulus.[10] The researchers also believed that ACC is basically a response to transition from fricative to vowel,[11] change in intensity, frequency, and phase modulations in continuous tones[22–24] and alteration in periodicity.[10] The ACC can also be recorded in two CV syllables (CVCV) combination.[25]

Jerger and Jerger recorded the amplitude of the averaged electroencepahlic response (AER) to frequency and intensity changes and compared it with the behavioral performance in subjects with normal hearing and sensorineural hearing loss.[22] They observed that the behavioral differences in both intensity and frequency resolution were paralleled in ACC amplitude response. Similarly, Martin and Boothroyd, in 1999, studied whether the N1–P2 (ACC) is evoked by a variation of periodicity in between continuous stimuli, without any changes of spectral envelope and root mean squared (RMS) intensity.[10] The stimuli used in the investigation were a complex tone and a noise band without any change of spectral envelope and RMS intensity. To evoke ACC, the signal was made in such a way to produce two stimuli that altered in the middle (noise-tone, tone-noise). Two stimuli were also generated as control stimuli for the investigation by attaching two copies of the noise and two copies of the tone (tone only, noise only). The stimuli were delivered in such a way that the onset-to-onset interstimulus interval was 3 seconds. The response from the control stimuli (tone only, noise only) showed a distinct N1–P2 complex, whereas noise-tone and tone-noise stimuli elicited an additional distinct N1–P2 ACC in response to the periodicity occurring in the middle. The conclusion made by the researchers was that ACC is very sensitive to study neural processing of any changes in periodicity.

Another study done by Ostroff et al. recorded ACC in eight young adults with normal hearing.[11] The stimuli taken was the syllable 'sei', with the sibilant 's' and the vowel 'ei' removed from the syllable. The recording was done at different sites of the scalp, that is, 'Fz, Cz, Pz, A1, and A2', referenced to the nose. The result revealed that, in the group's mean waveform, distinct responses were obtained for both sibilant and isolated vowels. It was also observed that even though the response of the 's' was weaker than that of 'ei', both had N1 and P2 components (ACC) with latencies according to sound onset. For the vowel, the onset response was conserved in the response to the complete syllable but with decreased amplitude. The study concluded that the ACC evoked in response to 'ei' within the complete syllable showed a shift of cortical stimulation due to change in spectrum at the transition from CV. It was also concluded by the researchers that changes from aperiodic to periodic stimulation may also produce changes in cortical to complex, time-varying speech waveform which showed features of acoustic change in the stimulus. So, it can be said that ACC can be used in the assessment of speech perception ability in individuals with a pathological condition. Martin and Boothroyd, in 2000, recorded ACC in 8 normal hearing young adults in response to change in amplitude and spectral envelope at the temporal center of a three vowels of 800 milliseconds.[26] A distinct ACC was observed to amplitude increments of 2 dB or more and decrement of 3 dB or more. It was also observed that change of second formant frequency (from perceived /u/ to perceived /i/), with amplitude increments increased the magnitude of the ACC, but amplitude decrements had little or no effect. The fact that the just detectable amplitude change is close to the psychoacoustic limits of the auditory system augurs well for the clinical application of the ACC.

Small and Werker recorded the ACC in 6 young adults and 24 4-month-old infants. English was their inherent language.[25] The stimuli were concatenated consonants pairs comprised from a dental /da/, plus either /ba/, Hindi retroflex /Da/, a second /da/, or a silent period (i.e., /dada/, /daba/, /daDa/ and /da_/). Acoustic change complex was recorded in adults to /dada/, /daba/, and /daDa/, with a trend showing a larger grand mean ACC for /daba/ compared with the other stimuli conditions. For infants, the responses to /da/ were similar to those of the adults' P1–N1–P2 complex in morphology but had much delayed latencies. They also observed that /daba/ was the only stimulus that consistently evoked ACC in infants. Additionally, they found that the ACC to /daba/ had less variable morphology, and the responses were clearer compared with both /dada/ and /daDa/, which showed that the infants perceived a bigger change from /da/ to /ba/ than from /da/ to either /da/ or /Da/. From the study, the authors concluded that ACC can be evoked in young infants and offer a starting point for further investigations of the infants. ACC can be used as a tool to study the auditory discrimination skill in infants. Shetty and Manjula, in 2012, investigated the effect of stimuli on the latency and amplitude of ACC in younger adults.[14] The naturally presented stimuli /sa/ and /si/ were presented through insert earphone to record the ACC. They reported a significant difference in the latency of 2N1 at the transition, with the latency of /sa/ taking place earlier. They also observed no significant difference in the amplitude of ACC between the stimuli. The authors concluded that ACC provides important insight in detecting spectral change in each stimulus.

Han and Dimitrijevic, in 2015, recorded the ACC from 64 scalp electrodes during passive listening in two conditions.[24] The first condition was ACC from white noise to 4, 40, 300 Hz amplitude modulation (AM), with changing AM depths of 100, 50, 25% lasting 1 second, and the second condition was 1 sec AM noise bursts at the same modulation rate. The result showed that N1 responses to ACC were big to 4 and 40 Hz and small to 300 Hz AM, whereas a different response was observed with bursts of AM showing a bigger response to increases in the AM rate. The authors concluded that the N1 response of ACC is similar to that of a low pass filter shaped like temporal modulation transfer function (TMTF). This study also indicated that in the ACC paradigm, the only stimulus parameter that changes is AM, and the N1 response showed an index for this AM change. On the other hand, the AM burst stimulus contains both AM and level change and is likely dominated by the rise time of the stimulus. From the above-mentioned literature, it can be concluded that ACC is a sensitive index of neural processing amplitude modulation depth in ongoing stimulus. Kalaiah, Jude and Malayil, investigated the effect of interstimulus interval (ISI) on ACC. They found a significant effect of interstimulus interval on peak latencies and peak-to-peak amplitudes.[27] A shorter interstimulus interval was found to elicit peaks with smaller amplitude and slightly longer latency, whereas a longer interstimulus interval elicited peaks with larger amplitude and shorter latency. Kalaiah, in 2018, reported that a frequency change greater than 50 Hz was required to evoke the ACC. The magnitude of frequency change had an effect on the latency and amplitude of the ACC peaks.[28] From the above-mentioned review of the literature, it can be concluded that ACC can be evoked even with a small change in the ongoing auditory stimulus, which makes ACC a perfect electrophysiological tool to evaluate the auditory discrimination capacity in different clinical populations.

The Effect of Transducer on ACC

Shetty and Manjula, in 2012, studied the effect of transducer on the ACC.[14] The naturally produced stimuli /sa/ and /si/ were presented through insert earphone and loudspeaker to record the ACC. It was found that the mean latencies of the onset of consonants (N1–P2) and transition from the frication to the onset of vowel (2N1–2P2) were shorter for the /sa/ and /si/ stimuli, presented through either transducer. Furthermore, the mean latencies of N1–P2 and 2N1–2P2 were shorter for the insert earphone than for the loudspeaker for both stimuli, although comparison between the transducers revealed no significant difference in latencies. It can be because the spectra of naturally produced speech stimuli /sa/ and /si/ are delivered within the frequency response of both transducers. They also reported no significant effect of transducer on the amplitude of the ACC. This could be due to the fact that both transducers had the same intensity of stimulus presentation. They reported that the mean amplitudes of 2N1 and 2P2 were larger for both stimuli when presented through the loudspeaker compared with the insert earphone. From the investigation of Shetty and Manjula, it can be concluded that the type of transducer used to deliver stimulus has an effect on the latencies and amplitude of ACC.[14]

Acoustic Change Complex in Cochlear Implant Users

Friesen and Tremblay, in 2006, investigated ACC with different speech sounds in cochlear implant users.[29] Eight adults using a Nucleus-24 (Sydney, Australia) cochlear implant participated in the study. The stimulus taken for the study was the naturally produced speech sound /si/, which evoked a distinct ACC waveform. Good stability and the feasibility with which it can be evoked in individuals with cochlear implant makes ACC a great clinical tool to investigate the central auditory function in cochlear implant users. Martin, in 2007, recorded ACC in a subject with cochlear implant.[30] The stimulus used was a synthetic vowel containing a change of F2 at midpoint ranging from 0 to 1,200 Hz, presented through loudspeaker at 75 dB SPL. The results showed that the ACC was present and could be set apart from stimulus artifact of the cochlear implant. Similarly, Friesen and Trembley, in 2006, also investigated acoustic change complex among cochlear implant users with the speech stimulus (si/ʃi).[29] They also reported that ACC can be constantly recorded in individuals with cochlear implant with good test-retest reliability. Hoppe et al. also showed ACC as an electrophysiological tool to assess the auditory discrimination ability at higher auditory level (auditory cortex) in individuals with cochlear implant. The above-mentioned literature reveals the importance of an objective tool (ACC) to measure the auditory discrimination ability in children and adults using cochlear implant. The above-mentioned studies also show the utility of the robust nature of ACC that can overcome the effect of stimulus artifact especially when assessing discrimination skill in cochlear implant users (►**Table 1**).

Table 1 Summary of the studies that showed ACC as a neurophysiological tool to assess the auditory discrimination skill in different clinical populations

References	Year	Participants	Method and stimuli	Outcome
Martin & Boothroyd[10]	1999	10 adults with normal hearing	Signals were concatenated to produce two stimuli that changed in the middle (noise-tone, tone-noise)	The noise-tone and tone-noise stimuli evoked N1–P2 acoustic change complex in response to the change in periodicity occurring in the middle.
Ostroff et al.[11]	1998	8 adults with normal hearing	Three naturally produced speech stimuli: 1. [sei], 2. [s], 3. [ei]	Clear responses were observed to both sibilants and isolated vowel.
Martinez et al.[12]	2013	3 adults and 5 children with normal hearing, 5 children with bilateral sensorineural hearing loss	Stimuli consisted of quasi-synthetic vowels, i.e., vowel place contrast and vowel height contrast	ACC can be used as a tool to investigate auditory resolution in children with hearing loss.
Ganapathy et al.[13]	2013	10 individuals with normal hearing	Stimuli used were consonant-vowel syllable and tonal complex stimuli with varying pre-transition durations	The speech stimulus required lesser duration of pre-transition than non-speech stimulus.
He at al.[15]	2015	19 children with bilateral Auditory Neuropathy Spectrum disorder	Two noise segments separated by gaps of different duration	Gap detection threshold measured using electrophysiological recordings of the ACC correlated well with those measured using psychophysical procedures
Brown et al.[16]	2008	Nine adults with cochlear implant	EEACC was recorded by introducing a change in the stimulating electrode 300 milliseconds after the onset of the pulse train.	Results showed the usefulness of recording the EACC in response to changes in stimulating electrode position
Harris et al.[18]	2007	10 younger and 10 older adults with normal hearing	ACC was elicited by an intensity increase in an otherwise continuous pure tone.	Outcome revealed decreased intensity discrimination and prolonged latencies in older subjects is an age-related decline in central auditory nervous system.
Tremblay et al.[19]	2006	Seven adults (50–76 years) with mild to severe sensorineural hearing	Consonant-vowel (CV) syllables	Neural detection of CV transitions can be measured with the help of ACC in hearing aid users.
Cowan at al.[21]	2017	60 hearing-impaired and 30 normal-hearing infants	Stimuli were spectral-ripple noise (SRN), sibilants /s-z/ and vowels /u-i/.	ACC might be preferred over VRISD for discrimination evaluation.
Han & Dimitrijevic[24]	2015	Ten normal hearing adults	Continuous white noise with occasional changes consisting of AM	N1 responses to the ACC resembled a low pass filter shape
Small & Werker[25]	2012	Six adults and twenty-five 4-month-old infants	Stimuli were concatenated consonant pairs	ACC have potential as an index of early speech-discrimination ability

Table 1 (*Continued*)

References	Year	Participants	Method and stimuli	Outcome
Friesen & Tremblay[29]	2006	Eight adults wearing the Nucleus-24 cochlear implant	Naturally produced speech tokens /si/ and /ʃi/.	ACC can be recorded using complex signals among CI users to study central auditory functioning.
Yau et al.[31]	2017	14 adults with normal hearing	Vowel changes in a synthetic vowel sound	ACC is a robust and efficient measure of simple auditory discrimination
Kang et al.[32]	2018	8 normal hearing listeners, 12 listener without cochlear dead region, 4 listeners with cochlear dead region	A pure tone of 1,000 Hz was used with an increment of 3 dB HL.	It is possible to detect the presence of cochlear dead region using ACC
Kumar et al.[33]	2020	Twenty normal-hearing individuals, 19 individuals with auditory neuropathy, and 23 individuals with cochlear hearing loss	For eliciting ACC, a 1,000 Hz pure tone with intensity increments of 1, 3, 4, 5, 10, and 20 dB were presented at 80 dB SPL.	ACC could be a useful objective tool to measure DLI in the clinical population
Kumar et al.[34]	2020	15, 17 and 18 subjects with normal hearing, auditory neuropathy, cochlear hearing loss respectively	ACC was recorded for naturally produced CV stimulus /sa/ of 380 milliseconds in duration.	Finding of the study showed ACC as a tool to investigate neural encoding of speech stimuli in different clinical population.
Kumar et al.[35]	2020	Twenty children diagnosed having CAPD and 20 normal hearing children	ACC was acquired using naturally produced CV syllable /sa/	Prolonged latencies of ACC indicated poor encoding of CV transition in children with CAPD.
Kumar et al.[36]	2020	Fifteen children with (C)APD and 15 normal hearing children	For eliciting ACC, a 1,000 Hz pure tone with intensity increments of 1, 3, 4, 5, 10, and 20 dB was presented at 80 dB SPL.	ACC could be a useful objective tool to measure DLI in the children with CAPD

Abbreviations: ACC, acoustic change complex; AM, amplitude modulation; CAPD, central auditory processing disorder; CI, cochlear implant; DLI, differential limen intensity; EACC, electrically evoked acoustic change complex; VRISD, visual reinforcement infant speech discrimination.

Discussion

The generation of ACC shows that the auditory system at a higher cortical level has perceived change(s) within an ongoing sound, and the patient's neural capacity is intact at higher neural centers, to perceive the change within an ongoing stimulus, which refers his/her auditory discrimination skill.[18] The outcomes of several investigations showed that the ACC amplitude rose with the increasing magnitude of acoustic changes in intensity, spectrum, and gap duration.[10,18,25] Therefore, the ACC can serve as a sensitive clinical tool to evaluate the speech discrimination capacity.[25] There are many advantages of recording ACC over other similar potentials (MMN, P300) as elicitation of ACC does not require attention and can be evoked even in the absence of attention besides requiring relatively less stimulus presentations to record a response with better SNR. In addition, ACC can be evoked reliably in individual participants with good test–retest reliability.[37] Given the consistency of ACC and the feasibility with which it can be evoked, it is a potential clinical tool to investigate the neural processing of speech in subjects with hearing loss, hearing aids, and cochlear implants.[19,26,30] Researchers have also used ACC to assess the central auditory function in individuals with cochlear implant, which makes ACC a valuable clinical tool to assess different auditory processes in individuals with cochlear implant.[29] It can also be an objective tool to assess auditory resolution in most young children with normal hearing.[12] The literature has proved that ACC is useful even in the assessment of speech perception ability in young children with hearing impairment, which may help the concerned professionals during rehabilitation.[11] Researchers showed that ACC is a sensitive tool to observe neural representation of the stimuli which changes in periodicity; however, ACC has advantages in terms of amplitude. The results of their findings increase the authenticity of ACC in the evaluation of speech perception ability in different pathological conditions. Acoustic change complex proves also its mettle in assessing behavioral discrimination among subjects.[30] It can be used in pediatric cochlear implantation as it provides important information on the auditory discrimination ability at the level of the auditory cortex.[38] Apart from that, the literature has shown that ACC can determine the capacity of the auditory pathway in detecting subtle spectral changes in the stimulus at the level of auditory cortex.[14] Investigators also concluded that ACC can assess temporal processing at the level of the cortex besides offering further indication of hemispheric specialization.[24] Many reports have shown that ACC is markedly successful in detecting simple auditory discrimination in the responses of individual participants.[12,31,39] A recent research article has shown that ACC is able to detect the presence of cochlear dead region, which can support the findings of behavioral tests.[32] A study has shown a strong positive correlation between subjective (behavioral) and objective (ACC) differential limen of intensity, which shows the utility of ACC as an objective tool to measure intensity discrimination in clinical populations, like those with cochlear hearing loss and auditory neuropathy spectrum disorder.[33] Researchers have also shown the utility of ACC in the study of CV transition in different clinical populations.[34–36]

Final Comments

The present review satisfactorily shows the utility of ACC as a tool to support behavioral measures in audiological evaluations. An objective tool, like ACC, can help professionals to assess the auditory discrimination skill in difficult-to-test populations, especially infants and young children. The current review also concluded the importance to find normative of different behavioral tests through ACC. From the outcome of previous investigations done using ACC, we deduce that extensive research must be done to explore the utility of ACC as an indispensable modality in mapping the various forms of hearing loss and its future impact across the spectrum.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Ethical Approval

Ethical approval was obtained from the ethical committee of the Sri Jagdamba Charitable Eye Hospital, Sri Ganganagar, Rajasthan, India.

Author Contributions

H. K. S.: Conception of the work, interpretation, and drafting

T. J.: Drafting, critical evaluation, interpretation, and accuracy

P. K.: Final approval, accuracy, integrity, and drafting

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Conflict of Interests

The authors have no conflict of interests to declare.

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