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ORIGINAL ARTICLE

Can Global Field Power be an Objective Tool to Assess Cortical Responses to Acoustic Change? A Study with Cochlear Implant Users

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Introduction: The aim of the present study was to record and analyse acoustic change complex (ACC) response with Global Field Power (GFP) in cochlear implant users.

Materials and Methods: Event- related potentials were recorded from 12 CI users.

Study participants were tested in sound-treated electrically shielded test booth in the Auditory Electrophysiology Laboratory at the Hacettepe University. For acoustic change complex recording /ui/ stimulus was used. The magnitude of the acoustic change complex was expressed as the ratio of GFP amplitude of ACC response to GFP amplitude of onset response and GFP measures.

Results: Recordings from each participant's 20 electrodes were plotted as butterfly plots and GFPs were computed. The GFP waveform of each subject was analyzed in terms of the peaks corresponding to suspected latency ranges of onset, ACC and off-set responses. Moreover ratio of GFP amplitude of ACC response to GFP amplitude of onset response was computed for each subject.

Discussions: In this study a new tool for adding objectivity to ACC response identification was applied, which was GFP measures. In addition, ratio of GFP peak amplitude corresponding to suspected ACC and onset response was computed, in order to find a cut-off score that differentiates a clear ACC response from a questionable one.

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Introduction

Acoustic change complex (ACC) is a relatively newly discovered auditory cortical potential which can be defined as the response of the auditory system to changes in stimuli. As stated by Freisen and Tremblay[1], traditional stimuli for eliciting P1-N1-P2 obligatory responses are relatively short in duration, which leads to responses being very similar to each other regardless of type of stimuli, whether speech or tonal. Responses in different morphology are also observed when stimuli of longer duration is used. ACC evoked by /ui/ stimuli 800 ms. in duration is shown in Figure 1. P1-N1-P2 complexes in response to onset, formant transition and offset can be observed[2,3].

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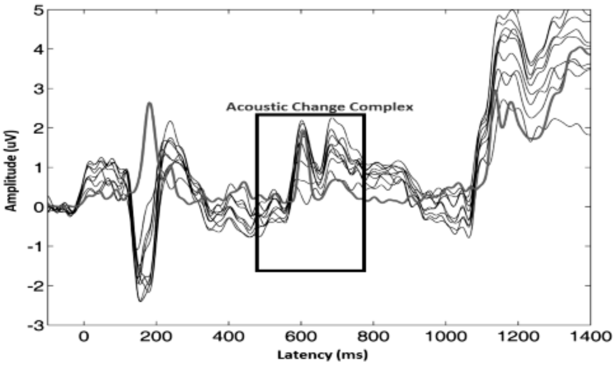

Figure 1. ACC evoked by /ui/

ACC evoked by formant transitions is dependent on spectral changes. In addition, ACC can also be recorded in response to amplitude changes. Martin and Boothroyd [4] recorded ACC to stimuli /uu/ containing amplitude change of +2 and -3 dB in the middle, which was measured as slightly higher than behavioral thresholds of amplitude detection. Amplitude increments produced larger responses; moreover, amplitude increments together with spectral change produced larger ACC compared to spectral changes alone.

ACC has been assessed not only in people with normal hearing but also in those with hearing impairments. In a study by Tremblay et al. [5], ACC was recorded in hearing aid users in response to /shee/ and /see/ stimuli. It was observed that similar latencies were found in both groups. Cochlear implant users were also assessed in a study by Freisen and Tremblay [1]. The study investigated ACC in cochlear implant users by using /si/ and /shi/ stimuli. Similar waveforms were observed in both groups and namely responses to voiced part of /shee/ were earlier in latency than that of /si/. On the other hand, all latencies were longer among cochlear implant users. The authors inferred this result as being due to cortical reorganisation after auditory deprivation or different speech processing strategies of the individual's devices. Electrophysiological responses were also found to be different in participants with good and bad speech discrimination. The study results suggest that ACC may be used as an index for speech discrimination ability among cochlear implant patients. In fact, as wide performance differences exist between cochlear implant users, assesment methods utilizing electrophysiology may be helpful in investigating these individual differences especially in difficult to test populations [6]. For such populations, in order to use ACC as an assesment method for speech discrimination ability, results from behavioral and psychophysical methods should be in agreement. Martin [7] has documented some research supporting results for this proposal. In that study, second formant change of /uu/ stimuli into /ui/ between 1000-150 Hz in attend conditon and 1200-300 Hz in ignore condition evoked ACC, the frequency ranges being well in agreement with the range of behavioral detection.

When considering ACC studies with cochlear implants, there are two ways to stimulate the auditory system. One is stimulating via the speech processor in free field and the other is directly stimulating the inner ear electrode, which was applied by Brown et. al. [8]. ACC response to electrode change produced ACC which was enhanced in amplitude when a larger distance between electrodes was introduced. This finding was attributed to non-overlapping neural activity due to larger distance in between the two electrodes.

Not only electrode change, but also stimulation changes on single electrode and resulting ACC was investigated by Kim et. al. [6] in a detailed study about ACC in cochlear implants. The point of interest was the effect of change on single electrode and the relation between N1-P1 amplitude growth function and ACC amplitude. Increasing and decreasing the stimulation on a single electrode evoked ACC, with the former resulting in larger amplitude, similar to the results of the Martin and Boothroyd study [9]. Stimulating the electrodes with steep ampitude growth function resulted in larger ACC response, although inter-individual variabilty existed.

When ACC response is visually inspected, consecutive P1-N1-P2 peaks in response to changes in stimuli parameters are observed. ACC peaks are therefore analysed in terms of latency and amplitude of these peaks. Although this latency and amplitude information is traditionally used in analysis of all evoked potentials, the spatial distribution and temporal characteristics of these potentials are important; which is not single reference dependent as all electrical fields in each electrode are compared against each other [10]. The method for topographical analysis mentioned above is “Global Field Power” (GFP), which is described by Brunet et. al [10] as standart deviation of potentials in all scalp electrodes. If sharp peaks and troughs do exist in recordings, GFP is high; flat appearence leads to low GFP. GFP may also be used for determining peak latencies in evoked potentials [11]. During visual inspection of ACC data, small but important waves may go unnoticed, some of which may be the responses to acoustic changes. GFP may be helpful in identifying these waves and decreasing false negatives.

In the light of this information, cochlear implant users at different ages with different etiologies are tested with ACC paradigm and the results are analysed with GFP measures. Results of participants are discussed as individual cases, as they have variety of characteristics like cochlear anomalies, age at implantation, and hearing status before implantation.

Materials and Methods

Subjects

Event-related potentials were recorded from 12 CI users (six females and six males, aged 7 to 20 yrs, mean = 13.75, SD= 5.04). Eight of the CI users have their implants on the right side, and four on the left. Demographic data of participants is shown in Table 1. Before electrohpysiological testing, maps of cochlear implant participants were analysed and necessary adjustments were applied. None of the participants had a history of neurological disorders which may compromise the EEG recordings. The study was approved by Hacettepe University ethics committee (011 D04 406 001, 27/10/2011). Informed consent from adult patients and parental consent for children patients were given.

Procedure

Testing procedure was approximately 1 hour (total time required for cap application and evoked potential recordings). Study participants were tested in a sound-treated electrically shielded test booth in the Auditory Electrophysiology Laboratory of Hacettepe University. Participants were instructed to ignore the stimuli presented to them and to remain as quiet as possible while sitting in a reclining chair. Participants were asked to remain awake and watch a movie of interest with subtitles. Breaks were given when needed during the recordings.

Stimuli

Experimental stimulus used for this study was created using Praat Programe [12] .The acoustic waveform and spectrogram of the stimulus was analysed using Praat software. The acoustic spectrogram of the stimulus /ui/ is shown in Figure 2. The basic stimulus was a synthetic vowel that contained 1000 Hz changes of second formant frequency. The stimulus was synthesized using a Klatt synthesier [13]. We modeled stimulus parameters initially used by Martin et al. [9] and the following parameters were used: Fo= 100 Hz, F1= 400 Hz, F2= 1000 Hz or 2000 Hz, F3= 3000 Hz, and F4= 4000 Hz. The transition between the lower and upper values of F2 occupied 40 ms. Perceptually, the change was from /u/ to /i/ synthesized vowels. Duration of /ui/ stimulus was 1000ms. A schematic of the stimulus parameters is shown in Figure 3. These stimuli differ in F2 transition at stimulus midpoint and so contain a contrast in vowel place of articulation.

After the stimulus was generated, it was perceptually tested by ten naive listeners. Listeners were asked to repeat which sound they heard. Both /u/ and /ui/ stimuli were perceived as /u/ and /ui/ , respectively.

Stimuli were calibrated to 75 dB SPL via a loudspeaker placed 1 m in front of participants at a zero-degree azimuth. The stimulus presentation was controlled and delivered with Presentation 15.0 programme (Neurobehavioral Systems).

Evoked Potential Recordings:

Evoked potentials were recorded using a Neuroscan 4.3 system and a 32-channel SynAmp amplifier. Electrodes were placed according to the International 10-20 system using a electrode cap [14]. A ground electrode was located on the subject’s forehead and a linked ear lobe reference electrode was used. Eye-

Table 1. Subject demographics of the cochlear implant users

Subject	Gender	Age (years)	CI side	CI type	Duration of CI use (months)	Aetiology
1	M	17	R	Medel	112	Congenital
2	M	8	R	Nucleus	74	Congenital
3	M	9	R	Nucleus	35	Congenital
4	F	20	R	Medel	65	Congenital
5	M	7	R	Nucleus	39	Congenital
6	F	12	R	Medel	94	Unknown
7	F	20	R	Medel	62	Inner ear malformation
8	M	17	L	Medel	57	Inner ear malformation
9	M	18	L	Nucleus	154	Inner ear malformation
10	F	11	L	Medel	95	Congenital
11	F	18	R	Nucleus	62	Inner ear malformation
12	F	8	L	Nucleus	62	Unknown

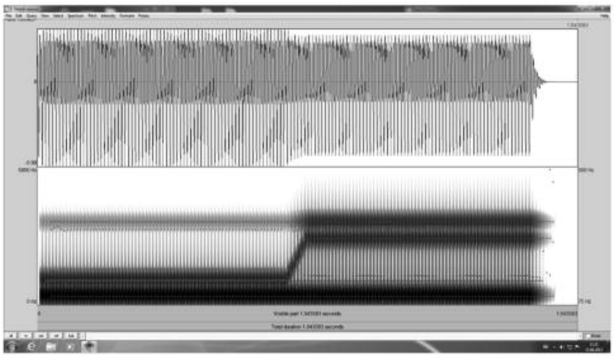

Figure 2. Acoustic spectrogram of the stimulus /ui/

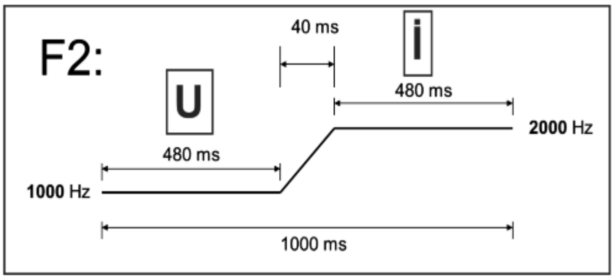

Figure 3. A schematic of second formant frequency (F2) as a function of time (in mili seconds)

blink activity was monitored using Fp1 and Fp2 electrodes. All impedances were kept below 5000 ohms. A 500 Hz sampling rate was used in recordings. Recordings were online filtered by a band bass filter of 0.5-70 Hz, and offline filtered by 1-30 Hz (2nd order, zero phase shift). Artifact rejection was set to ± 100 uV and Prestimulus base line correction was applied. The stimuli was presented 750 times to each subject.

Data Analysis:

Recordings from all active electrodes were analysed. For /ui/ stimulus, evoked response patterns in response to stimulus /ui/ was analysed in respect to onset of the /u/ vowel (50-200 ms after stimulus onset), followed by the ACC (response pattern to transition from /u/ to /i/ vowel) at approximately 550-700 ms relative to stimulus onset, and finally a small response to stimulus offset present at 1000-1200 ms after the stimulus onset. Points of interest for this specific study were amplitude and latencies of evoked responses to stimulus onset, acoustic change and offset. Initially, recordings from all electrodes were butterfly plotted with the response in black, and identified on the grand average global field power (GFP).

Quantification of ACC amplitude: The magnitude of the ACC was expressed as the ratio of GFP amplitude of ACC response to GFP amplitude of onset response. The aim in using this measure was to find a cut-off point of this ratio that may differentiate a clear ACC response from a questionable one. This ratio is labelled as "ratio of change to onset" (ROCTO). GFP was computed using the root of the mean of the squared potential differences between all possible electrode pairs within the field. The GFP provided a reference-free measure of cortical activity that was free of experimental bias in selecting a single electrode or set of electrodes [15,16].

Results

The latency and amplitude of evoked response potentials were obtained in all participants. Evoked responses to onset of the /u/ vowel, measured as 50-200 ms after stimulus onset, followed by the ACC responses (response pattern to transition from /u/ to /i/ vowel) at approximately 550-700 ms relative to stimulus onset, and finally to stimulus offset responses, present at 1000-1200 ms, after the stimulus onset were recorded.

Recordings from each participant's 20 electrodes were plotted as butterfly plots and GFPs were computed (red lines on the butterfly plots). The GFP waveform of each participant was analysed in terms of the peaks corresponding to suspected latency ranges of onset, ACC and off-set responses. The amplitude and latency of these peaks are given in Table 2 and Table 3, respectively. As mentioned in Methods section, ROCTO scores were computed for each subject (see Table 2). In some subjects, because onset, ACC, or off-set responses could not be observed, ROCTO could not be calculated; consequently, these responses were expressed as "not applicable" (NA).

Table 2. Amplitudes of peaks in GFP waveform

Subject	Onset (mμ)	ACC (mμ)	Offset (mμ)	ROCTO
1	0.87	NA	NA	NA
2	4.92	4.46	2.76	0,90
3	NA	NA	NA	NA
4	3.23	6.30	4.15	1,95
5	5.53	5.69	3.53	1,02
6	6.00	2.92	5.69	0,48
7	5.07	1.84	2.76	0,36
8-	3.23	0.31	0.76	0,09
9	6.46	2.46	4.61	0,38
10	NA	NA	NA	NA
11	6.30	5.53	5.53	0,87
12	1.38	NA	2.00	NA
Median	**4.99**	**2.69**	**3.14**	**0.43**
Min.-Max. Values	**0.87-6.46**	**0.31-6.30**	**0.76-5.69**	**0.09-1.95**

Table 3. The latency of peaks in GFP waveform

Subject no	Onset (mss)	ACC (mss)	Offset (mss)
1	150.94	NA	NA
2	152.38	647.61	1123.81
3	NA	NA	NA
4	114.28	647.61	1104.76
5	171.42	666.66	1142.85
6	95.23	647.61	1066.66
7	133.33	647.61	1161.90
8	95.23	628.57	1104.76
9	114.28	647.61	1085.71
10	NA	NA	NA
11	95.23	647.61	1180.95
12	95.23	NA	1200.00
Median	**114.28**	**647.61**	**1114.28**
Min.-Max. values	**95.23-171.42**	**628.57-666.66**	**1066.66-1200.00**

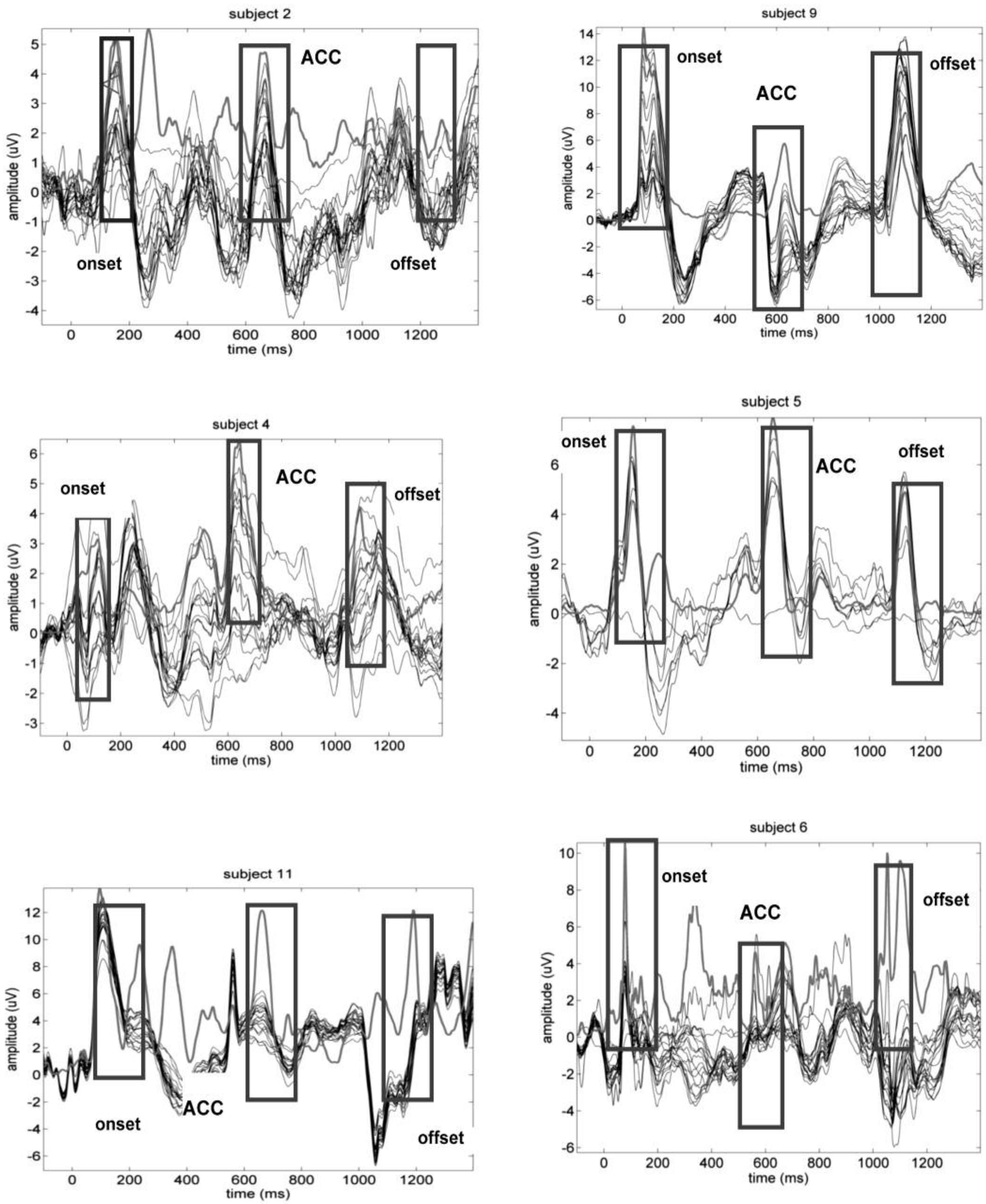

Figure 4. Butterfly plots and GFP of Group-1 Subjects

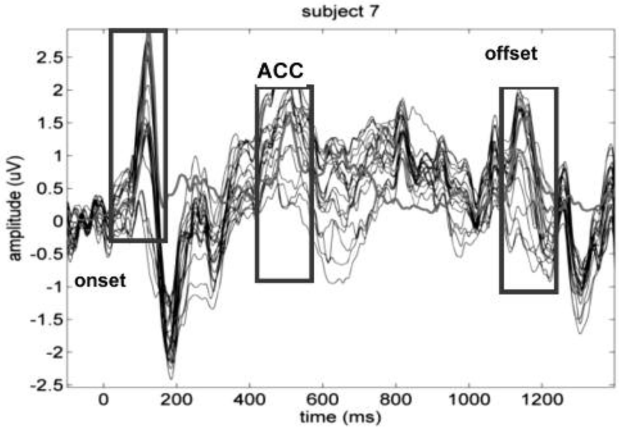

Figure 5. Butterfly plots and GFP of Group-2 Subject

The subjects were grouped into three based on their ACC responses which was determined via visual inspection of the waveforms. The groups are: Group 1- subjects with clear ACC response; Group 2- subjects with questionable ACC response; and finally Group 3- subjects with no ACC response. The waveforms of subjects in these groups are shown in Figure 4, Figure 5 and Figure 6, respectively. Onset, ACC, and offset responses were highlighted in the boxes. Each subject's GFP waveforms are given in Figure 7.

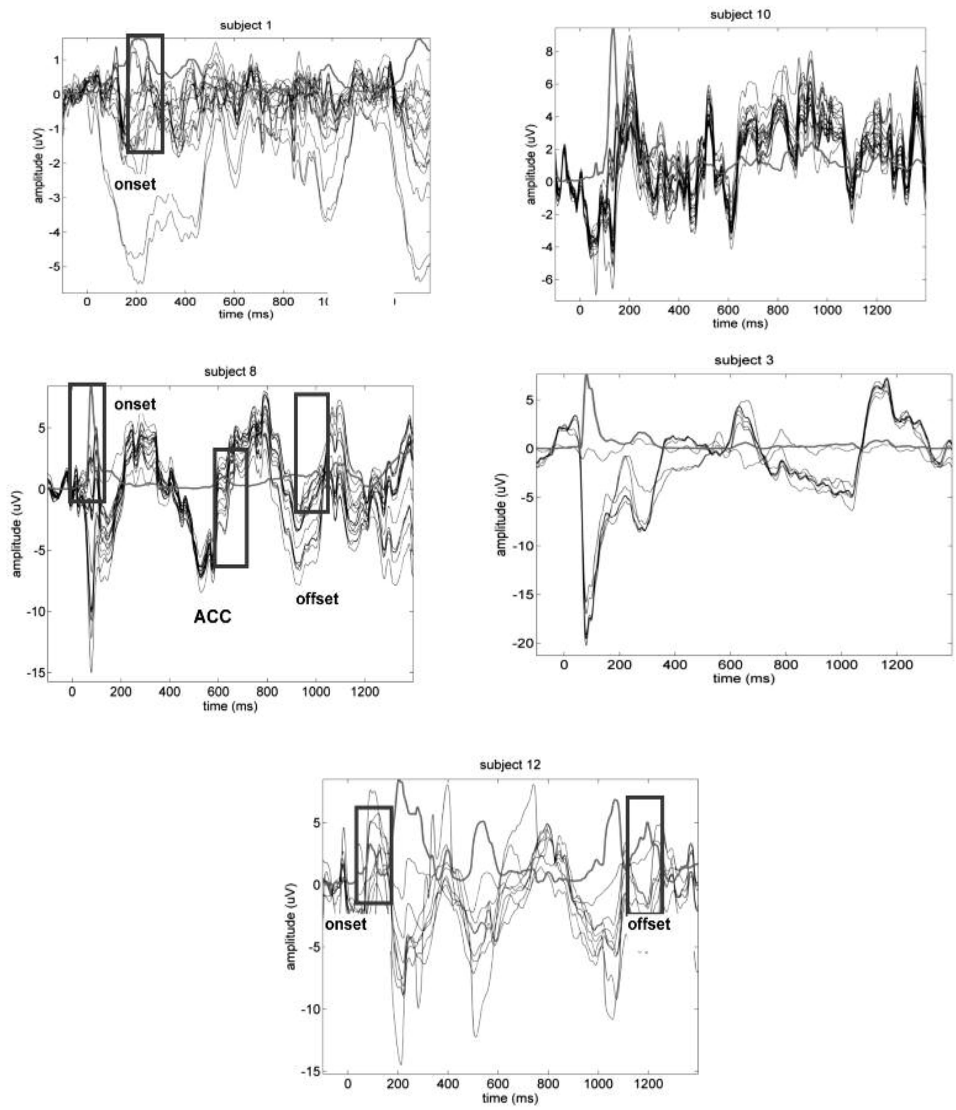

Figure 6. Butterfly plots and GFP of Group-3 Subjects (Subject-8 had no visually detected ACC, but GFP waveform had a peak in suspected latency range)

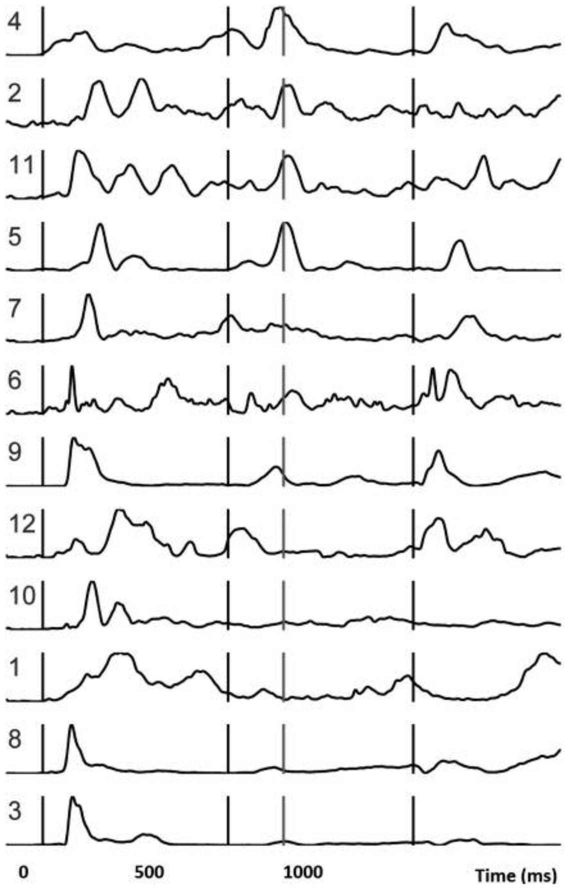

Figure 7. GFP waveforms of all subjects

Discussion

In this current study, a new tool for adding objectivity to ACC response detection was applied, which was GFP measures. In addition, the ratio of GFP peak amplitude corresponding to suspected ACC and onset response was computed in order to find a cut-off score that differentiates a clear ACC response from a questionable one. What is also interesting was the wide variety of subjects with cochlear implants, having different etiologies and a history of deafness.

Visual analysis of wave forms revealed 3 groups of subjects; the ones with clear ACC response, questionable response and no response. When ROCTO of group-1 and group-2 was compared it was found that lower limit of Group-1 was very close to that of Group-2; to which only one subject was assigned. This closure between two values makes it impossible to figure out a cut off point between clear ACC and a questionable one. This result makes ROCTO a somewhat unreliable measure for ACC analysis. The only result that can be inferred is that higher ROCTO scores are observed in subjects with visually detected clear ACC responses.

When Group-3 is considered, ROCTO scores could not be calculated due to the absence of ACC responses. An interesting finding was of the subject-8 for whom no ACC response could be visually detected, although a peak in GFP waveform with very low amplitude was clearly seen. This result complicates the findings: data from Group-1 and Group-2 showed a relation between presence of visually detected ACC and presence of GPF peaks. On the contrary subject-8 had no visually detected ACC, but GPF wave form had a peak in the latency range of ACC. This highlights the importance of cross-check — utilizing both visual detection and computing GFP while determining ACC peaks.

Cochlear implant users with different etiologies and implant usage histories revealed a variety of responses, as observed in our research results. In a previous study, Martin [7] applied ACC paradaigm to a CI user with auditory neuropathy and ACC response could be observed. In a study using post-linguel patients, Brown et. al [8] applied electrically evoked ACC in participants with etiologies of meniere, unknown cause, familial and oto-toxicity. Clear ACC responses were recorded in all of those participants. In another study by Kim et. al [6], authors could observe ACC responses from all CI users with etiologies similar to Brown et. al [8] except for a user with enlarged vestibular aquaduct, which is classified as cochlear anomaly. Our study can be considered as the first work to include a relatively larger number of participants with cochelar anomalies (4 users with cochlear anomalies). However, a drawback of our study is that most of the parameters belonging to implant usage and etiologies could not be controlled. Subsequently, each subject had to be was discussed as an individual case within each of the groups.

As an introduction to our research findings, subjects with clear ACC responses who belong to group-1 have to be discussed. Subject-2 was the only participant who has been implanted at an early age (at the age of 2), the age of implantation of others was between 4 and 15 yrs. This raises the concern that such differences may affect our research findings; it is possible that all of these participants might have received sufficent input before implantation, with the exception of subject-2 who has already implanted early. Sufficent input helps normal neural maturation and as ACC is response of auditory system to changes in stimuli, that may be why clear ACC responses could be observed.

Group-2 had only one subject. Subject-7 was implanted at the age of 15 and has been using her implant for 5 yrs by now. Questionable ACC peaks were observed. In terms of implant usage and implantation age, subject-7 was similar to subject-4 (Group-1). One notable difference between these 2 subjects is the cochlear anomaly diagnosed in subject 7, which may be the reason why onset and offset responses were observed, wtihout ACC peak; this might mean that onset and ofset of stimuli was detected by the system but no change was identified. The other subjects with cochlear anomailes were subject-11 and subject-9, implanted at ages of 13 and 6, respectively. Both subjects are in Group-1. The reason why clear ACC responses were observed in these two subjects and questionable response in subject 7 may be related to their post-implant auditory rehabilitation period, severity of anomaly etc., which is not the scope of this paper; more subjects with cochlear anomalies should be investigated in order to determine whether there is a coorelation.

Some subjects who were assigned to Group-3 had no ACC responses. Although none of the subjects in this groups had ACC responses, subject-1 and subject-12 had onset and offset response; which may mean that the auditory system detects a sound event is occuring, but no acoustic change is detected. In the other subjects, none of the 3 responses emerged.

When data from all subjects is considered, direct relationships between implant user parameters and presence-absence of responses can not be infered clearly, except for some speculations. The tests can be applied to a larger group of subjects while keeping the individual variables in control.

In conclusion, it can be stated that GFP may be applied to ACC analysis. It was clear that when an ACC response is visually detected, a GFP peak (with different amplitudes among subjects) was also observed. A contradictory finding was observed in a subject from Group-3, with no visually detected. ACC response but existence of a GFP peak. At this point, what may be suggested is to find out the minimum amplitude of GFP required for a suspected response to be meaningfull; the recommendation is that this issue be studied in another research. ROCTO method was similar to GFP, containing concerns about utilizing it in discriminating between a clear response from a questionable one; but no cut-off score could be stated for discrimination. Nevertheless, higher ROCTO values were observed for clear ACC responses.

The results of this study indicate that As a last word, ACC can be recorded in cochlear implant users. The variables affecting the absence or presence of the response is divergent which suggests that future research would require larger sample sizes, while still keeping inter-indvidual parameters in control. This current work can be seen as a preliminary study with cochlear implant users with cochlear anomalies but further research is crucial. ACC depends on system's detection of sound change; this test may be used as an objective tool to investigate speech perception skills in pediatric cochlear implant users. For this reason, the relation between subjective responses of change detection and presence of ACC can be investigated.

Disclosure Statement:

The authors declare there are no conflicts of interest regarding the data presented in this study.

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