Published in final edited form as:

Clin Neurophysiol. 2014 February ; 125(2): 370–380. doi:10.1016/j.clinph.2013.08.003.

Sensitivity of Offset and Onset Cortical Auditory Evoked Potentials to Signals in Noise

Lucas S. Baltzell¹ and Curtis J. Billings^{1,2}

¹National Center for Rehabilitative Auditory Research, Portland Veterans Affairs Medical Center, Portland, Oregon

²Department of Otolaryngology/Head and Neck Surgery, Oregon Health & Sciences University, Portland, Oregon

Abstract

Objective—The purpose of this study was to determine the effects of SNR and signal level on the offset response of the cortical auditory evoked potential (CAEP). Successful listening often depends on how well the auditory system can extract target signals from competing background noise. Both signal onsets and offsets are encoded neurally and contribute to successful listening in noise. Neural onset responses to signals in noise demonstrate a strong sensitivity to signal-to-noise ratio (SNR) rather than signal level; however, the sensitivity of neural offset responses to these cues is not known.

Methods—We analyzed the offset response from two previously published datasets for which only the onset response was reported. For both datasets, CAEPs were recorded from young normal-hearing adults in response to a 1000-Hz tone. For the first dataset, tones were presented at seven different signal levels without background noise, while the second dataset varied both signal level and SNR.

Results—Offset responses demonstrated sensitivity to absolute signal level in quiet, SNR, and to absolute signal level in noise.

Conclusions—Offset sensitivity to signal level when presented in noise contrasts with previously published onset results.

Significance—This sensitivity suggests a potential clinical measure of cortical encoding of signal level in noise.

Keywords

CAEP; Offset; Onset; Auditory; N1; N2; ERP; Evoked; Potential

1. Introduction

Successful perception of target auditory signals in a noisy or complex auditory scene depends on a number of factors, including the successful neural encoding of the signal in the auditory cortex. This encoding can be measured with scalp-recorded cortical auditory

Corresponding Author: Curtis J. Billings, National Center for Rehabilitative Auditory Research, Portland VA Medical Center, 3710 SW U.S. Veterans Hospital Rd (NCRAR), Portland, OR 97239, USA, Phone: 00-1-503-220-8262, Curtis.Billings2@va.gov.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

evoked potentials (CAEPs), a subset of electroencephalography (EEG) recordings, which can occur in response to both the onset and the offset of the stimulus. It has been suggested that the neural populations responsible for these two responses differ in important ways (Takahashi et al., 2004), and it is possible that they differ in their response to signals in noise. While the onset response has been used as a cortical measure of signal encoding in noise, the offset response has not. In this study we examine the effects of signal level and signal-to-noise ratio (SNR) on the offset response using two previously published onset datasets (Billings et al., 2007; Billings et al., 2009).

The extent to which the auditory evoked offset response differs from the auditory evoked onset response has been a central motivating question in the far-field study of offsets. Many of these studies have focused on shared physiological resources, and while many have suggested that the populations responsible for these two responses are the same or strongly overlapping (Hillyard & Picton, 1978; Hari et al. 1987; Joutsiniemi et al. 1989; Pantev et al. 1996), others have demonstrated significant differences (Noda et al. 1998; Wakai et al. 2007). Furthermore, near-field studies support the suggestion that different populations with different functional properties may be responsible for portions of the onset and offset responses. In general, onset units are far more prevalent than offset units and tend to be more tonotopically organized (Abeles & Goldstein, 1972; Phillips & Hall, 1990; He et al., 1997; Galazyuk & Feng, 1997; Recanzone, 2000; Phillips et al., 2002). It has been proposed that the offset response represents a rebound from inhibition, such that greater inhibition results in a larger offset response as inhibition is released (Henry, 1985b; Henry & Lewis, 1988; Phillips et al., 2002; Takahashi et al., 2004). However, other studies have shown that offset responses can occur in the absence of onset-evoked inhibition, and have suggested that different sets of synaptic inputs are contributing to the different responses (Qin et al., 2007; Scholl et al., 2010).

A number of near-field studies examining the onset response have demonstrated robust sensitivity to SNR rather than absolute signal level when signals were presented in noise (Phillips, 1985; Phillips & Cynader, 1985; Phillips & Hall, 1986; Phillips, 1990; Phillips & Kelly, 1992). Far-field evoked potential studies have investigated the effects of background noise on the onset response and have found similar effects, highlighting the encoding of SNR rather than absolute signal level when both cues are available (Burkard & Hecox, 1983; Burkard et al., 1997; Whitting et al. 1998; Kaplan-Neeman et al. 2006). Addressing this question directly, Billings et al. (2009) varied SNR for tonal stimuli at two different signal levels, and found that SNR and not absolute signal level had a significant effect on CAEP latency and amplitude. This sensitivity to SNR rather than signal level holds true for natural speech signals as well (Billings et al., in revision). In quiet however, previous studies have demonstrated robust effects of signal level (Adler & Adler, 1989; Billings et al., 2007). Psychophysical studies have demonstrated effects of both SNR and absolute signal level for signals presented in noise (Hawkins & Stevens, 1950; Dirks et al., 1982; Studebaker et al., 1999; Hornsby et al. 2005). These findings suggest that absolute signal level is a behaviorally relevant cue even in the presence of background noise. It is therefore unclear why onsets do not appear to encode absolute signal level in noise. The goal of the present study was to determine whether the offset response shows a similar sensitivity to SNR and absolute signal level cues as the onset response.

Cortical auditory evoked potentials (CAEPs) were used to determine the effects of SNR and signal level on offset responses. Our goal was to analyze the offset response and compare it to the onset response in two previously published datasets (Billings et al., 2007; Billings et al. 2009), and to investigate the extent to which effects of SNR and signal level differ between the two responses.

2. Methods

2.1 Experimental Conditions

Subject, stimulus, and recording procedures are described respectively in Billings et al. (2007) and Billings et al. (2009), and are summarized in Table 1. Briefly, Billings et al. (2007) presented 757 ms 1000-Hz pure tones (rise/fall time: 7.57 ms) at seven different intensity levels (30, 40, 50, 60, 70, 80, & 90 dB). Billings et al. (2009) used the same tone stimulus at two different signal levels (60 & 75 dB), but introduced continuous background noise at five different SNRs (20, 10, 0, -5, & -10 dB SNR) as well as testing in quiet. For all conditions in both studies, 400 trials were presented with an inter-stimulus interval (ISI; onset to offset) of 1910 ms using Neuroscan Stim2 and Scan systems (Charlotte, NC). All recordings were made while subjects watched a close-captioned movie of their choice, and responses were bandpass filtered offline from 1 to 30 Hz. While recordings were nose-referenced online in both studies, Billings et al. (2007) used a 32-channel electrode montage, while Billings et al. (2009) used a 64-channel electrode montage. Additionally, it should be noted that the original Billings et al. (2007) study looked at the effect of hearing aid amplification, and we included only the unaided data for analysis in the present study.

2.2 Data Analysis

For both datasets, we analyzed Cz and global field power (GFP) waveforms. GFP is the standard deviation of all channels as a function of time (Skrandies, 1989). While the N1, P2, and N2 waves are typically maximal at Cz, the GFP waveform captures more global cortical activity associated with the generating neural dipoles. Because it is a measure of the standard deviation of activity across electrodes, the GFP waveform is less sensitive to recording noise or electrical activity recorded from a specific location on the scalp. In the present study, GFP serves a confirmatory role demonstrating signal level and SNR effects across the scalp. An average reference (rather than a nose reference) was used to minimize noise specific to the reference electrode channel. We focus our analysis here only on the N1, P2, and N2 waves (shown in Figure 1), since it was determined that the P1 wave was not reliably present in the offset response. Peak latencies were calculated relative to stimulus onset, and peak amplitudes were calculated relative to baseline. Peak latencies and amplitudes for the N1, P2, and N2 waves of the offset response were determined by the agreement of two judges, who used electrode inversions, global field power traces, and grand averages in their determinations. Judges scored peaks independently, though neither was blind to experimental condition. As an unbiased measure of cortical activity, rectified area amplitudes were also calculated, which consisted of measuring the total area under the rectified trace (absolute value of the trace) to baseline within a certain latency window. As shown in Figure 2, the waveform was baseline corrected over the entire range of the offset, so as to minimize drift.

We fit the data with a linear mixed model representation of a repeated measures ANOVA, with different covariance structures for the peak latency, peak amplitude, and rectified area measures. Complex covariance structure models were chosen because standard repeated measures ANOVA models had undesirable properties of heteroskedasticity; that is, variance of the residuals depended on stimulus conditions. Models of covariance structure differed across measures to account for the distinct distributions of the residuals of each measure. Additionally, this allowed us flexibility with regards to missing measurements, since the maximum likelihood estimation used to fit the linear mixed model includes all measurements in the analysis, not just those of subjects with complete data. For latency measures, we fit the random intercepts model along with heterogeneous residual variance model for each of the SNR stimuli. For amplitude measures we allowed the residuals across SNR levels to follow a first-order autoregressive correlation structure. For area measures we

found that a simple random intercepts model, corresponding to the conventional repeated measures ANOVA was appropriate.

3. Results

Due to the large number of comparisons made in this study across individual waves (N1, P2, N2), electrode sites (Cz, GFP), and response type (onset, offset), Bonferroni corrections were applied across waves and electrode sites for each measure (peak latency, peak amplitude, and rectified area) independently, and p -values were modified accordingly. Also, since we used a statistical analysis that differed slightly from that reported in Billings et al. (2007) and Billings et al. (2009), we fit the onset data to the same statistical model used to fit the offset, and we report the results of both.

3.1 Billings et al. 2007: Effect of Signal Level in Quiet

Figure 3 plots the grand averaged CAEPs for all conditions from both Cz and GFP, and the effect of level on the offset response can be seen in the waveform morphology. The growth functions in Figure 4 show the shifts in latency and amplitude such that peak latencies decrease and peak amplitudes increase with increasing signal level. At Cz, the effect of level on peak latency was significant for N1 ($p=.021$) and P2 ($p=.005$), while the effect on peak amplitudes was significant for N2 ($p<.001$) and marginally significant for P2 ($p=.086$). This pattern of significance is less consistent than the uniform significance we observed for the onset response. These results are summarized in Table 2.

For GFP, it was determined that N1 and P2 could not be reliably measured manually, so only N2 was analyzed. As can be seen in Figure 3, the GFP offset response is dominated by the N2 wave, while the N1 and P2 waves are barely discernible if at all. However, the effect of level on the N2 offset wave for GFP was significant for both peak latency ($p=.038$) and peak amplitude ($p<.001$). It should be noted that N2 appears to be the dominant wave of the offset response, especially in the GFP waveforms.

Rectified area measures were analyzed at three different time ranges corresponding to the entire N1-P2-N2 response (790–1140 ms), the N2 response alone (970–1140 ms), and the N1-P2 response (790–970 ms). We decided to collapse the N1 and P2 response because the latency shifts associated with changes in stimulus level made selecting a latency value consistently in-between the two responses difficult. The growth functions in Figure 5 show that rectified area amplitude increases as signal increases, which is the same general effect observed in the peak amplitude measure described above. However, rectified area amplitude showed a more consistent effect of level than peak amplitude, in that for both Cz and GFP, the effect of level on rectified area amplitude was significant for all three ranges measured [Cz: N1-P2 ($p=.002$), N2 ($p<.001$), N1-P2-N2 ($p<.001$); GFP: N1-P2 ($p<.001$), N2 ($p<.001$), N1-P2-N2 ($p<.001$)].

3.2 Billings et al. 2009: Effect of SNR and Signal Level in Noise

3.2.1 Effects of SNR—Figure 6 plots the grand averaged CAEPs for all conditions from both Cz and GFP, and the effect of SNR on the offset response can be seen in the waveform morphology. The growth functions in Figure 7 illustrate the shifts in latency and amplitude such that peak latencies increase and peak amplitudes decrease with decreasing SNR. At Cz, the effect of SNR on peak latency was significant for all waves measured, while the effect on peak amplitude was significant only for N2 ($p=.017$). Results are summarized in Table 3. As reported above, N1 and P2 waves could not be reliably measured manually from GFP recordings, so only N2 was analyzed, though the effect of SNR was significant for both peak latency ($p<.001$) and peak amplitude ($p=.032$).

Rectified area amplitude measures once again showed a more robust effect than peak amplitude measures. The growth functions in Figure 8 show that rectified area amplitudes decrease with decreasing SNR. This effect of SNR was significant for all three ranges measured for both Cz [N1-P2 ($p < .001$), N2 ($p < .001$), N1-P2-N2 ($p < .001$)] and GFP [N1-P2 ($p < .001$), N2 ($p < .001$), N1-P2-N2 ($p < .001$)].

3.2.1 Effects of Level in Noise—Figure 6 overlays the grand averaged waveforms for both levels separately for each SNR, and we see that the 60 and 75 dB waveforms of the offset response are not entirely overlapping. The growth functions in Figure 7 illustrate that peak amplitudes are generally larger at the 75 dB level than they are at the 60 dB level. This effect of level on peak amplitude was significant for N2 at both Cz ($p = .002$) and GFP ($p = .0012$). The growth functions in Figure 7 also illustrate that peak latencies are generally *later* (larger) at 75 dB than at 60 dB. This effect of level was significant at Cz for N1 ($p = .003$), P2 ($p < .001$), and N2 ($p = .044$), such that peak latencies were significantly later at 75 dB than at 60 dB across SNR conditions. However, the effect of level on peak latency was not significant for GFP. Furthermore, no significant interactions (SNR x Level) interactions were found for any wave measured.

As shown in Figure 8 and Table 3, rectified area amplitude measures also showed an effect of level such that amplitudes were generally larger at 75 dB than at 60 dB. This effect was significant for the N2 range and for the entire N1-P2-N2 range for both Cz [N2 ($p < .001$), N1-P2-N2 ($p < .001$)] and GFP [N2 ($p = .002$), N1-P2-N2 ($p = .032$)]. Significant interactions were found for the N2 range at Cz ($p = .038$) and for the N1-P2-N2 range for GFP ($p = .022$), though as can be seen in Figure 8, this interaction is likely a result of floor effects at lower SNRs. It should again be noted that N2 appears to be the dominant wave of the offset response.

3.3 Onset Response: Effect of Level in Quiet, SNR, and Signal Level in Noise

The effect of signal level in quiet on the onset response can be seen in the waveform morphology in Figure 3, where it is visually apparent that peak latencies decreased and peak amplitudes increased with increasing signal level. This effect of level on the onset response was significant for all waves measured (see Table 2). The effect of SNR can be seen in Figure 6, illustrating that peak latencies increased and peak amplitudes decreased with a decreasing SNR. This effect of SNR was significant for all waves measured (see Table 3).

Looking at the onset response in Figure 6, we see that the 60 (dotted) and 75 (solid) dB waveforms are almost entirely overlapping, and a significant effect of level was not observed for any wave measured (see Table 3). This is consistent with the results of the standard repeated measures ANOVA used to analyze the data in Billings et al. 2009, which failed to find a significant effect of level in the onset response.

4. Discussion & Conclusions

We set out to determine the effects of signal level and SNR on the CAEP offset response, and to compare these effects to previously published data on the CAEP onset response. Our results indicate that while both the onset and offset response provide evidence for the encoding of signal level in quiet and of SNR, only the offset response provides evidence for the encoding of signal level in the presence of noise.

4.1 Effect of SNR

Our finding that both the onset and the offset response are sensitive to SNR is consistent with previous behavioral and physiological observations. Psychophysical studies have

shown that detection thresholds elevate as a function of elevation in masking noise; furthermore they show that once noise levels are elevated above the threshold for inducing elevations in detection threshold, this function is relatively linear (Hawkins & Stevens, 1950; Stevens & Guirao, 1967). Near-field studies of the auditory cortex have highlighted the adaptive tracking of cortical neurons in response to masking noise such that neural response thresholds elevate proportionally to increases in masking noise level (Phillips, 1985; Phillips & Cynader, 1985; Phillips & Hall, 1986; Phillips, 1990). As Phillips & Kelly (1992) point out, cortical auditory systems likely bear significant responsibility for signal discrimination in noise, to the extent that these systems are responsible for sensory gating, or the filtering of irrelevant stimuli. Specifically, the transient nature of cortical responses makes available the complete dynamic range of the neuron, while auditory nerve fibers respond continuously to the background noise. As the present study shows, large populations of neurons measured at the scalp are sensitive to changes in relative stimulus level, and this sensitivity is characteristic of the offset response as well as the onset response.

4.2 Effect of Level

When tested in quiet, we found that both the offset and the onset response varied as a roughly linear function of increasing signal level up to 90 dB. This effect is consistent with previous studies, which have also shown that increases in signal level result in decreased latencies and increased amplitudes (Polich et al., 1988; Billings et al., 2007). However, studies have also shown that these growth functions asymptote or even reverse direction at higher intensities (Picton et al., 1970; Adler & Adler, 1989). Our data do not show this reversal at higher intensities, and as Billings et al. (2007) point out, this is probably due to the long ISI used in the present study (Picton et al., 1970). It is therefore unlikely that these high intensity asymptotes can explain our result that response latencies to 75 dB tones were longer than latencies to 60 dB tones when presented in noise.

When the effect of level was tested in the presence of background noise, we found that the onset and offset response differed in their sensitivity to level cues. In noise, the onset response did not vary as a function of signal level, while both the latency and amplitude of the offset response increased as a function of increasing signal level. This is an interesting result, because based on our observations of the offset response to changes in signal level in quiet, we would expect latencies to decrease with increasing amplitude. As the growth functions for N1 and P2 in Figure 7 illustrate, the 75 dB latencies are less than or equal to the 60 dB latencies in quiet; however this function reverses when we move to 20 dB SNR. It appears that the introduction of noise, even at a high SNR, has the effect of shifting the latency of the offset response later. For example, introducing a 55 dB noise background to mask a 75 dB tone results in longer latencies than introducing a 40 dB noise background to mask a 60 dB tone. This would imply that it is not the absolute level of the signal, but rather the absolute level of the noise that may be driving this effect, especially since the difference is maintained as SNR decreases. However, while the signal tone itself was time-locked, the noise was continuous, and as mentioned above, the transient nature of the offset response allows it to encode the characteristics of the stimulus that are changing, and should target the stimulus itself rather than the continuous noise. We also know that transient responses adaptively track the level of background noise, and it seems plausible that an interaction between the time-locked tone and the continuous background noise could explain the increase in latency as a function of level that we observed in the offset response. Lending possible support to this notion, Burkard & Hecox (1983) found an effect of both masking noise level and signal level on wave V of the auditory brainstem response (ABR). It should be noted however, that in our study we did not observe a significant interaction between

SNR and level (the main effect of level did not differ significantly as a function of SNR), so these effects are mentioned here only qualitatively.

The degree to which the effect of level in background noise is driven by absolute noise level and absolute signal level respectively is hard to quantify, given the fact that both signal and noise level increase proportionally if SNR is fixed. However, the present results suggest that absolute noise level could be responsible for the fact that louder signals resulted in longer latencies. Support for this conclusion comes from the speech identification literature, where studies have shown that in noise, speech recognition thresholds increase as function of increasing intensity while SNR is fixed (Dirks et al., 1982; Studebaker et al., 1999; Hornsby et al. 2005). Studebaker et al. (1999) suggest that these decreases in intelligibility can be modeled as a function of increasing noise masking level. Further study is needed to better address the relative contribution of absolute signal level and absolute noise level cues on the CAEP offset response, and it is important to note that only two signal levels were used in the present study.

4.3 The Offset versus the Onset Response

As mentioned above, the offset response shares many characteristics with the larger and more easily elicited onset response. Indeed, it is the similarity between the onset and offset in terms of physiological function and location that has been largely responsible for the relative paucity of the offset literature. Furthermore, in far-field recordings, offsets are typically much smaller in amplitude than their onset counterparts and therefore harder to elicit. In the present study, we found that the offset response was smaller and less consistently observed on a wave by wave basis than the onset response, which showed strong and uniform effects of level and SNR. We also found that, with respect to changes in signal level in quiet and changes in SNR, the offset response shows an effect similar to that of the onset response.

Much of the offset literature has remarked on these similarities, and at a fundamental level, both responses appear to indicate changes in the auditory environment. Hillyard & Picton (1978) showed that shorter ISIs result in smaller onset responses and that shorter stimulus durations result in smaller offset responses, suggesting that each response reflects the build-up of an auditory image such that the distance between respective changes in the auditory environment are responsible for the magnitude of the response. Supporting this interpretation, Yamashiro et al. (2009) showed that at the cessation of a toneburst train stimulus, offset latencies were determined by the ISI, suggesting that it is not necessarily the cessation of the stimulus that triggers the offset, but change in auditory environment signaled by the failure of the next toneburst to sound.

To the extent that the onset and offset responses are functionally similar, we would expect their response sensitivities to be similar, and our results suggest that this functional overlap is significant. However, we also found significant morphological and functional differences, consistent with the suggestion that the neural populations responsible for the generation of the two responses (or at least the relative weighting of these populations) differ in some capacity, and that these differences are substantial enough to be measured by CAEPs.

We found that the N2 wave plays a far greater role in the magnitude of the offset response than it does in the onset response. In the CAEP literature, the N1 and P2 waves have received the most attention, as they are typically the largest and most sensitive waves of the onset response. This has carried over into the offset literature, where the N2 wave is virtually never reported. As our data show however, the offset N2 wave is somewhat less consistent at capturing latency effects, despite being the most reliable wave in capturing amplitude effects. The difficulty in measuring peak latency is probably due the sustained

nature of the N2 wave, and the resulting broadness of the N2 peak. However, the disproportional presence of the N2 wave in the offset response, especially given that it is virtually the only wave present in the GFP recordings, should be taken into account when characterizing the offset response.

Looking at the effects of maturation on the N2 wave of the onset response using a passive oddball paradigm, Ceponiene et al. (2002) found that amplitude of the N2 decreases substantially as a function of age. They suggested that with age, the N2 comes under increasing inhibitory control. The extent to which these results translate to the offset response is unclear, though it is possible that the large N2 in the offset response might represent a lack of inhibitory control. As infants mature, the size of the offset response decreases while the size of the onset response increases (Wakai et al., 2007). Presumably this is because the onset response assumes greater responsibility for the encoding of the auditory environment. If the N2 wave in particular reduces in size with greater inhibitory control, we might expect this reduction to be less apparent in the offset response, to the extent that the offset response is less sensitive to developmental changes.

However, in a similar oddball paradigm, Bertoli et al. (2005) found that the N2 amplitude of the onset response was either absent or severely reduced for elderly participants relative to young participants in passive listening conditions. They suggest that this reduction can be explained as an age-related loss of inhibition in the elderly participants, who are less able to inhibit unattended stimuli. They point out that sleep N2 (N350) amplitudes increase during sleep, when sensory processes are “disconnected”, and suggest that better inhibition of the unattended stimulus channel results in larger N2 responses. Ceponiene et al. (2008) found a similar N2 reduction in elderly listeners, though they point out that N1 and P2 enhancements observed in elderly listeners suggest that the reduction in N2 may reflect stimulus-level rather than channel-level inhibition. It is difficult to interpret the offset N2 in the context of these onset-related findings, though it seems clear that onset N2 is subject to unique inhibitory mechanisms, and possibly that these mechanisms might be at play in the offset N2 response.

We found that both the latency and amplitude of the offset N2, and not the onset N2, were sensitive to changes in signal level in noise. It could stand to reason that we did not see this effect in the onset because the responses to absolute level cues were inhibited in the presence of the more salient SNR cues, or at least weighted differently such that the effect of level was masked by the effect of SNR. In this case, greater inhibitory input allows the onset response to selectively target SNR cues, while the offset response lacks this degree of control. However, since we also observed this effect on the latency of both N1 and P2, it is also possible that the offset response is simply more sensitive to signal level in noise.

4.4 Rectified Area Amplitude

We introduce rectified area amplitude measures as an alternative to traditional peak picking in the case of the offset response because of the difficulty we encountered selecting these peaks manually. Despite the fact that we used uncharacteristically long stimuli that provided ideal conditions for offset recording, some peaks were simply unscorable, especially in high noise conditions (from the Billings et al. 2007 dataset, 97.8% of peaks were scored, and from the Billings et al. 2009 dataset, 92.5% of peaks were scored). We measured rectified area alongside peak latency and amplitude in order to see if they capture the same effects. Specifically, we wanted to see if rectified area measures are a viable alternative to manual peak picking, presumably to be used in experimental conditions less favorable to offset recording (shorter ISIs, complex stimuli, etc.), where peaks might be nearly impossible to identify manually.

We baseline corrected over the range of the offset response rather than over a pre-stimulus interval as is standard for baseline correction, so as to minimize drift. Furthermore, we wanted to compare the results of a courser but potentially more practical measure with the results of standard peak measurement, despite the fact that baseline correcting within the range being measured could significantly alter the respective amplitudes of the individual waves. Because of this potential confound, we suggest that the rectified area measures over the entire baseline correction range are more functional than measures made over sub-ranges, since these whole-range measures do not run the same risk of confound, as they make no assumption about the independence of individual waves.

We found that every main effect captured by peak amplitude measures was also captured by rectified area amplitude measures. Furthermore, each of these main effects was significant when measured over the entire range of the offset response. This suggests that rectified area amplitudes measured over the range of the offset response are sensitive to changes in signal level in quiet, changes in SNR, and changes in signal level in noise. Finally, it should be noted that the same main effects were observed for latency and amplitude measures, and while the timing and magnitude of the response are sensitive in different ways, we suggest that rectified area amplitude measures can be used when traditional peak picking is not a plausible option.

4.4 Conclusions

The CAEP offset response is sensitive to SNR, signal level in quiet, and signal level in noise. These offset results contrast with the CAEP onset response that does not appear to be sensitive to signal level in noise. We know that signal level is behaviorally relevant even in the presence of noise, so a measure that is sensitive to the encoding of signal level in noise could be useful in characterizing CAS encoding in populations with signal-in-noise difficulty.

Acknowledgments

We are grateful for helpful comments from Drs. Garnett McMillan, Erick Gallun, Melissa Papesh, and Tina Penman. This work is supported by the Department of Veterans Affairs through the Rehabilitation Research and Development Service with Career Development and Center of Excellence Grants (C6971M) and National Institutes of Health (NIDCD:DC010914). We are thankful to Kelly Tremblay and the Brain and Behavior Lab at the University of Washington where study design and collection of original data occurred with funding support from National Institutes of Health [T32-DC05361, R01-DC007705, P30-DC004661, and F31-DC007296].

References

- Abeles M, Goldstein MH Jr. Responses of single units in the primary auditory cortex of the cat to tones and to tone pairs. *Brain Res.* 1972; 42:337–352. [PubMed: 5050171]
- Adler G, Adler J. Influence of stimulus intensity on AEP components in the 80- to 200-millisecond latency range. *Audiology.* 1989; 28:316–324. [PubMed: 2597095]
- Bertoli S, Probst R. Lack of standard N2 in elderly participants indicates inhibitory processing deficit. *Neuroreport.* 2005; 16:1933–1937. [PubMed: 16272882]
- Billings CJ, McMillan G, Penman T, Ong S. Predicting perception in noise using cortical auditory evoked potentials. *J Assoc Res Oto.* in revision.
- Billings CJ, Tremblay KL, Souza PE, Binns MA. Effects of hearing aid amplification and stimulus intensity on cortical auditory evoked potentials. *Audiol Neurotol.* 2007; 12:234–246. [PubMed: 17389790]
- Billings CJ, Tremblay KL, Stecker GC, Tolin WM. Human evoked cortical activity to signal-to-noise ratio and absolute signal level. *Hear Res.* 2009; 254:15–24. [PubMed: 19364526]
- Burkard R, Hecox K. The effect of broadband noise on the human brainstem auditory evoked response. I. Rate and intensity effects. *J Acoust Soc Am.* 1983; 74:1204–1213. [PubMed: 6643843]

- Ceponiene R, Rinne T, Naatanen R. Maturation of cortical sound processing as indexed by event-related potentials. *Clin Neurophysiol.* 2002; 113:870–882. [PubMed: 12048046]
- Ceponiene R, Westerfield M, Torki M, Townsend J. Modality-specificity of sensory aging in vision and audition: Evidence from event-related potentials. *Brain Res.* 2008; 1215:53–68. [PubMed: 18482717]
- Dirks DD, Morgan DE, Dubno JR. A procedure for quantifying the effects of noise on speech recognition. *J Speech Hear Disord.* 1982; 47:114–123. [PubMed: 7176586]
- Galazyuk AV, Feng AS. Encoding of sound duration by neurons in the auditory cortex of the little brown bat, *Myotis lucifugus*. *J Comp Physiol A.* 1997; 180:301–311. [PubMed: 9106994]
- Hari R, Pelizzzone M, Makela JP, et al. Neuromagnetic responses of the human auditory cortex to on- and offsets of noise bursts. *Audiology.* 1987; 26:31–43. [PubMed: 3593099]
- Hawkins JE, Stevens SS. The masking of pure tones and speech by white noise. *J Acoust Soc Am.* 1950; 22:6–13.
- He J, Hashikawa T, Ojima H, Kinouchi Y. Temporal integration and duration tuning in the dorsal zone of cat auditory cortex. *J Neurosci.* 1997; 17:2615–2625. [PubMed: 9065521]
- Henry KR. Tuning of the auditory brainstem OFF responses is complementary to tuning of the auditory brainstem ON response. *Hear Res.* 1985; 19:115–125. [PubMed: 4055531]
- Henry KR, Lewis ER. Offset AP masker tuning curve and the FFT of the stimulus. *J Acoust Soc Am.* 1988; 84:1354–1362. [PubMed: 3198871]
- Hillyard SA, Picton TW. On and off components in the auditory evoked potential. *Percept Psychophys.* 1978; 24:391–398. [PubMed: 745926]
- Joutsiniemi SL, Hari R, Vilkmann V. Cerebral magnetic responses to noise bursts and pauses of different durations. *Audiology.* 1989; 28:325–333. [PubMed: 2597096]
- Kaplan-Neeman R, Kishon-Rabin L, Henkin Y, Muchnik C. Identification of syllables in noise: electrophysiological and behavioral correlates. *J Acoust Soc Am.* 2006; 120:926–933. [PubMed: 16938980]
- Noda K, Tonoike M, Doi K, Koizuka I, Yamaguchi M, Seo R, Kubo T. Auditory evoked off-response: its source distribution is different from that of on-response. *Neuroreport.* 1998; 9:2621–2625. [PubMed: 9721944]
- Pantev C, Eulitz C, Hampson S, Ross B, Roberts LE. The auditory evoked “off” response: Sources and comparison with the “on” and “sustained” responses. *Ear & Hearing.* 1996; 17:255–265. [PubMed: 8807267]
- Phillips DP. Temporal response features of cat auditory cortex neurons contributing to sensitivity to tones delivered in the presence of continuous noise. *Hear Res.* 1985; 19:253–268. [PubMed: 4066524]
- Phillips DP, Hall SE. Spike-rate intensity functions of cat cortical neurons studied with combined tone-noise stimuli. *J Acoust Soc Am.* 1986; 80:177–187. [PubMed: 3745663]
- Phillips DP, Hall SE, Boehnke SE. Central auditory onset responses, and temporal asymmetries in auditory perception. *Hear Res.* 2002; 167:192–205. [PubMed: 12117542]
- Qin L, Chimoto S, Sakai M, Wang J, Sato Y. Comparison between offset and onset responses of primary auditory cortex ON-OFF neurons in awake cats. *J Neurophysiol.* 2007; 97:3421–3431. [PubMed: 17360820]
- Recanzone GH. Response profiles of auditory cortical neurons to tones and noise in behaving macaque monkeys. *Hear Res.* 2000; 150:104–118. [PubMed: 11077196]
- Scholl B, Gao X, Wehr M. Nonoverlapping sets of synapses drive on responses and off responses in auditory cortex. *Neuron.* 2010; 65:412–421. [PubMed: 20159453]
- Stevens SS, Guirao M. Loudness functions under inhibition. *Percept Psychophys.* 1967; 2:459–465.
- Takahashi H, Nakao M, Kaga K. Cortical mapping of auditory-evoked offset responses in rats. *Neuroreport.* 2004; 15:1565–1569. [PubMed: 15232284]
- Wakai RT, Lutter WJ, Chen M, Maier MM. On and Off magnetic auditory evoked responses in early infancy: a possible marker of brain immaturity. *Clin Neurophysiol.* 2007; 118:1480–1487. [PubMed: 17502163]

HIGHLIGHTS

The cortical auditory evoked offset response shows sensitivity to signal level changes in noise, whereas the cortical auditory evoked onset response does not.

The N2 wave in the offset response was particularly pronounced, and was the clearest indicator of offset response magnitude.

Rectified area amplitudes computed over the range of the offset response captured the same main effects as peak measures.

Figure 1.

Example of the auditory evoked onset and offset response to a 90 dB tone showing Cz (solid black) and GFP (dotted gray) waveforms. The later 3 waves constitute the offset response to a stimulus with 757 ms duration (indicated with thick red line), with their onset counterparts shown earlier to the left. We also see that the GFP waveform is always positive, since it is plotting standard deviations across all electrodes.

Figure 2.

Illustration of the baseline correction procedure used in the calculation of rectified area. The red line illustrates the original pre-stimulus baseline correction used for peak measurements. The window over the offset response indicates the range over which the waveforms were baseline corrected (790 – 1140 ms), and the blue line indicates the new baseline corrected waveform used for area amplitude measurements. After baseline correction, rectified area amplitude was calculated for the entire range (as in this example) and for sub-ranges within the baseline correction window. This figure displays the grand averaged response to the 75 dB tone in quiet.

Figure 3.

Grand-averaged waveforms (n=13) for Cz and GFP. Overlaid are waveforms for the seven tone levels, ranging from 30 dB up to 90 dB. Notice that the N2 wave of the offset response is proportionally much larger than the N2 wave of the onset response, especially in the GFP waveforms.

Figure 4.

Growth functions for Cz and GFP waveforms illustrating the effect of absolute signal level on peak latency and peak amplitude of the offset response. Separate plots are given for each wave measured, which for Cz included N1, P2 and N2, and for GFP included N2. For each plot, values for all 7 signal levels are shown, and error bars represent one standard error of the mean.

Figure 5.

Growth functions illustrating the effect of absolute signal level on the rectified area amplitude of the offset response for Cz and GFP waveforms. Separate plots are given for each range measured, which included N1-P2 (790–970 ms), N2 (970–1140 ms) and N1-P2-N2 (790–1140 ms). Error bars represent one standard error of the mean. Notice that rectified area amplitude measures and peak amplitude measures (Figure 4) show a similar affect of level.

Figure 6. Grand-averaged waveforms ($n=15$) for Cz and GFP. Overlaid are waveforms for the 60 dB (dotted red line) and 75 dB (solid blue line) tones, displayed for SNRs ranging from quiet to -10 dB.

Figure 7. Growth functions illustrating the effect of SNR on peak latency and peak amplitude of the offset response recorded at Cz and GFP. Overlaid are growth functions for the 60 dB (dotted red line) and 75 dB (solid blue line) tones, displayed for the quiet condition and the 5 SNR conditions. Error bars represent one standard error of the mean. Notice that the effects of SNR and signal level in noise are more consistent on peak latency than on peak amplitude.

Figure 8.

Growth functions illustrating the effect of SNR on the rectified area amplitude of the offset response recorded at Cz and GFP. Separate plots are given for each range measured, which included N1-P2 (790–970 ms), N2 (970–1140 ms) and N1-P2-N2 (790–1140 ms). Overlaid are growth functions for the 60 dB (dotted red line) and 75 dB (solid blue line) tones, displayed for the quiet condition and the 5 SNR conditions. Error bars represent one standard error of the mean. Notice that the effect of signal level in noise appears most pronounced at the highest SNR.

Table 1

Outline of the experimental conditions used in Billings et al. (2007) and Billings et al. (2009), the data from which we reanalyze in the present study.

Subjects		Experimental Design				Electrophysiology		
n	Characteristics	Signal	Noise	Duration (ms)	ISI (ms)	Signal Level (dB)	SNR (dB)	Recording
(A) Billings et al., 2007	Young adults; normal hearing	1000-Hz tone	None	757	1910	30, 40, 50, 60, 70, 80, & 90 dB SPL	N/A	<ul style="list-style-type: none">Passive recording; 400 sweeps for each stimulus
								<ul style="list-style-type: none">32-electrode montage; nose-referencedBandpass filtered from 1 Hz to 30 Hz
(B) Billings et al., 2009	Young adults; normal hearing	1000-Hz tone	Continuous White Noise	756	1910	(a) 60 dB SPL (b) 75 dB SPL	Quiet, 20, 10, 0, -5, & -10 dB SNR	<ul style="list-style-type: none">Passive recording; 400 sweeps for each stimulus
								<ul style="list-style-type: none">64-electrode montage; nose-referencedBandpass filtered from 1 Hz to 30 Hz

Table 2

Statistical results for Cz and GFP waveforms from Billings et al. (2007) dataset.

	ONSET			OFFSET		
	Effect of Level			Effect of Level		
	<i>F</i> -statistic (df)	<i>P</i> -value	<i>Bonferroni P</i> -value	<i>F</i> -statistic (df)	<i>P</i> -value	<i>Bonferroni P</i> -value
Cz						
Peak Latency						
N1	16.4 (6,22.6)	<0.001	<0.001	4.1 (6,24.7)	0.005	0.021
P2	10.5 (6,24.0)	<0.001	<0.001	5.2 (6,25.2)	0.001	0.005
N2	3.8 (6,24.4)	0.008	0.049	1.3 (6,32.4)	0.268	1
Peak Amplitude						
N1	20.3 (6,23.9)	<0.001	<0.001	1.6 (6,23.0)	0.185	0.741
P2	7.6 (6,23.6)	<0.001	<0.001	3.1 (6,23.1)	0.021	0.086
N2	8.8 (6,14.3)	<0.001	0.002	35.5 (6,23.6)	<0.001	<0.001
Rectified Area						
N1-P2	*	*	*	5.0 (6,25.5)	0.002	0.01
N2	*	*	*	22.6 (6,15.3)	<0.001	<0.001
N1-P2-N2	*	*	*	19.4 (6,23.1)	<0.001	<0.001
GFP						
Peak Latency						
N1	19.7 (6,23.6)	<0.001	<0.001	**	**	**
P2	4.3 (6,72)	<0.001	<0.001	**	**	**
N2	3.5 (6,23.0)	0.013	0.078	3.4 (6,32.6)	0.01	0.038
Peak Amplitude						
N1	27.2 (6,20.8)	<0.001	<0.001	**	**	**
P2	9.9 (6,23.7)	<0.001	<0.001	**	**	**
N2	11.4 (6,23.6)	<0.001	<0.001	17.1 (6,19.6)	<0.001	<0.001
Rectified Area						
N1-P2	*	*	*	7.4 (6,27.6)	<0.001	<0.001
N2	*	*	*	16.7 (6,28.8)	<0.001	<0.001
N1-P2-N2	*	*	*	18.1 (6,28.4)	<0.001	<0.001

* Rectified area amplitude was only measured for the offset response, since all peaks in the onset response could be identified directly.

** N1 and P2 peaks could not be reliably measured, and were therefore excluded from the analysis.

Table 3

Statistical results for Cz and GFP waveforms from Billings et al. (2009) dataset.

	ONSET			Effect of Level			SNR*Level Interaction		
	Effect of SNR			F-statistic (df)			Bonferroni P-value		
	F-statistic (df)	P-value	Bonferroni P-value	F-statistic (df)	P-value	Bonferroni P-value	F-statistic (df)	P-value	Bonferroni P-value
Cz									
Peak Latency									
N1	51.5 (6,55.8)	<0.001	<0.001	0.1 (1,45.2)	0.77		1 2.5 (4,55.8)	0.052	0.924
P2	22.6 (6,55.4)	<0.001	<0.001	0.3 (1,56.8)	0.593		1 2.1 (4,55.4)	0.087	1
N2	23.6 (6,55.7)	<0.001	<0.001	0.1 (1,91.3)	0.734		1 0.6 (4,55.7)	0.643	1
Peak Amplitude									
N1	12.4 (4,34.2)	<0.001	<0.001	3.6 (1,95.9)	0.06		1 0.4 (4,95.9)	0.806	1
P2	12.8 (4,41.4)	<0.001	<0.001	1.6 (1,83.5)	0.203		1 0.7 (4,83.3)	0.603	1
N2	12.3 (4,67.2)	<0.001	<0.001	0.8 (1,123.1)	0.377		1 0.2 (4,123)	0.957	1
Rectified Area*									
N1-P2	134.5 (4,126)	<0.001	<0.001	1.2 (1,126)	0.272		1 0.9 (4,126)	0.451	1
N2	21.8 (4,126)	<0.001	<0.001	2.2 (1,126)	0.136		1 0.8 (4,126)	0.53	1
N1-P2-N2	89.6 (4,126)	<0.001	<0.001	3.9 (1,126)	0.051		0.91 1.3 (4,126)	0.281	1
GFP									
Peak Latency									
N1	70.3 (4,54.6)	<0.001	<0.001	1.5 (1,63.6)	0.232		1 2.0 (4,54.6)	0.102	1
P2	100.4 (4,56.2)	<0.001	<0.001	1.1 (1,101.7)	0.294		1 2.4 (4,56.2)	0.061	1
N2	57.2 (4,56.3)	<0.001	<0.001	0.5 (1,107.2)	0.503		1 1.6 (4,56.4)	0.193	1
Peak Amplitude									
N1	62.9 (4,74.1)	<0.001	<0.001	6.2 (1,124.1)	0.014		0.251 0.4 (4,124.1)	0.823	1
P2	16.4 (4,27.5)	<0.001	<0.001	0.7 (1,90.8)	0.418		1 0.6 (4,90.8)	0.678	1
N2	15.8 (4,31.3)	<0.001	<0.001	0.4 (1,86.2)	0.522		1 0.4 (4,86.1)	0.824	1
Rectified Area*									
N1-P2	60.6 (4,126)	<0.001	<0.001	1.5 (4,126)	0.215		1 0.3 (4,126)	0.904	1
N2	32.3 (4,126)	<0.001	<0.001	1.7 (4,126)	0.201		1 0.6 (4,126)	0.641	1
N1-P2-N2	70.7 (4,126)	<0.001	<0.001	0.1 (4,126)	0.802		1 0.5 (4,126)	0.74	1

OFFSET

	Effect of SNR			Effect of Level			SNR* Level Interaction		
	<i>F</i> -statistic (df)	<i>P</i> -value	<i>Bonferroni P</i> -value	<i>F</i> -statistic (df)	<i>P</i> -value	<i>Bonferroni P</i> -value	<i>F</i> -statistic (df)	<i>P</i> -value	<i>Bonferroni P</i> -value
Cz									
Peak Latency									
N1	5.6 (4,55.7)	<0.001	0.009	14.0 (1,112.8)	<0.001	0.003	1.1 (4,55.6)	0.378	1
P2	7.8 (4,53.1)	<0.001	<0.001	21.9 (1,101.9)	<0.001	<0.001	0.4 (4,53.6)	0.835	1
N2	16.0 (4,58.8)	<0.001	<0.001	8.8 (1,109.4)	0.004	0.044	0.7 (4,58.8)	0.618	1
Peak Amplitude									
N1	0.4 (4,31.5)	0.804	1	1.6 (1,97.5)	0.205	1	1.1 (4,96.3)	0.377	1
P2	0.9 (4,34.4)	0.481	1	0.6 (1,92.8)	0.431	1	3.2 (4,92.2)	0.016	0.19
N2	5.2 (4,46.6)	0.001	0.017	14.6 (1,123)	<0.001	0.002	2.3 (4,123)	0.061	0.727
Rectified Area									
N1-P2	16.9 (4,126)	<0.001	<0.001	8.4 (1,126)	0.004	0.08	1.5 (4,126)	0.193	1
N2	9.2 (4,126)	<0.001	<0.001	20.5 (1,126)	<0.001	<0.001	4.4 (4,126)	0.002	0.038
N1-P2-N2	14.0 (4,126)	<0.001	<0.001	20.2 (1,126)	<0.001	<0.001	4.1 (4,126)	0.004	0.065
GFP									
Peak Latency									
N1	**	**	**	**	**	**	**	**	**
P2	**	**	**	**	**	**	**	**	**
N2	9.6 (4,47.2)	<0.001	<0.001	2.7 (1,77.8)	0.103	1	0.6 (4,47.6)	0.671	1
Peak Amplitude									
N1	**	**	**	**	**	**	**	**	**
P2	**	**	**	**	**	**	**	**	**
N2	5.0 (4,34.3)	0.003	0.032	11.6 (1,83.7)	0.001	0.012	0.8 (4,82.9)	0.527	1
Rectified Area									
N1-P2	7.0 (4,126)	<0.001	<0.001	5.5 (1,126)	0.021	0.38	3.4 (4,126)	0.011	0.197
N2	14.4 (4,126)	<0.001	<0.001	15.9 (1,126)	<0.001	0.002	4.2 (4,126)	0.003	0.057
N1-P2-N2	12.6 (4,126)	<0.001	<0.001	10.2 (1,126)	0.002	0.032	4.8 (4,126)	0.001	0.022

* Rectified area amplitude was measured for both the onset and offset response to provide a basis for comparison.

** N1 and P2 peaks could not be reliably measured, and were therefore excluded from the analysis.