Clinical Neurophysiology 127 (2016) 1589–1602

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Effects of rate (0.3–40/s) on simultaneously recorded auditory brainstem, middle and late responses using deconvolution

Fred Holt [a], Özcan Özdamar [a,b,*]

[a] Department of Biomedical Engineering, University of Miami, P.O. Box 248294, Coral Gables, FL 33124, USA
[b] Departments of Otolaryngology, Pediatrics and Neuroscience, School of Medicine, University of Miami, Miami, FL, USA

ARTICLE INFO

Article history:
Accepted 9 October 2015
Available online 6 November 2015

Keywords:
Auditory evoked potentials
Deconvolution
Transient response
Rate effects
Adaptation
Chirp

HIGHLIGHTS

- Transient auditory evoked potentials (AEPs) to chirps for several rates 0.3–40/s are obtained using deconvolution.
- ABR and middle latency response (MLR) are mostly stable across rate, late response morphology changes significantly in latency and amplitude below 3.5/s.
- P_1 of the late responses and P_b of the middle latency responses appear indistinguishable.

ABSTRACT

Objective: Auditory evoked potentials (AEPs) are typically acquired in either transient (low-rate) or steady state (high-rate) conditions. This study utilizes deconvolution to obtain transient responses over a range of rates from 0.3 to 40/s, to establish a rate profile of transient responses employing uniform recording conditions.
Methods: Deconvolution is used to obtain transient responses from quasi steady state recordings for rates 3.5–40/s, and components are scored and waveform morphologies are compared across rates.
Results: All component latencies remain stable across all rates other than P_2, which decreases for rates up to 3.5/s. Amplitudes for brainstem (V, N_a), middle latency (P_a, N_b), and late (P_b/P_1, N_1 and P_2) responses increased for rates below 1, 2 and 3.5/s, respectively. Rates between 3.5 and 25/s undergo a gradual morphology transition, above which oscillations begin to occur after 100 ms.
Conclusions: Auditory brainstem, middle and late latency components other than P_2 show stable latencies across 0.3–40/s with varying amplitude rate dependencies.
Significance: Obtaining a transient response rate profile utilizing uniform acquisition parameters is useful for an improved understanding of how individual AEP components interact with stimulation rate, and can provide a more comprehensive assessment of the ascending auditory pathway and primary auditory cortices.

1. Introduction

Auditory evoked potentials (AEPs) are small amplitude electrical potentials generated by overlapping streams of neural activity in response to any sufficiently intense stimulus. For clinical purposes, AEPs are commonly acquired via scalp surface electrodes to assess the function and integrity of the auditory system. The recorded AEP is sensitive to the stimulus content, intensity, presentation rate, subject age, and sex among others. Two types of responses are typically acquired depending on stimulus presentation rate: transient or steady state responses. Lower stimulus repetition rates (<2/s) are capable of eliciting transient (or unitary) responses, where evoked neural activity subsides fully prior to subsequent stimulation. Auditory steady state responses (ASSR) are commonly acquired with stimulation (or modulation) rates of 20, 40 and 80/s, resulting in quasi-sinusoidal waveforms that are often evaluated objectively using spectral analysis.

The transient response (TR) is typically segregated into three epochs relative to stimulus onset: early (the auditory brainstem

* Corresponding author at: Department of Biomedical Engineering, University of Miami, P.O. Box 248294, Coral Gables, FL 33124, USA. Tel.: +1 305 284 2136; fax: +1 305 284 6494.
E-mail address: oozdamar@miami.edu (Ö. Özdamar).

http://dx.doi.org/10.1016/j.clinph.2015.10.046
1388-2457/

response, ABR), middle latency (MLR), and late latency response (LLR) or cortical AEP (CAEP), and is typically evaluated in the time domain (Picton et al., 1974). Each epoch is comprised of several characteristic waves that represent progressive stages of neural processing, and is typically studied in isolation as a result of filtering and for historical and technological reasons.

The ABR (occurring 1.5–15 ms after stimulus onset) is considered to be an entirely exogenous response with well-established neuroanatomical correlates (Jewett and Williston, 1971; Picton, 2011), thus is highly dependent on neural synchrony in cochlea and early auditory pathway. When using click stimuli, there are seven identifiable waves in the ABR (Jewett and Williston, 1971) with the prominent positive peaks I, III, and V followed by a slow negativity (SN_{10}) or N_a. The detectability of peaks and peak-to-peak amplitudes of the ABR can be utilized to objectively estimate hearing thresholds, evaluate the integrity of the brainstem pathway, detect lesions using interaural differential diagnosis, to assess neurodegenerative disorders such as Ménière's, and to evaluate potential hearing loss during recovery of infections such as bacterial meningitis (e.g., Don et al., 2005; Irimajiri et al., 2005; Özdamar and Kraus, 1983b; Özdamar et al., 1983; Prasher et al., 1993).

The MLR (15–60 ms) contains waves P_a, N_b and P_b that are generated along the thalamocortical pathway (Özdamar and Kraus, 1983a; Kraus and McGee, 1995; Kraus et al., 1982). It can be utilized to assess cortical lesions, binaural interactions, to evaluate echo suppression, fusing speech elements to form auditory objects, and for diagnostics related to central auditory processing disorders (Kraus et al., 1982; Musiek et al., 1994; Özdamar and Kraus, 1983a; Starr and Hamilton, 1976).

The cortical AEP (CAEP) responses are typically significantly larger in amplitude than ABR and MLR when stimulating less than 2/s (Hall, 1992), occur more than 60 ms after stimulus onset and signify broad activation of the various regions of the auditory and associational cortices (Picton, 2011). The presence and magnitude of CAEP waves is heavily dependent on subject attentiveness, wakefulness and stimulation rate (Näätänen and Picton, 1987; Picton et al., 1974; Picton and Hillyard, 1974; Rosenberg et al., 1984). CAEPs have been difficult to study due to large inter-subject and intra-subject variability, long testing durations due to the requisite low stimulation rates, and typically lack substantive normative data for clinical usage (Burkard et al., 2007; Ch. 23).

As stimulation rate increases above 2/s, responses evoked by individual stimuli begin to experience overlap with adjacent responses, resulting in increasingly convolved waveforms where neuroanatomically correlated waves elicited by individual stimuli become difficult or impossible to evaluate independently in the time domain. Stimulation rates of 40 or 80/s are commonly used to acquire steady state (or SS) responses (Picton et al., 2003), since the responses at these rates are characterized by a quasi discrete spectrum and high signal-to-noise ratio (SNR) that can be readily evaluated objectively.

Typical studies of AEPs involve averaging responses to several 10s (CAEP) to several 1000s (ABR) of stimuli in order to obtain a waveform with sufficiently high SNR to detect characteristic peaks. Recommended acquisition parameters for the ASSR and transient responses typically render these paradigms mutually exclusive.

1.1. Rate dependence

AEP components within the MLR and CAEP exhibit sensitivity to stimulus presentation rate (Azzena et al., 1995; Davis et al., 1966; Özdamar et al., 2007; Sussman et al., 2008) and the subject's state of wakefulness. For example, wave P_2 of the CAEP can be several 10 s of microvolts when stimulating once per second in awake adult subjects, but can diminish significantly in sleep or anesthesia (Thornton and Sharpe, 1998; Crowley and Colrain, 2004).

Conventional AEP recordings (both TR and SS) are often acquired using stimulation trains with constant inter-stimulus intervals (ISIs), and involve averaging over windows of one to several ISI periods, depending on the AEP epoch studied (e.g., Özdamar and Kraus, 1983a; Picton, 2011; Tucker et al., 2002). The amount of neuroanatomically correlated information available in a given recording depends partly on the filters used, but is mostly limited by stimulation rate relative to the epoch of the AEP to be studied.

However, several methods have been proposed to overcome the rate limitation, and recover an estimate of the transient response by using special sequences containing stimulus onset jitter. Appropriately designed sequences can alleviate the otherwise ill-posed inversion problem and allowing for an estimate of the transient response to be mathematically recovered.

Several deconvolution methods have been applied to acquire AEPs, such as maximum length sequences (MLS) (Eysholdt and Schreiner, 1982), the continuous loop averaging deconvolution (CLAD) method (Delgado and Özdamar, 2004), the adjacent response (ADJAR) method (Woldorff, 1993), quasi-periodic sequence deconvolution (QSD) (Jewett et al., 2004), the randomized stimulation and averaging method (RSA) (Valderrama et al., 2012), least-squares (LS) deconvolution (Bardy et al., 2014b), and Weiner deconvolution (Wang et al., 2013), among others.

Deconvolution has been used for numerous diagnostic and basic research applications. For example, a relationship between MLR components and the 40/s ASSR has been apparent since the beginning (Galambos et al., 1981), suggesting that at 40/s the ASSR comprised of superimposed MLR components of the responses to individual stimuli. However, initial efforts to model the ASSR using transient responses acquired at low rates were unsuccessful (Conti et al., 1999). A subsequent report demonstrated that the 40/s ASSR can be fully explained using simple superposition of the TR obtained using the CLAD deconvolution method (Bohórquez and Özdamar, 2008).

The general relationship between stimulation rate and adaptation (or response refractoriness) has primarily been investigated for each epoch of the AEP independently, or each peak in isolation. Attempts to acquire and compare multiple representations or epochs of the AEP simultaneously have resulted in acquisition of early responses (ABR or frequency following responses, FFR) and cortical ERPs separately or concurrently with different acquisition parameters for each (Bidelman, 2015; Irimajiri et al., 2005; Krishnan et al., 2012; McFadden et al., 2010). For example, studies investigating rate function of the CAEP primarily rely on repetition rates $\leqslant$2/s (Hall, 1992), and occasionally extend to 10/s (Budd and Michie, 1994; Wang et al., 2008), but are typically limited by their stimulation, averaging methodology and filters. Studies involving the MLR typically eliminate any potential contributions of the CAEP by filtering, or use stimulation methodologies that do not allow for later waves to be observed. Additionally, stimulation rates of 5–20/s are intermediate to recommended conventional transient or steady state acquisition protocols. These intermediate rates elicit responses that are often complex and difficult to interpret in the temporal or spectral domains as a result of adjacent stimulus overlap. While few studies have utilized these intermediate rates (5–20 Hz, *see*: Tlumak et al., 2011), this region has not been as thoroughly studied as lower or higher rates.

True simultaneous recordings of brainstem and cortical AEPs would be advantageous in individual subjects as it would allow for a more complete assessment of the ascending auditory pathway (from early neural transcription and pitch coding, to behaviorally relevant processing of the middle latency responses, to complex cognitive processing in the cortex), and thus provides for multiple representations of auditory processing hierarchy under uniform stimulation and acquisition conditions. For example, such an assessment utilizing speech stimuli may provide