Research paper

The relation between auditory-nerve temporal responses and perceptual rate integration in cochlear implants

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ABSTRACT

The purpose of this study was to examine auditory-nerve temporal response properties and their relation to psychophysical threshold for electrical pulse trains of varying rates ("rate integration"). The primary hypothesis was that better rate integration (steeper slope) would be correlated with smaller decrements in ECAP amplitude as a function of stimulation rate (shallower slope of the amplitude-rate function), reflecting a larger percentage of the neural population contributing more synchronously to each pulse in the train. Data were obtained for 26 ears in 23 cochlear-implant recipients. Electrically evoked compound action potential (ECAP) amplitudes were measured in response to each of 21 pulses in a pulse train for the following rates: 900, 1200, 1800, 2400, and 3500 pps. Psychophysical thresholds were obtained using a 3-interval, forced-choice adaptive procedure for 300-ms pulse trains of the same rates as used for the ECAP measures, which formed the rate-integration function. For each electrode, the slope of the psychophysical rate-integration function was compared to the following ECAP measures: (1) slope of the function comparing average normalized ECAP amplitude across pulses versus stimulation rate ("adaptation"), (2) the rate that produced the maximum alternation depth across the pulse train, and (3) rate at which the alternating pattern ceased (stochastic rate). Results showed no significant relations between the slope of the rate-integration function and any of the ECAP measures when data were collapsed across subjects. However, group data showed that both threshold and average ECAP amplitude decreased with increased stimulus rate, and within-subject analyses showed significant positive correlations between psychophysical thresholds and mean ECAP response amplitudes across the pulse train. These data suggest that ECAP temporal response patterns are complex and further study is required to better understand the relative contributions of adaptation, desynchronization, and firing probabilities of individual neurons that contribute to the aggregate ECAP response.

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1. Introduction

Today's cochlear implants (CIs) offer stimulation rates that range from 250 pulses per second per channel (pps/ch; Cochlear's SPEAK strategy) to over 5000 pps/ch (Advanced Bionics' HiResolution). Speech understanding with a CI has been shown to vary as a function of per-channel stimulation rate both within and across recipients (e.g., Brill et al., 1997; Friesen et al., 2005; Holden et al., 2002; Kiefer et al., 2000; Loizou et al., 2000; Vandali et al., 2000). At a more basic perceptual level, speech-processor program levels

also differ with stimulation rate (e.g. Botros and Psarros, 2010; Kreft et al., 2004; McKay et al., 2005; McKay and McDermott, 1998; Shannon, 1985; Zhou et al., 2012). As the stimulation rate increases, behavioral thresholds (T levels) and upper-comfort (C or M) levels typically decrease. The extent to which these levels decrease with increased stimulation rate differs across individuals as well as across electrodes within an individual, although no systematic trends have been reported (Donaldson et al., 1997; Kreft et al., 2004; Pfingst et al., 2011; Zhou et al., 2012). Finally, at the most peripheral physiological level, auditory neural responses also vary with stimulation rate, and these response patterns likewise differ across electrodes and across individuals (Hughes et al., 2012). The primary goal of this study was to examine the extent to which physiological response patterns at the level of the auditory nerve relate to changes in behavioral threshold as a function of stimulation rate for pulse trains. Understanding these relations may provide insights to performance differences across stimulation rates.

Abbreviations: AB, Advanced Bionics; BEDCS, Bionic Ear Data Collection System; CI, cochlear implant; ECAP, electrically evoked compound action potential; MPI, masker-probe interval; NRT, Neural Response Telemetry; pps, pulses per second; SD, standard deviation.

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1.1. Physiological effects of stimulation rate

The electrically evoked compound action potential (ECAP) is an aggregate response from a collection of auditory-nerve fibers. ECAP amplitudes change as a function of stimulation rate because of variations in neural excitability across fibers and across time. For relatively slow stimulation rates (≤200 pps), ECAPs measured in response to individual pulses within a train exhibit relatively large, equal-amplitude responses because the stimulation rate is sufficiently slow to allow for full recovery from depolarization to each pulse (Haenggeli et al., 1998; Matsuoka et al., 2000; Wilson et al., 1997). For rates ranging from approximately 400–2400 pps, ECAPs show an alternating pattern of amplitudes as a function of pulse number, reflecting differences in refractory periods across the underlying neural population (Finley et al., 1997; Hughes et al., 2012; Matsuoka et al., 2000; Rubinstein et al., 1999; Wilson et al., 1997). The depth of this alternating pattern increases with rate until a maximum depth is reached. The rate that produces the maximum alternation is expected to occur within the relative refractory period of the stimulated neural population (Hughes et al., 2012; Matsuoka et al., 2000). Matsuoka et al. (2000) described the maximum alternation as a "resonance" between the refractory period and the period of the stimulus pulse train, where the two periods are "synchronized". As the stimulation rate increases beyond the point of maximum alternation, the alternating pattern diminishes and the overall amplitudes decrease (Finley et al., 1997; Hughes et al., 2012; Miller et al., 2008; Wilson et al., 1997). This reduced-amplitude, relatively flat pattern reflects a stochastic state (or desynchronization) across the individual fibers that contribute to the ECAP, and typically occurs for rates ≥2400 pps (Hughes et al., 2012). Each pulse therefore elicits a response from a sub-population of neurons because of differences in refractory-recovery times across fibers. In addition, there is likely some amount of neural adaptation (i.e., extended period of no response) that contributes to the overall amplitude reduction (Hay-McCutcheon et al., 2005; Miller et al., 2008; Zhang et al., 2007); however, the extent to which adaptation and desynchronization each contribute to the overall amplitude reduction remains unclear.

The rate at which the alternating pattern ceases is henceforth termed the "stochastic rate." Hughes et al. (2012) examined ECAP responses to pulse-train stimuli for 29 ears in 26 CI recipients and found that for the majority of subjects, the stochastic rate differed across the three electrode regions tested (basal, middle, and apical). That study also examined the rate that yielded the maximum alternation in the ECAP amplitude pattern, and found that the maximum alternation occurred most often for 1800 pps for basal and apical electrodes, and 1200 pps for middle electrodes. These rates correspond to stimulus periods of 556–833 μs, which are slightly longer than the absolute refractory period for the human auditory nerve (approximately 300–500 μs), and therefore within the earlier portion of the relative refractory period (~0.5–8 ms; Brown et al., 1996, 1998; Finley et al., 1997). There was a trend toward shorter refractory-recovery time constants for electrodes that reached the maximum alternation at faster rates, suggesting that the alternating pattern is influenced by neural refractory effects, as noted by Matsuoka et al. (2000). However, there was no significant relation between refractory-recovery time constants and stochastic rate, suggesting that multiple mechanisms (e.g., variability of individual spike rates, firing probability, adaptation) likely contribute to stochastic independence in a complex way. It has been proposed that variations in neural refractory times underlie differences in how loudness (or behavioral threshold) changes with stimulation rate across individuals (Botros and Psarros, 2010; McKay et al., 2005; discussed further in the next section). Individual variability in auditory-nerve temporal-response properties (e.g., refractory-recovery time constants, adaptation, desynchronization) may therefore contribute to behavioral threshold differences and potentially performance differences across rates.

1.2. Perceptual effects of stimulation rate

The effect of stimulation rate on threshold and upper-comfort levels for CI users has been well documented (e.g. Botros and Psarros, 2010; Kreft et al., 2004; McKay et al., 2005; McKay and McDermott, 1998; Shannon, 1985; Zhou et al., 2012). As stimulation rate increases, thresholds tend to decrease more than upper-comfort levels because the mechanisms that contribute to each measure differ slightly (McKay et al., 2005; McKay and McDermott, 1998; Zhou et al., 2012). For threshold changes, Pfingst et al. (2011) and Zhou et al. (2012) described two mechanisms (central and peripheral) that presumably contribute to threshold decreases with increased stimulation rate. The first is a form of temporal integration, which they termed "multi-pulse integration." Temporal integration is presumed to be a central mechanism and is defined as a reduction in behavioral threshold for increased stimulus *duration* (using a fixed rate). Multi-pulse integration describes a reduction in behavioral threshold for increased stimulus *rate* (using a fixed duration). As the stimulation rate increases, the total number of pulses presented during the fixed period of time increases, resulting in increased overall power of the stimulus. Temporal integration and multi-pulse integration are similar in that the total number of pulses in each listening interval increases, thus resulting in better detectability. The second mechanism contributing to perceptual threshold changes with stimulation rate occurs at the peripheral level, and involves integrative properties of the nerve-fiber membrane. At low stimulation levels, sub-threshold charge from multiple pulses accumulates within the integrative time constant of the neural membrane, resulting in increased probability of neural discharge for sub-threshold stimulation (e.g., Cartee et al., 2000; Middlebrooks, 2004). This phenomenon will only occur if the period between pulses is short enough for multiple pulses to occur within the integrative time window of the neural membrane (i.e., faster rates). Membrane charge integration will not occur for very slow rates due to the longer period between pulses exceeding the integrative time window. Data from animals and humans show integrative (summative) effects for inter-pulse intervals of approximately 400 μs or less (Cartee et al., 2000; Morsnowski et al., 2006), which corresponds to stimulus rates of approximately 2500 pps or greater. In the present paper, we will use the term "rate integration" to refer to the collective effects of central multi-pulse integration (the rate-based version of temporal integration) and peripheral integration of charge along the auditory neural membrane for sub-threshold current levels, both of which contribute to the perceptual detection of the stimulus.

For behavioral upper-comfort levels, McKay and McDermott (1998) and McKay et al. (2005) suggested two somewhat opposing mechanisms (again, central and peripheral) that contribute to loudness as a function of stimulation rate. The first is multi-pulse integration, which is the same central mechanism that acts at threshold, summing peripheral input across a given time window. The second mechanism, neural refractory effects, occurs at the peripheral level and counterbalances the first to some extent by reducing the overall amount of neural input to the central integrator. Zhou et al. (2012) further proposed that fibers located near the edge of the excitation region likely receive sub-threshold stimulation, which temporally sums according to the neural-membrane integration mechanism described previously. Because there are fewer fibers that receive sub-threshold stimulation at high levels (near upper-comfort) than at low levels (near threshold), neural-membrane charge integration contributes less to