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Mapping the 40-Hz auditory steady-state response using current density reconstructions

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Abstract

We mapped the 40-Hz aSSR from nine normal subjects using PET-independent low-resolution electroencephalographic tomography (LORETA) as well as PET-weighted LORETA and minimum norm (MinNorm) current density reconstructions. In grand mean data, PET-independent LORETA identified seven sites with peaks in current density in right temporal lobe, right brainstem/cerebellum, right parietal lobe, left cerebellum/temporal lobe, and right frontal lobe. PET-weighted LORETA found six of the same sites as the PET-independent LORETA: the right brainstem source was eliminated and two right-frontal sources were added. Both LORETA analyses revealed considerable phase dispersion across identified sources. In both LORETA analyses, the relative time course of activation measured from an arbitrary starting phase progressed from right temporal lobe to right mid-frontal lobe to right parietal–frontal to right inferior parietal and finally to left cerebellum and left temporal lobe. MinNorm analysis incorporating PET information identified sources in the same locations as specified in the PET data. These sources were synchronized, with their amplitudes peaking almost simultaneously.

Both PET-independent and PET-weighted LORETA results suggest that the aSSR is: (1) the result of a reverberating network with two or more groups of sources that recurrently excite each other or (2) the result of sequential auditory processing through various levels of a hierarchical network. In contrast, the PET-weighted MinNorm results suggest that the 40-Hz response represents simultaneous activation over widely spaced areas of the brain, perhaps due to synchronization of γ-band activity to a common neural clock.

Keywords: Auditory steady-state response; Source localization; Auditory pathways; Evoked potentials; LORETA; MinNorm

Abbreviations: AM, amplitude modulated; aSSR, auditory steady-state response; CAR, common average reference; EP, evoked potential; LORETA, low resolution electroencephalogic tomography; MEG, magnetoencephalography; MinNorm, minimum norm; MNI, Montreal Neurological Institute; PAL, left preauricular point; PAR, right preauricular point; PCA, principal component analysis; PET, positron emission tomography; SNR, signal-to-noise ratio

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1. Introduction

The aSSR is an oscillation of the electrical potential on the scalp that follows the envelope of periodic stimuli such as amplitude modulated (AM) tones or click trains. First reported as a 40-Hz aSSR in 1981 by Galambos et al. (1981), SSRs have been found at other modulation rates (Rickards and Clark, 1984), and in other sensory systems (Snyder, 1992; Tallon-Baudry et al., 1997). While higher modulation frequencies are less dependent on subject state, the 40-Hz aSSR is typically larger and can be used as a rapid, objective hearing screening test in adults (Aoyagi et al., 1993).

The proposed models of aSSR generation can be divided into focal models, with activity dominated by either cortical or subcortical sites, and distributed models, involving resonance between thalamic and cortical structures. There is conflicting evidence as to which of these models best describes the origin of the aSSR.

The focal cortical hypothesis is supported by source-localization studies in humans (Gutschalk et al., 1999; Pantev et al., 1996) using magnetoencephalography (MEG). Pantev et al. (1996) used MEG to record the 40-Hz aSSR over the contralateral scalp with a 37-channel magnetometer and modeled the generator as a single moving dipole in the superior temporal gyrus. The position of this dipole oscillated from medial to lateral and back to medial as the aSSR varied sinusoidally at the modulation frequency. They also confirmed the results of Romani et al. (1982), who found that the aSSR is tonotopically arranged in the cortex when modeled by a single moving dipole, with high carrier frequencies located medial to low frequencies. Gutschalk et al. (1999) used a 122-channel whole-head magnetometer to localize the generators of a deconvolved aSSR near 40 Hz. They modeled the sources as two pairs of symmetric fixed dipoles, one pair in the superior temporal gyrus on each side. Changes in the 40 Hz aSSR with alertness (Dobie and Wilson, 1998), attention (Tiitinen et al., 1993), and anesthesia (Gilron et al., 1998; Plourde, 1993) also suggest a predominantly cortical generation site. The cortical hypothesis is supported by the morphologic similarity between the 40-Hz aSSR electrical waveform recorded from the surface of cat cortex (Makela et al., 1990), and the scalp potential recorded from humans. In the rat, the phase of this response reversed as the electrode advanced through the outer layer of the cortex, providing strong evidence that the aSSR is generated in the cortex (Franowicz and Barth, 1995).

Rickards and Clark (1984) found large phase shifts between the aSSR at low (25–70 Hz) and high (75–200 Hz) modulation rates. This phase shift, which represents a change in response latency, was interpreted as a change in the response generator. Moreover, John and Picton (2000) found latencies of 10 ms for the aSSR evoked by stimuli with modulation frequencies of 150–190 Hz. This is consistent with a generator at the same level as wave V of the auditory brainstem response (ABR), supporting the subcortical hypothesis at high modulation rates.

Lesion studies have also suggested subcortical generation sites for the aSSR, even at 40 Hz. Investigators have found that aspiration of the feline auditory cortex did not change the 40-Hz aSSR (Kiren et al., 1994). They also found that ipsilateral inferior colliculus lesions reduced the amplitude of the aSSR and contralateral inferior colliculus lesions abolished it. Others have found decreases in amplitude and increases in latency of the 40-Hz aSSR when patients with thalamic lesions were compared to controls (Spydell et al., 1985). However, only one of the five patients with temporal lobe lesions had amplitudes or latencies outside the control range. They concluded that the aSSR was generated subcortically.

A recent case report (Santarelli and Conti, 1999) suggests that while subcortical sites may be necessary for generating the aSSR, they may not be sufficient. They recorded a robust middle latency response (MLR), but no aSSR, in a patient in which both auditory cortices were intact, but multiple ischemic lesions were found in the white matter connecting cortex to thalamus. As the MLR is thought to reflect activity in both primary and non-primary thalamo-cortical pathways (Kraus and McGee, 1995), the presence of the MLR suggests that ascending auditory pathways are intact. The absence of the aSSR in this patient suggests that a thalamo-cortical network in addition to the pathway responsible for the MLR is required to generate the aSSR. Assuming that the sources of the aSSR at 40 Hz were broadly distributed from temporal cortex to thalamus, Ribary et al. (1991) found MEG source-localization data supporting a thalamo-cortical network generating the aSSR.

The results of other studies have suggested that the aSSR may influence activity in even more widely distributed regions of the brain. Patel and Balaban (2000) studied changes in the phase of the 40-Hz aSSR across carrier frequency. They found significant coherence between frontal and occipital sources when the carrier frequency changed in melodic fashion. This suggests that the 40-Hz aSSR may have additional components generated by frontal and occipital sources. Frontal sources are not without precedence in the auditory evoked potential literature. For example, Picton et al. (1999) found mN100 sources in the temporal lobes, as well as frontal regions using focal and distributed source models.

The lack of consensus concerning the generators of the aSSR prompted us to conduct additional studies to help define the origins of the aSSR. Using positron