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Intracranial mapping of auditory perception: Event-related responses and electrocortical stimulation

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ABSTRACT

Objective: We compared intracranial recordings of auditory event-related responses with electrocortical stimulation mapping (ESM) to determine their functional relationship.
Methods: Intracranial recordings and ESM were performed, using speech and tones, in adult epilepsy patients with subdural electrodes implanted over lateral left cortex. Evoked N1 responses and induced spectral power changes were obtained by trial averaging and time-frequency analysis.
Results: ESM impaired perception and comprehension of speech, not tones, at electrode sites in the posterior temporal lobe. There was high spatial concordance between ESM sites critical for speech perception and the largest spectral power (100% concordance) and N1 (83%) responses to speech. N1 responses showed good sensitivity (0.75) and specificity (0.82), but poor positive predictive value (0.32). Conversely, increased high-frequency power (>60 Hz) showed high specificity (0.98), but poorer sensitivity (0.67) and positive predictive value (0.67). Stimulus-related differences were observed in the spatial-temporal patterns of event-related responses.
Conclusions: Intracranial auditory event-related responses to speech were associated with cortical sites critical for auditory perception and comprehension of speech.
Significance: These results suggest that the distribution and magnitude of intracranial auditory event-related responses to speech reflect the functional significance of the underlying cortical regions and may be useful for pre-surgical functional mapping.

1. Introduction

Multi-channel recording studies have shown that cortical auditory event-related responses are widely distributed across the cortex, occurring at multiple sites in the same individuals (Woods and Wolpaw, 1982; Näätänen and Picton, 1987). Cortical event-related responses to auditory stimuli can be evoked or induced. Stimulus-evoked responses, such as the early cortical N1, are phase-locked to the stimulus and obtained by trial averaging in the time domain. Stimulus-induced responses refer to modulations in the spectral power of the EEG signal that are not strictly phase-locked to the stimulus and are derived using time-frequency analyses. Both types of auditory event-related responses are considered indices of cortical sound processing (Näätänen and Picton, 1987; Tallon-Baudry and Bertrand, 1999; Crone et al., 2001; Edwards et al., 2005). However, their functional relationships to each other and to the cortical regions that are essential for auditory perception remain poorly understood.

Although electrophysiologic methods provide adequate temporal resolution for investigating cortical sound processing, which occurs on the millisecond time-scale, the spatial resolution of scalp recordings is relatively poor due to signal attenuation and spatial distortion from intervening cranial tissues (Pfurtscheller and Cooper, 1975). Similarly, information about which cortical areas are functionally critical in individuals undergoing scalp recordings is generally lacking and must be inferred from stroke or other lesion studies. In contrast, intracranial recordings are not subject to the same limitations.

Intracranial recordings, also known as electrocorticography or ECoG, are performed routinely in patients with medically intractable seizures who have subdural electrodes implanted for seizure localization and pre-surgical functional mapping. Intracranial recordings provide better spatial resolution than scalp recordings because the electrodes are located directly on the surface of the cortex. They are also less vulnerable than scalp recordings to ocular

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and muscle artifacts (Sinai et al., 2005). Another advantage is that intracranial recordings can be performed in conjunction with electrocortical stimulation mapping (ESM), which is used to identify cortical areas that are functionally critical for motor, language, and sensory processing for pre-surgical planning (Lesser et al., 1987; Ojemann et al., 1989; Boatman, 2004). Previous ESM studies have identified sites critical for perception and discrimination of speech and other complex sounds in the left posterior temporal lobe, corresponding to auditory association cortex (Boatman et al., 1995; Boatman and Miglioretti, 2005). Conversely, auditory processing of simple tones is rarely disrupted by ESM.

Previous intracranial recording studies have identified task-related changes in spectral power, especially in the gamma frequency range (>30 Hz), during motor, language, and sensory tasks (Liegeois-Chauvel et al., 1994; Crone et al., 1998, 2001, 2006; Sinai et al., 2005; Miller et al., 2007). Recent intracranial studies have also identified changes in the gamma band during tasks involving attention, memory, and reading (Brovelli et al., 2005; Mainy et al., 2007, 2008; Sederberg et al., 2007). Intracranial recordings are well suited for investigating these high-frequency neural responses because they are not subject to the low-pass filtering effects encountered in scalp recordings. Induced spectral changes, especially in the high gamma frequencies (>60 Hz), have been observed during auditory tasks in previous intracranial recording studies (Crone et al., 2001; Ray et al., 2003, 2008; Edwards et al., 2005; Lachaux et al.,2007; Towle et al., 2008). A study by Edwards et al. (2005) demonstrated good spatial agreement between auditory evoked responses and high-frequency gamma responses to tones. Towle et al. (2008) recently reported good spatial agreement for auditory evoked responses and high gamma responses to tones. Although auditory evoked responses to speech were not described, they found increased gamma band responses to words at cortical sites identified as essential for receptive language processing by ESM. In a separate study, increased gamma responses to speech were identified at temporal lobe sites where ESM also impaired speech perception in the same patient (Lachaux et al., 2007). These studies suggest overlap in the distributions of intracranial auditory evoked and induced responses to simple tones and in the distributions of spectral responses to complex sounds, such as speech, and cortical sites that are critical for speech perception or comprehension. However, no studies to date have compared directly auditory event-related responses, evoked and induced, to ESM using the same auditory stimuli.

In this study, we used within-subject, repeated measures testing to compare directly auditory event-related responses, stimulus-evoked and stimulus-induced, to ESM results from the same patients using the same speech and tone stimuli. The targeted evoked response was the auditory N1, an early and prominent cortical response to the onset of a novel sound, occurring 70–120 ms after stimulus onset, and considered a relatively robust and reliable index of sound perception (Näätänen and Picton, 1987; Tremblay et al., 2003). Stimulus-induced spectral responses were identified using a matching pursuit time-frequency analysis method (Mallat and Zhang, 1993). We computed the sensitivity, specificity, and positive predictive value of cortical auditory evoked and induced responses to evaluate their accuracy in identifying cortical sites that are essential for auditory perception.

2. Methods

2.1. Patients

We tested six consecutive adult epilepsy patients, three males and three females ages 23–58 years (mean 35.7), undergoing extraoperative ESM for pre-surgical motor and language mapping (Table 1). All had medically intractable complex partial seizures, left hemisphere dominance for language as determined by intracarotid amobarbital injection, and subdural implantation of electrode arrays (6×8, 8×8) over lateral left cortex. Pre-surgical volumetric MRI studies showed no co-morbid neurological disorders (e.g. neoplasm). Two patients had previous anterior frontal or anterior temporal lobe resections ($\leqslant$3 cm), with seizure recurrence (Pts 3 and 6). Implanted electrodes were platinum-iridium disks, 3-mm diameter, embedded 10 mm apart in medical-grade silastic arrays (Ad-Tech, Racine, Wisconsin). Electrode locations were determined by co-registration of each patient's post-surgical CT to a pre-surgical volumetric MRI and by intraoperative photographs (Boatman et al., 2000; Boatman and Miglioretti, 2005). All patients had electrodes covering the posterior superior and middle temporal gyri for clinical language mapping; five also had coverage of the anterior temporal lobe. All patients had electrodes covering the parietal lobe; five also had coverage of the inferior frontal lobe. Individual differences in the number and location of electrodes were determined by clinical circumstances. Intracranial EEG recordings localized seizure foci to the anterior temporal lobe in five patients and the anterior frontal lobe in one patient (Pt 6).

Behavioral audiometric testing confirmed that all patients had normal hearing bilaterally ($\leqslant$20 dB HL, 250–8000 Hz) and normal performance on tests of auditory processing, including speech recognition in quiet and under adverse listening conditions (e.g. background noise). There was no history of speech-language, motor, or attention disorders. One patient (Pt 5) participated in a previous ESM study (Boatman and Miglioretti, 2005). Informed written consent was obtained for all participants in compliance with The Johns Hopkins Institutional Review Board.

2.2. Stimuli and tasks

2.2.1. Stimuli

Fifteen 200-ms speech and tone stimuli were generated (10-ms rise/fall times). Five were digitized consonant–vowel syllables (/ba, da, pa, ta, ga/) produced by a male speaker (44.1 kHz, 16 bit sampling; SoundForge™, Sony Inc.). The 10 tone stimuli included six steady-state tones and four frequency-modulated (FM) tones (NCH Tone/Waveform Generator, NCH Software). Steady-state tones were sine-waves generated at 500 Hz, 1000 Hz, 1200 Hz,

Table 1
Patient demographics.

Patient	Sex	Age (years)	Handedness	FSIQ	Seizure onset age (years)	Epilepsy duration (years)	MRI results
1	M	33	Right	94	31	2	Normal
2	F	26	Right	109	14	12	Normal
3	F	40	Right	102	20	20	Prior resection
4	M	58	Right	104	30	28	Normal
5	M	23	Left	99	4	19	Normal
6	F	34	Right	89	2	31	Prior resection
Mean		35.7		99.5	16.8	18.7	
SD		12.5		7.2	12.5	10.7	