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INTRODUCTION

Information from multiple sensory systems has been shown to interact surprisingly early in the cortical information processing stream, occurring at latencies consistent with the earliest stages of sensory processing. Intra-cortical electrical recordings in macaques have revealed that multisensory interactions can occur not only early in time, but also in what have traditionally been considered unisensory cortices (Schroeder & Foxe, 2002; Schroeder et al., 2001; Fu et al., 2003). High-density electrical mapping from the scalp surface has extended this finding to humans, revealing early latency multisensory interactions with scalp topographies consistent with generators in sensory cortices (Foxe et al., 2000; Molholm et al., 2002; Murray et al., in review). However, source localization based on scalp recordings is subject to the "inverse problem": a given scalp topography can be produced by multiple generator configurations. Thus to date there has been no direct evidence to tie the early multisensory interactions in humans to sensory processing areas. To this end intracranial recordings were made in patients with intractable epilepsy who were being evaluated for possible surgery, while they were presented with randomly interleaved visual, auditory, and simultaneously presented visual and auditory stimuli. These recordings revealed an early multisensory effect in auditory cortex. This finding clearly indicates that visual and auditory inputs interact early on in the information-processing stream to affect sensory processing.

METHODS

Subjects:

Recordings were made from patients with intractable epilepsy who were surgically implanted with intracranial electrodes. Data from the 8 in whom we clearly identified putative auditory P1s are reported here. In 2 of these subjects a P1 was identified in both the right and left hemisphere, leading to a total of 10 data points. All subjects were on anti-seizure medication at the time of recording.

Stimulus conditions:

Auditory alone (AUD-alone) – a 1000Hz tone of 60ms duration (~75dB SPL)

Visual alone (VIS-alone) – a disk subtending 1.2° in diameter (60ms duration) and appearing red on a black background. The disk was presented in the right upper quadrant of the monitor, 1.6° vertical and lateral from fixation.

Auditory + visual (MULT-AV) – the above auditory and visual stimuli were presented simultaneously.

Procedure:

Subjects performed a simple reaction-time task in which they responded to Aud-alone, Vis-alone and MULT-AV stimuli presented in random order. SOA ranged from 750 to 3000 ms. The tone was presented over headphones and the visual stimulus was presented on a monitor placed 100 cm from the subject. Subjects maintained fixation on a centrally placed cross and the experimenter monitored subjects' attentiveness and fixation.

Data acquisition and analysis:

Event-related potentials (ERPs) were acquired from 32 to 128 intracranial electrodes. A frontally placed intracranial electrode served as the reference. The data were online bandpass-filtered from 0.05 to 100Hz, amplified with a gain of 250, and digitized at 500Hz or 1000Hz. An artifact rejection criterion of $\pm 600 \mu V$ was used on the -100 to 300 ms portion of the stimulus locked epoch.

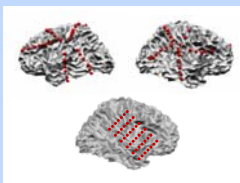
Statistical analyses:

We tested whether the auditory P1 (i.e., early auditory processing) was modulated by the simultaneous presentation of auditory and visual stimuli. Data from all electrode sites of a given subject were examined for the largest auditory P1 response, and this individual subject data was entered into the statistical analyses. This was done separately for each hemisphere when there was bilateral coverage.

To test for modulation of the auditory P1, we compared 1) the ERP elicited by the AUD-alone stimulus to the ERP elicited by the MULT-AV stimulus (simultaneously presented auditory and visual stimuli); and 2) the ERP elicited by the MULT-AV stimulus to the "summed ERP" (the sum of the ERPs elicited by the AUD-alone and the VIS-alone stimulus conditions). This was done for a 20ms window centered at the peak of the P1 as defined in the grand mean waveform.

As a secondary analysis, we performed point-wise running paired two-tailed t-tests on the two above comparisons. This allowed us to assess the onset and offset of the possible multisensory P1 effect. The onset was defined as the first time point where the t-test exceeded the 0.05 alpha criterion for at least 10 consecutive data points (>20ms for a 500 Hz digitization rate), in the latency range of the P1 (the requirement of 10 consecutive significant data points minimizes the likelihood of a Type 1 error; see Guthrie and Buchwald, 1991).

SAMPLE ELECTRODE ARRAYS



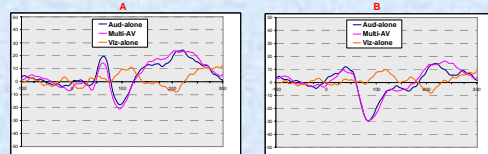
PARADIGM

Randomly interleaved: 1000 Hz tones presented alone (60ms duration); red circles presented alone (for 60ms); and 1000 Hz tones and red circles presented together (for 60ms). SOA = 750-3000ms



THE MULTISENSORY P1 EFFECT

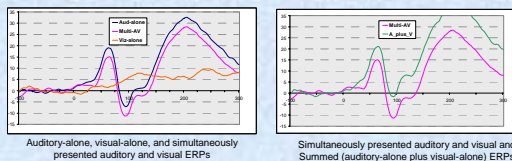
INDIVIDUAL SUBJECT DATA



(A) the multisensory P1-effect at a site over the right superior temporal gyrus.

(B) data from a site 1 cm away on the STG illustrates the specificity of the recorded P1 response.

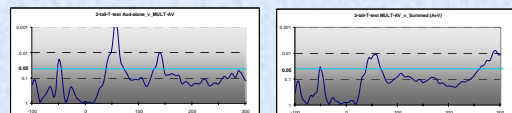
GROUP WAVEFORMS



Auditory-alone, visual-alone, and simultaneously presented auditory and visual ERPs

Simultaneously presented auditory and visual and Summed (auditory-alone plus visual-alone) ERPs

RUNNING T-TESTS



Plot of the p values from the running two-tailed t-test comparing the Aud-alone and Multi-AV ERPs. The light blue bar represents the cutoff for the 0.05 significance level.

Plot of the p values from the running two-tailed t-test comparing the Multi-AV and Summed (A plus V) ERPs. The light blue bar represents the cutoff for the 0.05 significance level.

RESULTS

In the latency range and cortical region of the auditory P1 the MULT-AV ERP was significantly smaller in amplitude than either the Aud-alone ERP or the summed ERP (respectively $t=3.79$, $p=.004$ and $t=2.83$, $p=.019$). See Group Waveforms.

The running t-tests revealed that this multisensory effect onset at 38ms for both the MULT-AV versus Aud-alone and the Multi-AV versus summed comparisons, and offset at about 70ms for both comparisons (74ms and 70ms, respectively). The p values of the running t-tests for each of the comparisons from -100 to 300ms are shown under 'Running t-tests'.

CONCLUSIONS

WE SHOW A MULTISENSORY AUDITORY-VISUAL EFFECT LOCALIZED TO PUTATIVE AUDITORY CORTEX

THE EFFECT ONSET AT THE EARLY LATENCY OF 38ms POST STIMULUS ONSET

Possible accounts of the multisensory effect include:

1) Direct inputs from visual to auditory cortex.

Neuroanatomical tracer studies by Falchier et al. (2002) and Rockland and Ojima (2003) show monosynaptic connections between visual and auditory cortices in the primate cortex. This demonstrates feasibility of a direct visual to auditory corticocortical account. The early timing profile of the multisensory effect suggests that such inputs would be through the "fast" visual pathway, i.e., the magnocellular pathway.

2) Inputs from a subcortical region to auditory cortex.

Another possibility is that inputs from the superior colliculus, known to have multisensory neurons that respond to input from both the auditory and visual sensory modalities (Stein & Meredith, 1993), account for the observed multisensory effect.

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