

High-frequency gamma activity (80–150 Hz) is increased in human cortex during selective attention

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Accepted 23 September 2007

Available online 26 November 2007

Abstract

Objective: To study the role of gamma oscillations (>30 Hz) in selective attention using subdural electrocorticography (ECoG) in humans.

Methods: We recorded ECoG in human subjects implanted with subdural electrodes for epilepsy surgery. Sequences of auditory tones and tactile vibrations of 800 ms duration were presented asynchronously, and subjects were asked to selectively attend to one of the two stimulus modalities in order to detect an amplitude increase at 400 ms in some of the stimuli.

Results: Event-related ECoG gamma activity was greater over auditory cortex when subjects attended auditory stimuli and was greater over somatosensory cortex when subjects attended vibrotactile stimuli. Furthermore, gamma activity was also observed over prefrontal cortex when stimuli appeared in either modality, but only when they were attended. Attentional modulation of gamma power began ~400 ms after stimulus onset, consistent with the temporal demands on attention. The increase in gamma activity was greatest at frequencies between 80 and 150 Hz, in the so-called high-gamma frequency range.

Conclusions: There appears to be a strong link between activity in the high-gamma range (80–150 Hz) and selective attention.

Significance: Selective attention is correlated with increased activity in a frequency range that is significantly higher than what has been reported previously using EEG recordings.

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Keywords: Attention; ECoG; Gamma oscillations; High-gamma activity; Sensory cortex; Intracranial EEG

1. Introduction

Human scalp EEG studies have suggested that high-frequency activity in the gamma band (>30 Hz) is correlated with selective attention (Tallon-Baudry and Bertrand, 1999; Kaiser and Lutzenberger, 2005), and this finding

has been supported by microelectrode recordings in awake behaving monkeys (Fries et al., 2001). However, high frequency cortical activity is significantly attenuated by intervening cranial tissues in scalp recordings (Cooper et al., 1965; Pfurtscheller and Cooper, 1975). Indeed, the extended frequency response of invasive EEG recordings has shown that during functional activation of cerebral cortex, gamma activity occurs over a much broader range of frequencies that extend far beyond the traditional 40-Hz gamma band typically observed in scalp EEG (Crone et al., 1998a, 2006). These non-phase-locked responses in

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“high-gamma” frequencies, typically greater than 60 Hz and extending as high as 200 Hz, have been observed during functional activation in a variety of cortical domains, including sensorimotor (Crone et al., 1998a; Ohara et al., 2000; Pfurtscheller et al., 2003; Leuthardt et al., 2004), oculomotor (Lachaux et al., 2006), auditory (Crone et al., 2001a; Ray et al., 2003; Edwards et al., 2005), visual (Crone et al., 2001b; Lachaux et al., 2005; Tanji et al., 2005), and language (Crone et al., 2001b; Sinai et al., 2005) cortices. However, their correlation with selective attention has not yet been unequivocally established. In one recent study, high-gamma responses were observed in two visual areas known to play a role in visual object processing: the lateral occipital cortex and the fusiform gyrus (Tallon-Baudry et al., 2005). Modulations of this high-gamma activity appeared to be correlated with attention, but these modulations were complex. For example, in the lateral occipital cortex, gamma-range activity increased during baseline but decreased during stimulus presentation. On the other hand, gamma activity in fusiform gyrus remained unchanged during the baseline period and increased during stimulus presentation.

In the present study, we investigated subdural electrocorticographic (ECoG) activity while human subjects performed a selective attention task. We recorded from subdural electrodes implanted in patients with intractable epilepsy before undergoing surgery while controlling their attentional state. Because gamma oscillations induced by stimulus presentation typically occur early after stimulus onset (less than 400 ms, peaking between 200 and 300 ms,

see Tallon-Baudry and Bertrand, 1999; Bauer et al., 2006) and may be modulated by stimulus strength (Henrie and Shapley, 2005; Siegel et al., 2007), our experimental task required the subjects to pay attention 400 ms after stimulus onset. This was designed to dissociate the effects of attention on induced gamma activity from stimulus-related effects (although, as mentioned in Section 4, the two effects may be interrelated). We addressed the following two questions: (1) what is the effect of selective attention on ECoG recorded from sensory (auditory and somatosensory) and frontal cortices, especially at higher frequencies (>60 Hz) not accessible in non-invasive EEG recordings? (2) Can the attention-related modulation in gamma power be dissociated from stimulus-induced gamma modulations, and if yes, is there a difference in the frequency range of gamma modulation associated with stimulus onset versus attention to the stimulus?

2. Methods

2.1. Experimental design

Stimuli were presented in both the tactile and auditory modalities (Fig. 1). The tactile stimuli consisted of a sinusoidal vibration (200 Hz) of 800 ms duration, delivered parallel to the skin surface by a stimulator consisting of an acrylic cylinder (32 mm diameter \times 160 mm long) driven by a linear motor mounted within the cylinder (Brisben et al., 1999). The auditory stimuli consisted of pure tones (200 Hz) of 800 ms duration, delivered through insert

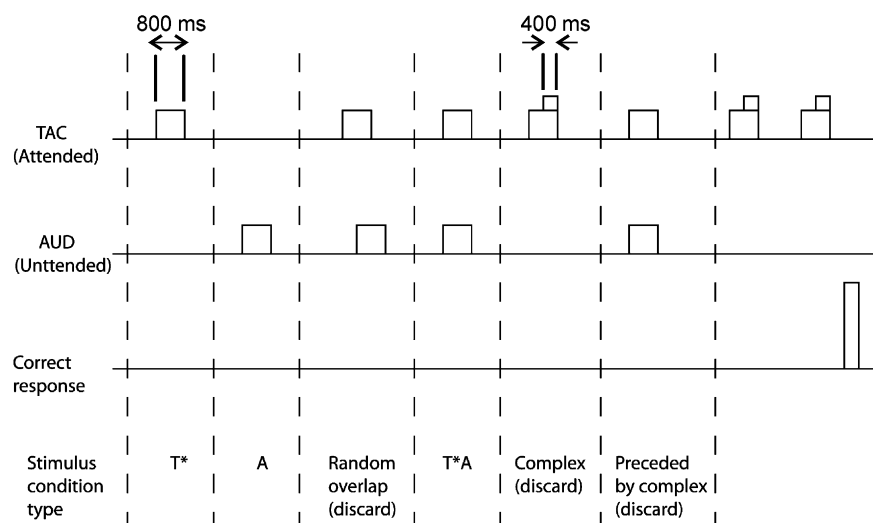


Fig. 1. Task Design. Subject was asked to pay attention to only one modality (tactile or auditory) for the duration of each set. Shown here is an example set in which the subject attended to the tactile modality (Aud and Tac correspond to Auditory and Tactile, respectively). A continuous sequence of tactile (vibrations at 200 Hz, 800 ms duration) and auditory stimuli (tones at 200 Hz, 800 ms duration) was presented with pseudorandom inter-stimulus interval (ISI). Stimuli were of two types: (1) Simple: no change in intensity throughout the duration of stimulus and (2) Complex: intensity increased after 400 ms. The subject was asked to press the response button when two consecutive complex stimuli were detected. Only the simple stimuli that were preceded and followed by more than a second of baseline activity (no other stimulus in any modality) were chosen for analysis; complex stimuli, stimuli with partial overlap or stimuli preceded by a complex stimulus were excluded from analysis. Each set contained about 80 stimuli in both modalities and lasted about 6 minutes, yielding 22 stimuli of types T*, A and T*A (T = Tactile, A = Auditory, TA = both tactile and auditory with complete temporal overlap, * indicates the attended modality). A similar set with attention directed to auditory stimuli yielded 22 stimuli of type T, A* and TA* each. Three sets were presented in each modality, yielding 66 trials for each of six stimulus conditions: T*, T, A*, A, T*A, and TA*.

earphones (Etymotic ER-3A). A frequency of 200 Hz was chosen so that the stimulus frequency lay outside of frequencies of interest. The frequency of auditory stimuli was matched to that of tactile stimuli so that the stimulus types could be as similar as possible. Although 200 Hz is towards the lower end of the audible range (and hence the auditory stimulus may be in a different perceptual range than the tactile stimulus), the spectral/temporal pattern of high-gamma activity due to a stimulus frequency of 200 Hz was similar to that observed in previous studies using a stimulus frequency of 1000 Hz (Ray et al., 2003). Stimulus amplitudes in both modalities were chosen as described under *Threshold and performance* below.

Auditory and tactile stimuli were of two types: simple (amplitude constant for duration of stimulus) and complex (amplitude increased after 400 ms). The subject was asked to comfortably grip the cylinder with the hand contralateral to the ECoG recording array and not to change the grip during the experiment. In the beginning of each set the subject was asked to attend to one of the two modalities (tactile or auditory) and to ignore stimuli in the other modality. Fig. 1 shows an example set of trials in which the subject attended to the tactile modality. Each set consisted of about 80 stimuli in both the attended and unattended modalities, out of which 15 stimuli were complex (in the attended modality only). All complex stimuli were excluded from the analysis to rule out gamma activity due to an increase in stimulus amplitude or to motor responses. The subject was asked to press a switch with the other hand following two consecutive complex stimuli (this occurred 5 times in each set). This response contingency was designed to prevent motor preparation during simple stimulus presentation. In addition, simple stimuli immediately following any single complex stimulus were excluded from analysis to reduce the effects of motor preparation in anticipation of another complex stimulus. To discourage subjects from switching their attention back and forth between the attended and unattended modalities, the inter-stimulus interval was pseudo-randomized and in several trials there was a partial overlap between stimuli in the two modalities. The partially overlapping stimuli were included to encourage the subject to maintain attention in the specified modality; a stimulus in that modality could potentially appear before a stimulus in the unattended modality finished. These partially overlapping stimuli were also excluded from analysis. Analyses were performed on only two classes of stimuli: (1) simple stimuli in both modalities that completely overlapped (22 stimuli per set) and (2) simple stimuli in one modality alone (attended or unattended) with at least one second pre- and post-stimulus without stimuli in either modality (22 stimuli per set). The first class of stimuli was useful in studying the effects of a competing stimulus in the unattended modality. It also increased the proportion of overlapping stimuli, again discouraging attentional switching between stimulus modalities. Each set lasted about 6 minutes. A total of six sets were recorded (three with attention

directed to tactile stimuli and three with attention directed to auditory stimuli), thus generating 66 stimuli for each of the following six stimulus conditions: Tactile-attended (T*), Tactile-unattended (T), Auditory-attended (A*), Auditory-unattended (A), overlapping stimuli of both modalities with attention on tactile stimuli (T*A), and overlapping stimuli with attention on auditory stimuli (TA*). Error trials were excluded from analysis.

2.2. Subjects

Subject 1 was a 53-year-old male, Subject 2 a 17-year-old female, and Subject 3 a 32-year-old female. All three subjects were right handed and had IQs in the normal range. Their seizures started at the age of 49, 1.5 and 17 years, respectively. Experiments were conducted with informed consent under a protocol approved by the Institutional Review Board of Johns Hopkins University.

Apart from these three subjects, three more subjects were able to satisfactorily complete the study (other subjects could not understand the experimental task or could not perform satisfactorily due to inattention or drowsiness). One of these three additional subjects had good coverage of auditory areas, but almost all the channels recording from temporal cortex were noisy, and no significant gamma activity could be observed. The other two subjects had bilateral strips (instead of grids) that did not cover auditory or somatosensory cortices. Some parietal recording sites close to auditory/SII cortex showed multimodal gamma responses due to both auditory and somatosensory stimuli (similar to [Supplementary Fig. 3](#)). The gamma power modulations were confined to higher gamma frequencies (80–150 Hz) in these channels, consistent with the results from the three subjects reported in this paper.

2.3. Threshold and performance

In general, in studies like these the estimation of optimal stimulus amplitudes is difficult. The short time available for the experiment under the given clinical circumstances prevented more detailed psychophysical testing. Furthermore, the perceived amplitude of auditory stimuli depends on a number of factors, including the presence of fluid and post-operative edema in the external auditory meatus. Likewise, perceived tactile amplitude may depend upon grip strength, and accurate measurement of EMG activity is difficult in this clinical setting. Nevertheless, the main experimental results, i.e. modulation of gamma responses during selective attention, could not be explained by these factors (see Section 4).

The tactile and auditory amplitudes were set as follows: first, the simple auditory amplitude was set to a level that was clearly audible without being uncomfortably loud to the subject. Then both the auditory and tactile stimuli were presented simultaneously, and the amplitude of the tactile stimulus was adjusted until its perceived intensity was equal to that of the auditory stimulus (neither stimulus

dominated the other). Then, a series of complex stimuli of varying difficulty levels (different amplitude step magnitudes) were presented, and the subject was asked to choose one that was just detectable, i.e. requiring significant attention. Subjects 1 and 2 held the stimulator with their left hand while Subject 3 used her right hand so that in each case, the stimulated hand was contralateral to the recording grid.

For Subject 1, the complex auditory stimulus had a 35% increase in amplitude. At this level of difficulty, the subject was able to detect all 15 complex pairs in the three sets (5 pairs per set), with no false alarms (FA). The complex tactile stimulus initially used a 50% increase during set 1 (1/5 correct, 1 FA), but was increased to 62.5% for set 2 (1/5 correct, 1 FA) and to 87.5% for set 3 (3/5 correct, 0 FA). Although the subject was able to detect a change of 50% during the initial setting (when no distracting auditory stimulus was present), his performance was poor in the presence of auditory distracters, requiring an increase in the amplitude step to get adequate performance. This did not create any inconsistency in the data analysis since the complex trials were excluded. Even with repetition of the same task, the level of attention required by the task remained high, evidenced by the subject detecting only 3 out of 5 tactile target stimuli even in the third set.

For Subject 2, the complex auditory stimulus had an increase of 23% in all 3 sets. This subject also detected all 15 auditory complex pairs, with no false alarms. The complex tactile stimulus had an increase of 78% in all sets (14/15 correct, 8 FA). For Subject 3, the complex auditory and tactile stimuli had an increase of 56% (15 correct, 1 FA) and 100% (13/15 correct, 2 FA), respectively. Although all the subjects detected all the 15 complex auditory stimuli, they confirmed that the task was difficult and that they had to pay close attention to detect the complex stimuli. In general, we saw that while the presence of a tactile distractor did not affect performance under the attend-to-auditory condition, an auditory distractor did affect attend-to-tactile performance (the subjects also verbally confirmed this).

2.4. ECoG data acquisition

Continuous ECoG was digitally recorded (Stellate Systems Inc., Montreal, Quebec) with 1000 Hz A/D conversion rate and a bandwidth of 0.1–300 Hz. Tactile and auditory stimulus markers and response markers were recorded simultaneously to marker channels. Subdural

ECoG electrodes consisted of 4-mm diameter platinum–iridium disks embedded in a silastic sheet with 2.36 mm diameter exposed surfaces arranged in rectangular arrays with evenly spaced intervals (1 cm center-to-center). The locations of subdural electrodes with respect to cortical gyral anatomy were determined by computerized co-registration of each subject's pre-implantation volumetric brain MRI with their post-implantation volumetric brain CT (Curry, Herndon, VA).

ECoG was recorded from 89 (Subject 1), 96 (Subject 2) and 83 (Subject 3) electrodes, illustrated in Fig. 2a–c, respectively. Note that some electrodes are not visible in the lateral projection used in the figures.

All ECoG recordings were initially made with a referential montage, in which each subdural electrode was referenced to a single subdural electrode that was selected for its relative inactivity and its relatively remote location in relation to the majority of the electrodes, usually at one corner of an electrode array or at the distal end of an electrode strip. Nevertheless, the proximity of the subdural reference electrode to the recording array made it necessary to remontage ECoG signals to a reference-independent derivation prior to further analyses. The common average reference was used as the best compromise between competing concerns regarding the spatial representation of ECoG power spectra (Crone et al., 2001a; see below for further discussion).

2.5. Data analysis

2.5.1. Preprocessing

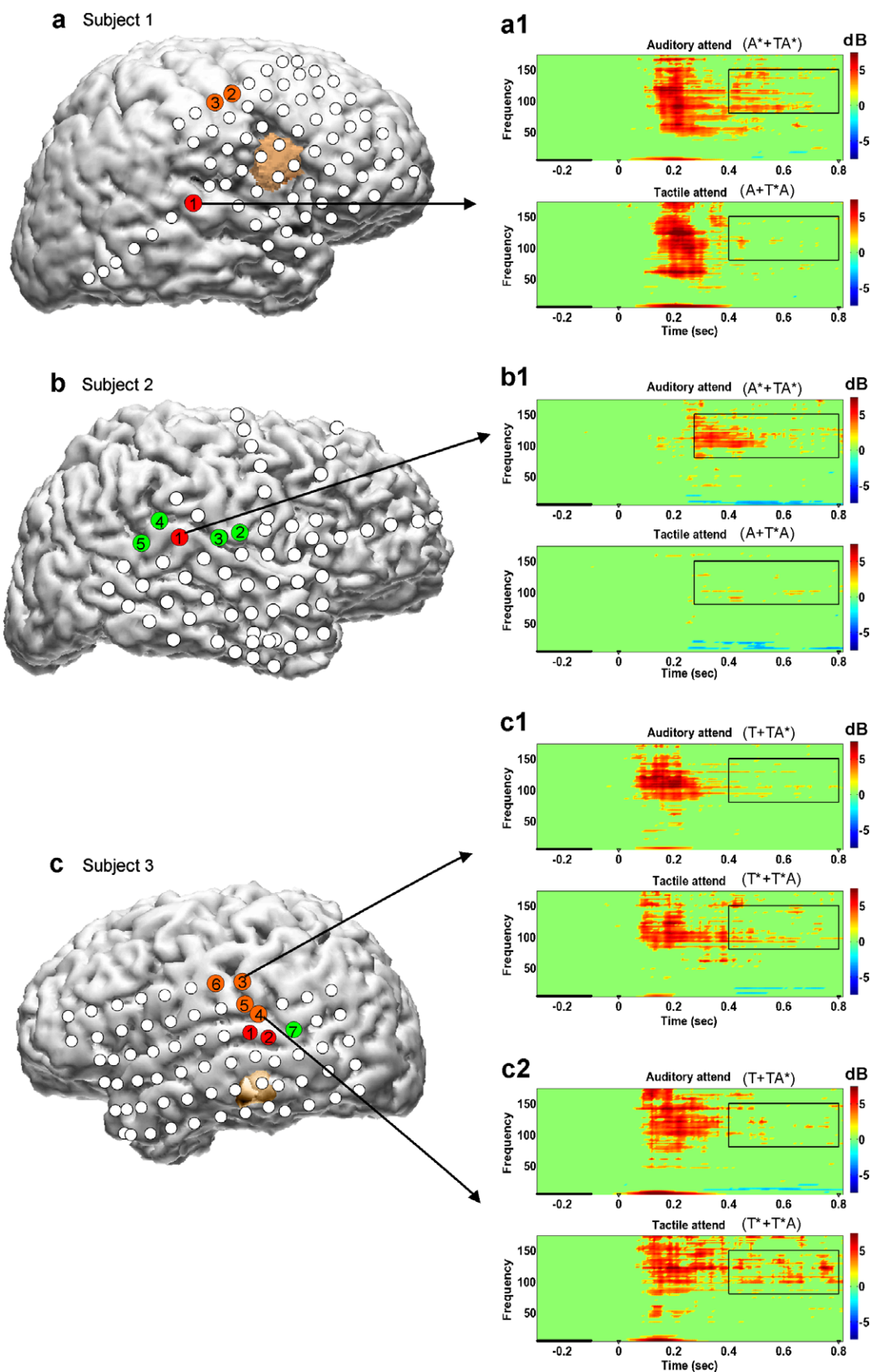
First, channels with excessive artifacts or epileptiform activity were identified by visual inspection of the data traces and excluded from further analysis. The remaining channels were used to compute the common average reference. For Subject 3, a large number of channels were excluded because of irregular spiking activity around a lesion in the left temporal lobe (Fig. 2c). Nonetheless, an additional analysis was performed with inclusion of these channels, and no significant gamma responses were found in any of these channels (they were excluded to prevent contamination of the common average reference). Six stacks of 66 trials each, corresponding to the T*, T, A*, A, TA* and T*A conditions, were obtained for each electrode site. Based on visual inspection of ECoG signals, trials with excessive artifacts were also excluded from further analysis (ca. 20% of trials overall), leaving about 50 trials per stack.

Fig. 2. Subdural electrode coverage and results for select recording sites in 3 subjects. (a–c) The electrode coverage of Subjects 1, 2 and 3. The electrodes over the auditory and somatosensory cortices showing significant gamma activity are shown in red and orange, respectively. Electrodes showing both auditory and tactile induced responses are shown in green and are described in the supplementary section. (a1, b1, c1 and c2) show the change in power (in dB) with respect to power in the baseline (–300 to –100 ms, indicated by a thick black line). The stimulus starts at $t = 0$ and stays on until $t = 800$ ms. Only simple trials (no change in stimulus after 400 ms) were used for analysis. Only the power changes significantly different (t -test, $p < 0.01$, no Bonferroni correction) from baseline are plotted (the rest are set to zero). For clarity, the frequency range of 80 to 150 Hz and the time period of significant differences between the attentional conditions (400–800 ms for Subjects 1 and 3 and 275–800 for Subject 2) are outlined by the rectangular boxes. The brown patches in (a) and (c) show pre-existing lesions in Subjects 1 and 3.

2.5.2. Time-frequency analysis

Time-frequency analysis was performed using the matching pursuit (MP) algorithm (Mallat and Zhang,

1993). This algorithm represents a signal as a sum of Gabor atoms, taken iteratively from a large, overcomplete dictionary (usually Fourier and Dirac atoms are also included).



The algorithm first finds the atom that represents the maximum energy of the signal. Thereafter, the algorithm iteratively finds atoms from the dictionary that represent the maximum energy of the residual (the part of the signal not represented by previously chosen atoms). This algorithm is well suited for EEG or ECoG studies, especially at high frequencies (Ray et al., 2003; Zygierevicz et al., 2005). Further details can be found in the [supplementary section](#) (under the heading ‘Matching Pursuit Algorithm’).

For each signal (taken from -0.623 to 1.424 s, where zero is the time of stimulus onset), we fitted 500 atoms so that high frequency atoms (generally of a much lower energy) could also be selected: typically this number of atoms accounted for more than 99.9% of the signal energy. The time-frequency spectrum was computed by taking the Wigner distribution of the selected atoms (Mallat and Zhang, 1993). This representation is especially useful because it has no cross terms. The power as a function of time and frequency was computed by summing the spectrum on the frequency-axis and the time-axis, respectively. The original MP was performed on a signal of length 2048 samples (-0.623 to 1.424 s at 1 ms resolution), yielding a 2048×2048 array of time-frequency values (with a time resolution of 1 ms and frequency resolution of $500/2048 \sim 0.25$ Hz). This was later down-sampled by a factor of 8 (the mean of every 8×8 pixels was taken to get one time-frequency bin), yielding a time resolution of 8 ms and a frequency resolution of about 2 Hz.

With matching pursuits, line noise is represented by long atoms (spread along the time axis) concentrated around 60 Hz or harmonics of 60 Hz. Such atoms were excluded from analysis to eliminate this artifact. This procedure is more powerful than traditional notch filtering because some of the energy at 60 Hz due to a physiological origin is preserved. For example, a short burst of activity, which MP represents as an atom localized in time but spread in frequency, would not be excluded from the analysis. Longer bursts of activity in the 60 Hz range (of a physiological origin) may, however, get excluded as they are less distinguishable from noise.

A potential drawback of the average reference derivation is that if strong oscillatory activity occurs locally (involving a limited number of electrodes), it could contaminate the signal at all electrode contacts referenced to the average reference. To investigate this possibility, we performed a time-frequency analysis on the average reference signal itself (similar to the analysis performed on other electrodes). We found no significant time-frequency points in the stimulus period compared to baseline in the average reference signal. Furthermore, we restricted our analysis only to electrodes in which the power was significantly greater than the power in the common average reference signal during the period of signal analysis. All electrodes with results reported in this paper met this criterion.

For time-frequency plots of event-related ECoG power changes, baseline power at each frequency point (mean power between -300 and -100 ms) was compared to the

power at each time-frequency point after stimulus onset (t -test, $p = 0.01$, using log power throughout, assuming unequal variances). To increase the clarity of the plots, time-frequency points for which power did not differ significantly from baseline were set to zero. The analyses were first performed without any correction for multiple comparisons because there were no a priori assumptions regarding particular electrode sites, times, or frequencies at which event-related power changes would occur. Although this method did not control for overall type I error, it preserved the nominal statistical power of the individual test results and gave a graphical representation of the significant time-frequency patches. The analyses were then repeated using the false detection rate (FDR) method (Genovese et al., 2002), to account for multiple comparisons.

2.5.3. FDR analysis

The details of this method can be found elsewhere (Genovese et al., 2002). Briefly, this procedure controls the expected proportion of the rejected hypotheses that are falsely rejected. Using the map of p -values of the time-frequency spectrum (obtained using t -tests as described above), the FDR method is used to find an appropriate significance level below which all time-frequency points are considered significant. To use the FDR method on V time-frequency points, the V p -values are first ordered from smallest to largest (denoted by $p_{(i)}$, $i = 1, 2, \dots, V$). The cut-off level is then given by $p_{(r)}$, where r is the largest i such that

$$p_{(i)} \leq \frac{i}{V} \frac{q}{c(V)} \quad (1)$$

where q is the desired FDR (set to 0.05 in this paper) and $c(V)$ is a predetermined constant that depends on assumptions about the joint distribution of the p -values. Two values of $c(V)$ are used: (i) $c(V) = 1$ and (ii) $c(V) = \sum_{i=1}^V 1/i$. The first choice of $c(V)$ holds when the p -values at different time-frequency points are independent and the noise is Gaussian with non-negative correlation between the time-frequency points. The second condition applies for any joint distribution of p -values across the time-frequency space. However, the second condition yields a smaller significance level and hence fewer significant time-frequency points. The results are shown for both conditions.

Comparison of ECoG high-gamma power as a function of time: for comparisons of event-related ECoG power changes under different attentional conditions, a t -test was performed for each individual time value ($p < 0.01$, no correction for multiple comparisons). To test whether the average power over a larger time interval was also significantly different under different attentional conditions, the average power was computed by convolving the raw power with a boxcar window of 50 and 200 ms (and shifted by 8 ms). A t -test was performed on the averaged power (for the different attentional

conditions) and the corresponding p -values were plotted. FDR analysis was then performed to find the significant cut-offs.

3. Results

Subdural ECoG was recorded in three patients using arrays of subdural electrodes positioned over frontal, temporal, and parietal lobes (Fig. 2). The amplitude of ECoG signals was regionally attenuated in and around pre-existing surgical lesions (tumors resected in previous surgeries) in Subjects 1 and 3 (brown patches in Fig. 2a and c). Electrodes showing gamma activity due to auditory stimuli only (marked red in Fig. 2) were located over auditory association cortex in the posterior lateral surface of the superior temporal gyrus, and somatosensory responses (marked orange in Fig. 2) were located over somatosensory cortex (SI or SII) at the frontoparietal junction and parietal operculum. Gamma responses were also observed at some electrodes during both somatosensory and auditory stimuli (marked green in Fig. 2). These electrodes, located near the sylvian fissure and temporal-parietal junction, are described in the [supplementary materials](#). In addition, gamma responses were modulated by attention at electrodes over prefrontal regions in Subject 2 (Fig. 5a and b). We first discuss responses over sensory cortices and then those over frontal cortex.

3.1. High-gamma responses in sensory cortices

In Fig. 2, time-frequency plots of event-related power changes are shown for electrodes over auditory association cortex in Subjects 1 and 2 (numbered 1 in Fig. 2a and b and plotted in Fig. 2a1 and b1, respectively), and for two electrodes over somatosensory cortex in Subject 3 (numbered 3 and 4 in Fig. 2c and plotted in Fig. 2c1 and c2, respectively). In the two electrodes over auditory association cortex, tactile stimuli (T^* and T) induced a very small gamma response following the initial stimulus-related response, which was not statistically different (t -test, $p = 0.01$) between the attended and non-attended conditions ([Supplementary Fig. 1](#)). This allowed us to combine the A^* and TA^* trials and the A and T^*A trials to generate the “Auditory attend” and “Tactile attend” sets of trials, respectively, plotted in Fig. 2a1 and b1 (conditions A^* versus TA^* and A versus T^*A were compared in detail later, see Fig. 9). Similarly, for the electrodes over somatosensory cortex in Subject 3, the responses to auditory stimuli were small and not statistically different (t -test, $p = 0.01$) in the two attentional conditions ([Supplementary Fig. 1](#)). Thus the T and TA^* and the T^* and T^*A trials were combined to generate the “Auditory attend” and “Tactile attend” conditions, respectively, plotted in Fig. 2c1 and c2 (conditions T^* versus T^*A and T versus TA^* were compared in detail later, see Fig. 9). The time frequency plots (Fig. 2a1, b1, c1 and c2) show the change in power (in dB) with respect to the baseline (−300 to −100 ms relative

to stimulus onset, marked by a horizontal black line on the x -axis). For clarity of presentation, only the regions significantly different from baseline are shown (other points are set to zero).

Stimulus presentation resulted in short-latency (150–300 ms following stimulus onset) event-related gamma responses over sensory cortices in all subjects according to stimulus modality. These responses are illustrated in the plots of selected electrodes (Fig. 2a1, c1, and c2). When observed, this early stimulus-related increase in gamma power was not statistically different between the two attentional conditions (t -test, $p = 0.01$). This short-latency response was absent at the electrode site plotted in Fig. 2b1 but was present at nearby electrodes in Subject 2 (like electrode 2 in Fig. 2b, shown in [Supplementary Fig. 3A](#)).

We observed a larger increase in gamma power during the attended condition at longer latencies following the stimulus, i.e. 400–800 ms for Subjects 1 and 3, and 275–800 ms for Subject 2 (denoted by the horizontal dimensions of the black rectangles in Fig. 2a1, b1, c1, and c2) that was largely confined to higher gamma frequencies, i.e. 80–150 Hz (denoted by the vertical dimensions of the aforementioned black rectangles). These results indicate a correlation between high-gamma activity and the attentional requirements of the experimental task (which were maximal about 400 ms after stimulus onset, when stimulus intensity changed in target stimuli). We observed the same phenomenon when, instead of pooling the trials, the trials of types A^* and TA^* were compared to A and T^*A separately ([Supplementary Fig. 1](#)). Trials were pooled to increase the statistical power of the comparison. The black rectangles are shown only for clarity; the differences between the two attended conditions were not restricted to these time-frequency ranges. For statistical comparisons, we compared the entire time period from −300 to 800 ms (Fig. 3, details below) as well as other frequency bands (Figs. 6 and 7, details below).

The time-frequency plots shown in Fig. 2 were used only for a graphical description of the range of high-gamma activity, since the statistics used to construct these plots did not account for multiple statistical tests. [Supplementary Fig. 2](#) shows the same time-frequency plots using FDR analysis (which sets an appropriate significance level to account for multiple comparisons, see Section 2). When $c(V)$ in Eq. (1) was set to 1, the results were very similar to the results shown in Fig. 2. Even for the stricter criterion ($c(V) = \sum_{i=1}^V 1/i$), the results were qualitatively similar, with significant time-frequency patches at longer latencies for the attended condition in all four plots. The table below [Supplementary Fig. 2](#) shows the p -values obtained from the FDR analysis.

Significance analysis shows whether each time-frequency point is different from the baseline period, but this difference is meaningful only when it is consistent for a physiologically sufficient period of time. To compare event-related power changes in the two attentional conditions, we plotted high-gamma ECoG power (80–150 Hz)

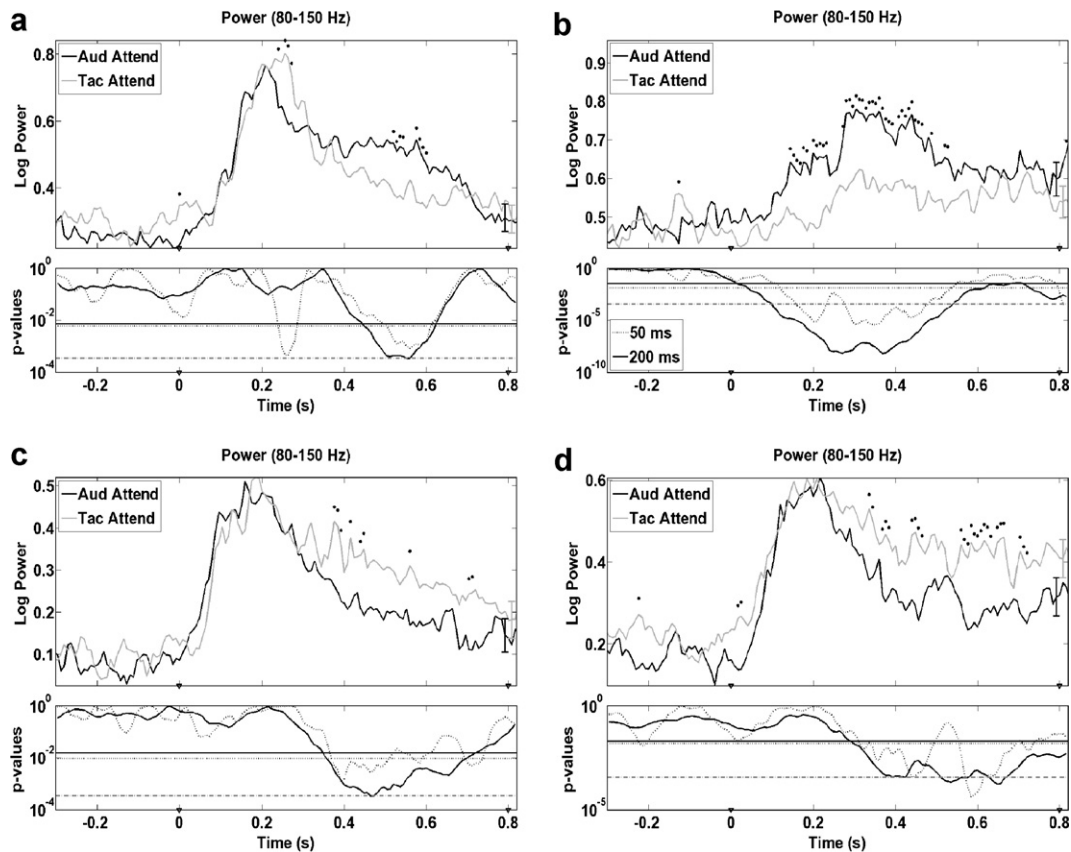


Fig. 3. Comparison of high-gamma (80–150 Hz) power as a function of time. (a–d) Correspond to the time-frequency plots in Fig. 2a1, b1, c1 and c2. The upper panels in each plot show the high-gamma power as a function of time for the two attentional conditions. The maximum standard deviation of the mean is denoted by the error bar at $t = 800$ ms. Time values for which high-gamma power values are significantly different under the two attentional conditions (t -test, $p < 0.01$) are shown by black dots. The lower panels show the p -values (in log scale) computed from a t -test performed on the average power in 50 ms (dotted lines) or 200 ms (solid line) intervals between the two attentional conditions (the average power was computed by convolving the power with a boxcar filter). The significance level obtained from the FDR analysis on these p -values (using $c(V) = 1$) is shown in dotted and solid straight lines, respectively. The significance level after a Bonferroni correction at 0.05 level (at $p = 0.05/140 = 3.57 \times 10^{-4}$) is shown by the broken gray line.

as a function of time (Fig. 3, upper panels in each plot) for the four electrodes plotted in Fig. 2. First, the power in each time bin (8 ms resolution) was compared (t -test, $p = 0.01$) between the attentional conditions (trials pooled as in Fig. 2, plots); the time bins with significantly different power were denoted by black dots. Next, we estimated the average power over a longer interval of time by convolving the power with a boxcar filter, and then compared (using t -tests) the average power between the attention conditions. The lower panels in each plot in Fig. 3 show the p -values (on a log scale) obtained from the t -tests, for a boxcar window of size 50 ms (dotted line) and 200 ms (solid line). The corresponding significance levels obtained from FDR analysis on these p -values are also shown (dotted and solid straight lines, the levels correspond to $c(V) = 1$). For comparison, the significance level from a Bonferroni correction was also shown (broken gray line at $p = 0.05/140 = 3.57 \times 10^{-4}$, since the analysis was performed at 140 time points). The dotted line for the 50 ms window, as expected, captured the local differences in power for the two attentional conditions and was similar to the analysis performed at individual time points

(black dots in the upper panels). The analysis was performed for a 100 ms window as well and the results were intermediate between the 50 and 200 ms windows (not shown).

No significant difference in the two attentional conditions could be observed in the baseline period. Although a few time points appeared to have significant differences with uncorrelated t -tests (Fig. 3, upper panels), there were no differences when multiple comparisons were accounted for with FDR analysis. For the early stimulus-induced gamma activity (150–300 ms), there was a smaller increase in the attended stimulus than during the unattended stimulus in Subject 1 (Fig. 3a), and no difference in Subject 3 (Fig. 3c and d). This was not inconsistent with our hypothesis of a correlation between high-gamma power and selective attention, since the stimulus was expected to change only after 400 ms and thus attention during this time period was not critical for task performance.

We observed a significant increase in gamma power in the attended condition at longer latencies after stimulus onset, i.e., ~ 400 ms, when the subject could expect to detect a change in stimulus intensity. This increase in

gamma power was not related to changes in stimulus intensity because ECoG signal analysis was restricted to the simple trials in which the stimulus intensity did not change throughout the duration of the trial. Thus, modulation of high-gamma power could only be attributed to selective attention. The solid lines in the lower panels (Fig. 3), corresponding to the differences in average power (in 200 ms intervals), showed maximum significance (lowest p -values) between 400 and 600 ms in Subjects 1 and 3 and between 250 and 400 ms in Subject 2. Similar results were obtained from the analysis performed on average power in 50 ms intervals (dotted line in lower panels) or power at individual time points (black dots, upper panels).

The other two electrodes near somatosensory cortices in Subject 3 (numbered 5 and 6 in Fig. 2c) showed very similar results to those plotted in Fig. 2c1 and c2. In both of these electrodes, we observed greater high-gamma responses when attention was directed to the tactile modality; this difference began to be significant 450 ms after stimulus onset (data not shown).

Similar results were obtained from sensorimotor cortex in Subject 1 (electrodes 2 and 3 in Fig. 2a) and auditory association cortex in Subject 3 (electrodes 1 and 2 in Fig. 2c). The results obtained from the electrodes marked 2 and 1 in Fig. 2a and c, respectively, are shown in Fig. 4. The comparison of gamma responses between the two attention conditions (Fig. 4b and d) showed a small but significant effect of attention. The small size of the

effect could have been due to suboptimal electrode placement or due to the effect of a nearby lesion. Nonetheless, we observed a delayed modality-specific increase in high-gamma power in the attended condition, similar to the results obtained from regions well removed from any lesion. Similar results were obtained from the other two channels (numbered 3 and 2 in Fig. 2a and c, respectively), but the gamma power increase associated with attention was not sufficient to be statistically significant (data not shown). Even for the two electrodes shown in Fig. 4, the increase was significant only after pooling the no-overlap and full-overlap trials (e.g., combining T* and T*A for the “Tactile attend” condition and combining T and TA* for the “Auditory attend” condition in Fig. 4a).

Several electrodes close to the sylvian fissure or at the junction between temporal and parietal cortex (shown in green in Fig. 2b and c) recorded significant gamma activity during both auditory and tactile stimuli. The results obtained from these channels were consistent with the results obtained at other electrode sites with only one stimulus modality and are illustrated in detail in Supplementary Fig. 3.

3.2. High-gamma responses in prefrontal cortex

In Subject 2, several electrodes over prefrontal cortex showed significant attention-dependent gamma responses (Fig. 5). In contrast to our results in and around sensory

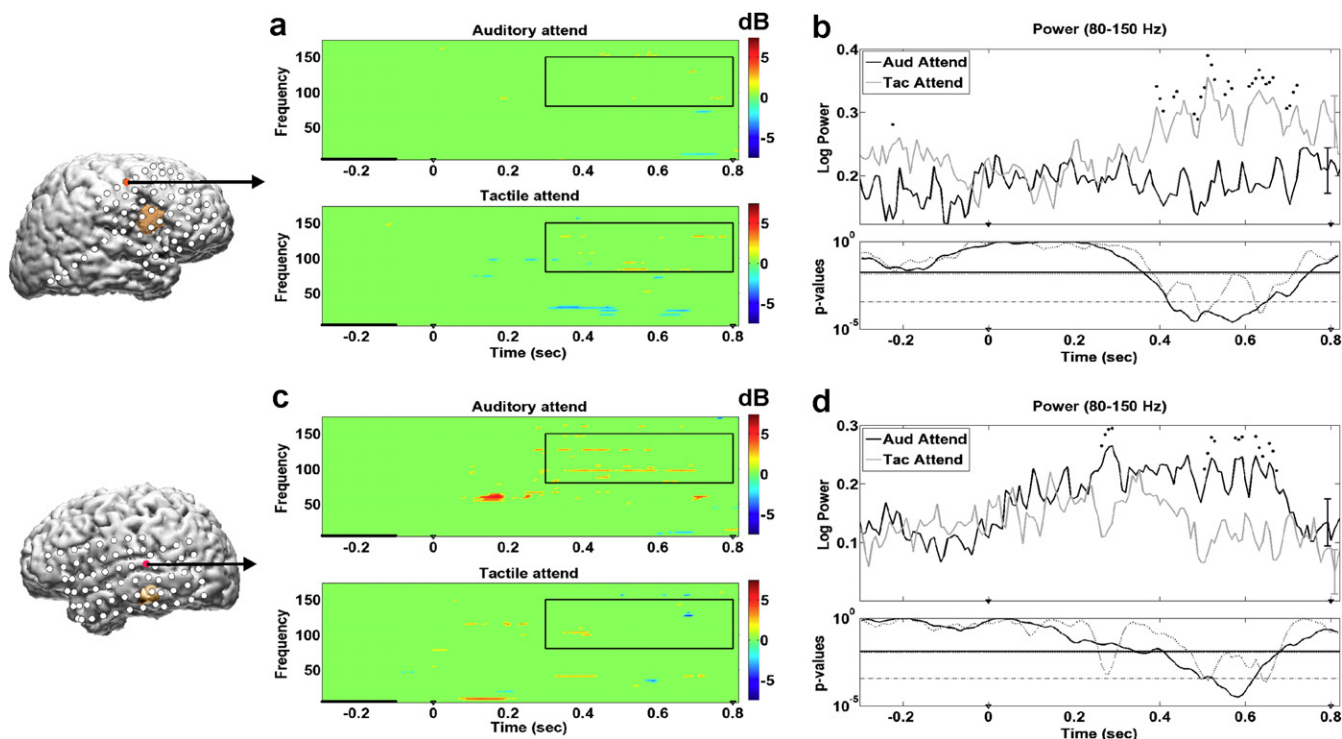


Fig. 4. Time-frequency plots (left column) and plots of high-gamma power (80–150 Hz) vs. time for the lesion-affected regions in Subjects 1 and 3. Top row shows results for an electrode on the somatosensory cortex of Subject 1 (electrode location shown on left, same as the electrode marked 2 in Fig. 2a); bottom row shows results for an electrode on the auditory cortex of Subject 3 (shown on left, same as the electrode marked 1 in Fig. 2c) (same conventions as in Figs. 2 and 3). The rectangular box is from 300 to 800 ms and from 80 to 150 Hz.

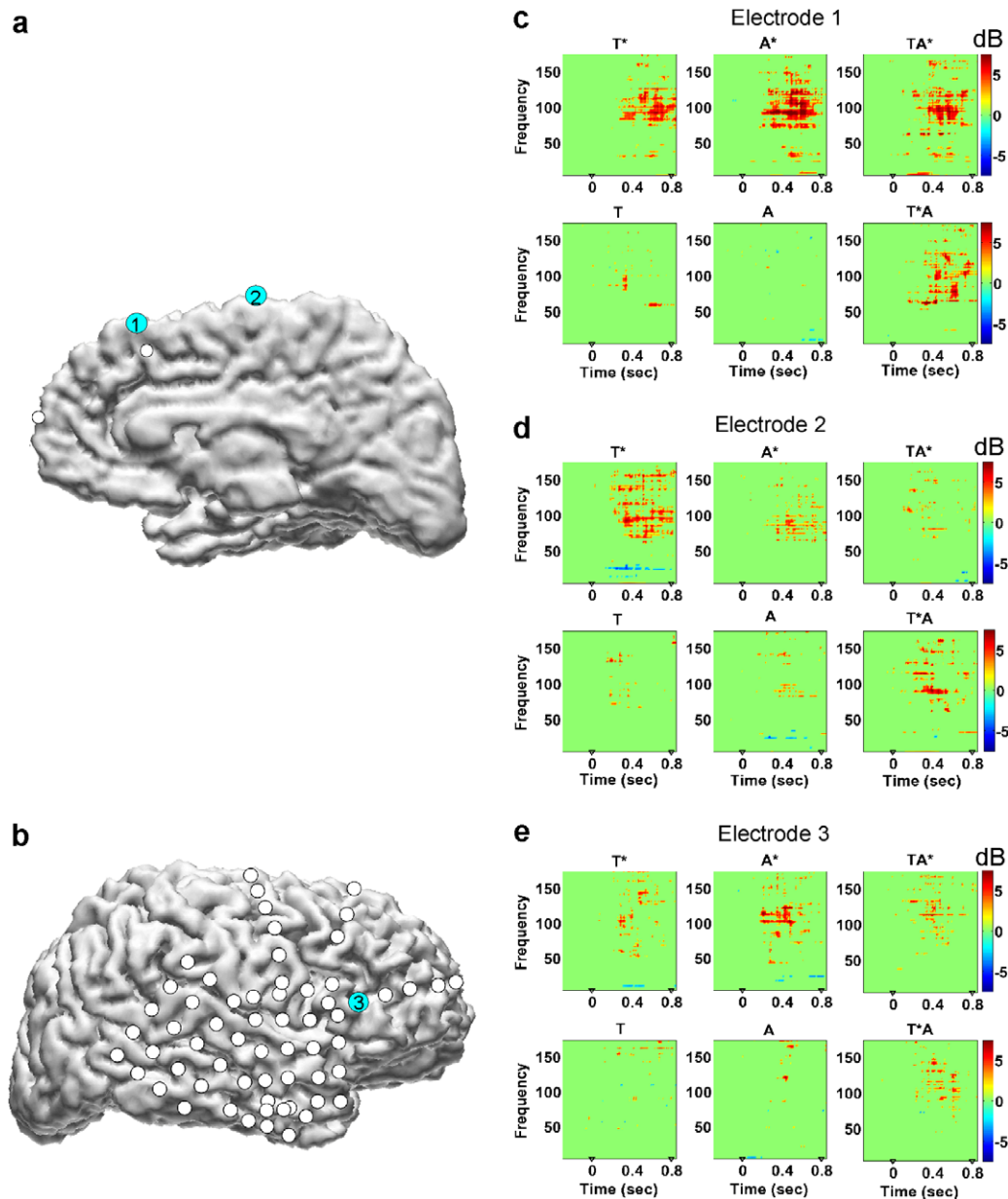


Fig. 5. Time-frequency plots of the six experimental conditions for electrodes over frontal regions in Subject 2. (a) (Medial view of the right hemisphere) and (b) (lateral view of the right hemisphere) show the electrode positions. The spectra shown in (c–e) correspond to the electrodes marked 1, 2 and 3, respectively, in (a) and (b).

cortices, we observed a large increase in gamma power at these prefrontal sites only when a stimulus was presented in the attended modality (for both auditory and tactile stimuli), but gamma responses were absent or insignificant when a stimulus was presented in the unattended modality. We observed this response from midline frontal regions (electrodes 1 and 2 in Fig. 5) and inferior frontal gyrus (electrode 3). These responses were also significant when the analysis of significance was repeated using the FDR criteria (Supplementary Fig. 4). Due to a lack of comprehensive coverage of frontal cortex in our subjects it was difficult to draw conclusions about which frontal regions were consistently involved in attentional modulation. However, visual inspection of the plots in Fig. 5 indicates that

the attention-modulated gamma responses are broadband, with the strongest power modulations in high-gamma frequencies (80–150 Hz), consistent with our findings of attention-modulated gamma activity in sensory cortices.

3.3. Stimulus-induced gamma activity versus attentional modulation of gamma activity

Gamma activity induced by the stimulus at shorter latencies (observed between 100 and 300 ms in some electrodes) was not typically modulated by attention in this experimental paradigm, which allowed us to compare this stimulus-induced activity with the attention-related modulation of gamma activity at longer latencies (>400 ms). For

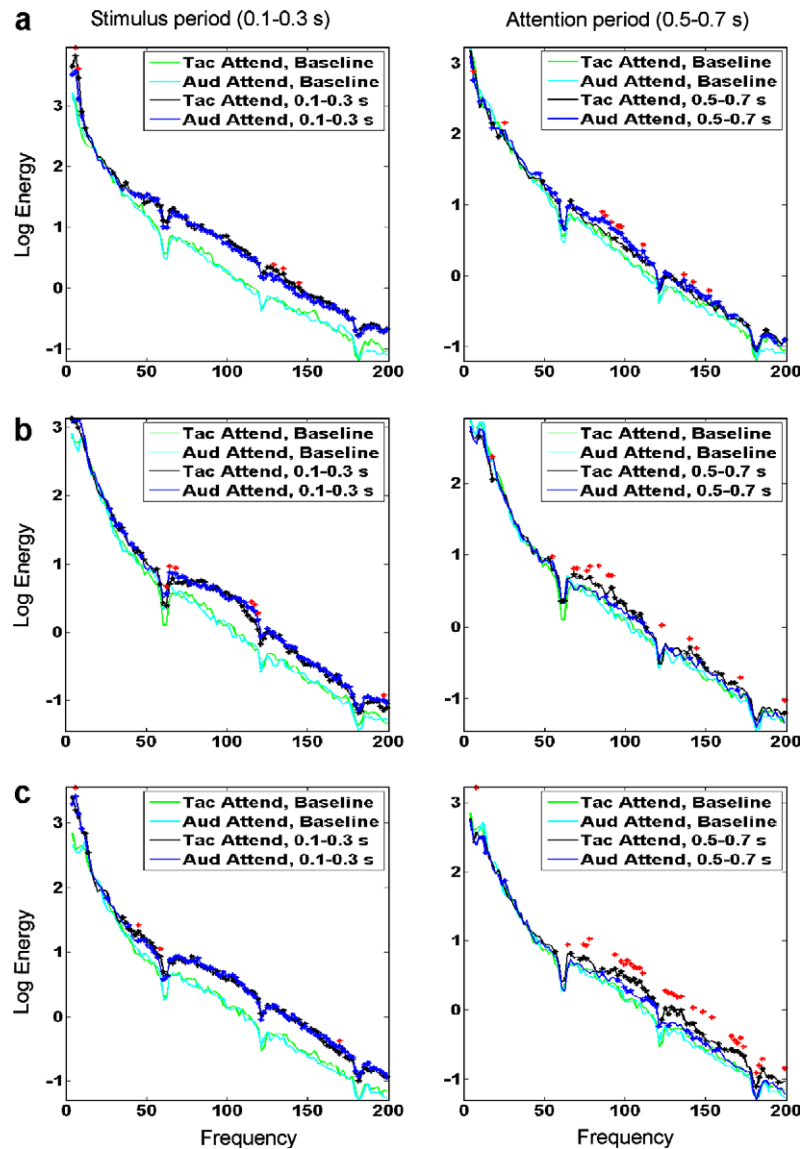


Fig. 6. Comparison between the stimulus-induced and attention-related activity. (a–c) Correspond to the time-frequency plots in Fig. 2a1, c1 and c2, respectively, in which significant stimulus-induced activity was observed. The left column compares ECoG power spectra during the baseline (–300 to –100 ms) with spectra during early post-stimulus latencies (100–300 ms) during which prominent stimulus-induced activity was observed. The right column compares the baseline spectra with the spectra between 500 and 700 ms, during which maximum attention-related modulation was observed. The red asterisks mark the frequency points for which the auditory attend and tactile attend conditions have significantly (t -test, $p < 0.05$) different power.

the electrode sites with prominent stimulus-induced activity (Fig. 2a1, c1 and c2), we compared the power spectra during the baseline (–300 to –100 ms) with the spectrum at short latencies (100–300 ms, Fig. 6, left column) and longer latencies (500–700 ms, Fig. 6, right column) to compare the effect of stimulus vs. attention on the power spectrum, respectively. Electrodes Fig. 6a–c correspond to plots Fig. 2a1, c1 and c2, respectively. For proper comparison of the power spectra under different conditions, the same time interval of 200 ms was chosen for analysis. As shown in Fig. 6, the attention-related changes in the power spectra were slightly different from the stimulus-induced effects. The stimulus-induced gamma activity (left column) was broadband, starting as low as 40 Hz and extending up to

200 Hz and beyond. As expected, the tactile attend and auditory attend conditions were similar, confirming that attention had little effect during this period. In contrast, the attention-related effects were more prominent in the high-frequency range (>60 Hz), with negligible energy differences in the 40–60 Hz range in all the conditions (right column in Fig. 6). The frequency ranges of maximum modulations were 80–100, 60–100 and 80–150 Hz for the three electrodes. The absence of low-gamma activity (40–60 Hz) modulation suggests that low and high-gamma activities may have different functional significance, and while stimulus-induced activity occurred in the entire gamma range, attention specifically modulated higher gamma frequencies. Alternatively, the increase in high-gamma activity at longer

latencies could have been due to an enhanced processing of the stimulus (i.e. an extension of the stimulus-induced gamma activity). This is discussed in more detail in Section 4.

3.4. Comparison with other gamma frequency bands studied in the literature

We compared the frequency band where we typically observed an attentional effect (80–150 Hz) with two other frequency bands that have been previously used to denote gamma activity: 60–95 Hz (Bauer et al., 2006) and 31–60 Hz (Aoki et al., 2001). As can be seen in the plots in Figs. 2 and 6, there is indeed some activity in these lower frequencies (30–80 Hz), although the maximum change typically occurs at higher frequencies. Fig. 7 plots ECoG signal power in the attended and unattended conditions from six electrodes over sensory cortices (four shown in Fig. 2 and two in Fig. 4). We observed a significant increase in power during attention at 60–95 Hz, consistent with previous results (Bauer et al., 2006). However, the difference appeared to be greater, with more statistically significant time points, in the 80–150 Hz frequency range. The results

did not depend on the specific choice of frequency band. For example, we performed this analysis on different sets of frequencies (40–60 and 60–80 Hz) and obtained results that were very similar to those for 31–60 and 60–95 Hz (data not shown).

We also compared two other frequency bands – alpha (8–12 Hz) and beta (16–24 Hz) – across the two attentional conditions at all electrode sites. Even though there was a decrease in power (desynchronization) after stimulus onset in several channels, the decrease was not significantly different in the two attentional conditions (t -test, $p = 0.01$).

3.5. Comparison of no overlap versus full overlap conditions

Although the analysis was performed only on electrodes that showed no cross-modal activation, it is possible that the full overlap conditions (T*A and TA*) demanded a more acute selective attention and had a different time course of cortical activation than the conditions with only one stimulus. To test this possibility, we compared the time course of high-gamma activation for A* versus TA* conditions and A versus T*A conditions for Subjects 1 and 2 (these correspond to the components of the ‘Auditory

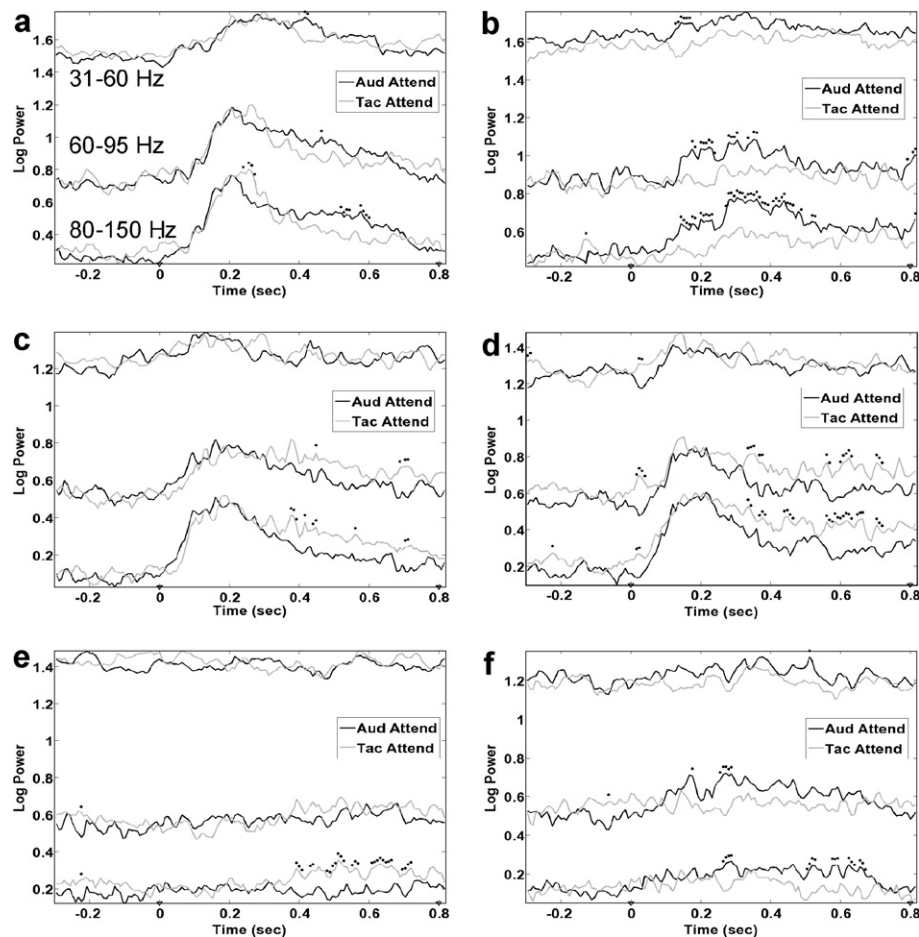


Fig. 7. Comparison of ECoG power under two attentional conditions in three different frequency bands – 31–60 Hz (top trace in each figure), 60–95 Hz (middle trace) and 80–150 Hz (bottom trace). (a–d) Correspond to Fig. 3a–d while (e and f) correspond to Fig. 4b and d, respectively (same conventions as in Fig. 3).

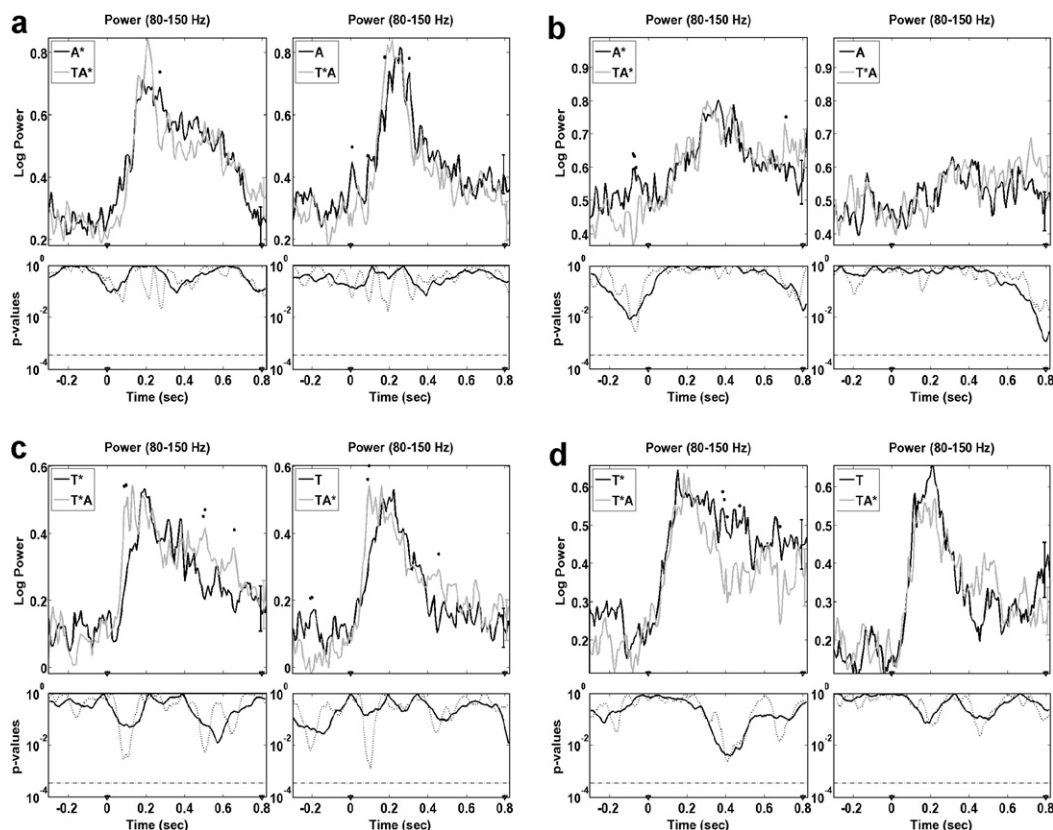


Fig. 8. Comparison of full overlap versus no overlap conditions. (a–d) Correspond to the time-frequency plots in Fig. 2a1, b1, c1 and c2 (same conventions as in Fig. 3). FDR analysis did not show any significant differences between the no overlap and full overlap conditions and hence the significance levels (dotted and solid straight lines in the lower panels in Fig. 3) are not shown.

attend' and 'Tactile attend' conditions, respectively). Similarly, we compared T versus TA* and T* versus T*A conditions for Subject 3. The results are shown in the upper panels of Fig. 8. The lower panels show the *p*-values (similar to Fig. 3). No significant differences were obtained from the FDR analysis (hence no significance levels are shown in the lower panels). This lack of significant differences between the no overlap and full overlap conditions further justified the pooling of these conditions for the analysis shown in Fig. 2.

Finally, we compared event-related ECoG spectral changes with event-related potentials (ERPs) recorded from the same subdural electrodes. ERPs recorded at the sites illustrated in Fig. 2 are shown in Fig. 9. The ERPs were significantly different from baseline only at shorter latencies (<300 ms) and had response contingencies similar to the stimulus-induced gamma activity. Subject 1 (Fig. 9a) showed a decrease in amplitude of the main negative deflection of the ERP at ~200 ms during attention, consistent with the smaller increase in gamma power observed between 200 and 300 ms (Fig. 3a). In Subject 2 (Fig. 9b) only a weak evoked response was observed at a site where stimulus-induced gamma activity was relatively small (Fig. 3b). Subject 3 (Fig. 9c and d) showed very small differences in the ERP between attention conditions and had no significant difference in gamma activity at similar latencies

(see Fig. 3c and d). In summary, event-related potentials were present only at short latencies and were only weakly modulated by attention. These findings support the notion that our experimental task did not critically depend on attention at shorter post-stimulus latencies (before 400 ms), and are consistent with the findings of our spectral analyses, i.e. that early stimulus-related gamma activity was not significantly modulated by attention.

4. Discussion

We found that significant modulations of gamma activity (60–150 Hz) were correlated with the attentional state of our human subjects. In addition to early stimulus-related gamma responses that were localized in modality specific sensory cortices but not modulated by attention, gamma responses occurring in the same cortical regions at longer latencies were enhanced when the respective stimuli were attended. These responses could not be attributed solely to sensory stimulation since they were observed 300 to 800 ms after stimulus onset, beyond the typical duration of stimulus-induced gamma oscillations and at a time when maximal attention was required by the task. Likewise, these responses could not be attributed to the change in stimulus intensity that occurred at 400 ms in target stimuli because signal analyses were performed only on the simple

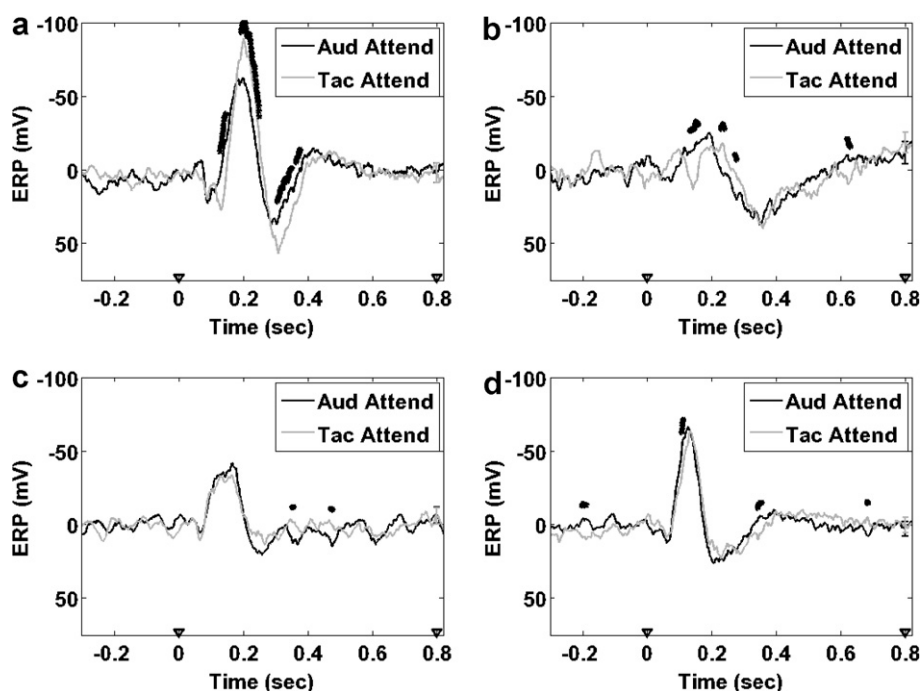


Fig. 9. Event-related potentials: the event-related potentials for the four electrodes with time-frequency plots shown in Fig. 2. (a–d) Correspond to Fig. 2a1, b1, c1 and c2, respectively. The black asterisks show the time values at which the event-related potentials for the two attention conditions are significantly different (t -test, $p < 0.05$).

stimuli (~80%, i.e. non-targets), in which there was no change in stimulus intensity. Apart from these responses in sensory cortices, gamma-frequency responses were also observed in frontal regions, but only when a stimulus appeared in the attended modality. While the stimulus-induced gamma modulation was broadband (40–200 Hz), the increase in power modulated by attention appeared to be restricted to higher frequencies (>60 Hz) with the maximal modulation in a high frequency gamma range (80–150 Hz).

Our results are generally consistent with previous scalp EEG studies of gamma activity. These studies have shown a correlation between gamma-range activity and attentive processing in all non-chemical senses, including vision (Gruber et al., 1999), audition (Galambos et al., 1981; Tiitinen et al., 1993; Debener et al., 2003) and somatic sensation (Desmedt and Tomberg, 1994). However, scalp EEG studies have typically focused on gamma activity in lower frequencies (<50 Hz). Signal changes in higher gamma frequencies are difficult, if not impossible, to observe in scalp EEG recordings (Pfurtscheller and Cooper, 1975). Although such frequencies are accessible in microelectrode recordings of local field potentials in animals, the small change in signal energy observed at high-gamma frequencies in ECoG is likely to occur at the network level and might be overlooked at such a fine resolution. For example, the behavior of local field potentials may be influenced by the firing rate of a small population of neurons rather than a change in synchronization within this population that occurs during attention (Steinmetz et al., 2000). Although the spatial

resolution of subdural ECoG is not sufficient to directly measure synchronization between single neurons, the increases in ECoG gamma power observed herein with macroelectrodes are presumed to require the synchronization of dendritic potentials in a relatively large population of cortical neurons. ECoG could therefore be useful for studying network activity during selective attention.

Subdural ECoG recordings offer a spatial resolution that is intermediate between scalp EEG and local field potential recordings and are thus well suited to study gamma activity at the level of cortical networks. Indeed, subdural ECoG recordings have demonstrated event-related gamma activity in topographic and temporal patterns that are consistent with the functional anatomy and processing dynamics of sensorimotor, auditory, visual, and language function (Crone et al., 2006), oculomotor function (Lachaux et al., 2006) and memory (Fell et al., 2001; Howard et al., 2005; Sederberg et al., 2003; Mainy et al., 2007). From the perspective of ECoG, this gamma response is not limited to a single gamma band, e.g. the traditional 40-Hz band, but consists of a broadband response with variable lower and upper frequency limits, often extending as low as 30 Hz and as high as 200 Hz, but appearing most robust in the middle of this range (Crone et al., 2006). Similar broadband gamma responses have been reported in animals, including primate auditory cortex during tones (Brosch et al., 2002) and cat visual cortex during saccades (Buser and Rougeul-Buser, 2005).

Recently, ECoG studies of attention in humans have been reported in which electrodes are positioned over premotor or visual areas. Brovelli et al. (2005) reported

high-gamma activity (60–200 Hz) reflecting attentional/mnemonic processes in premotor cortex and suggested that this high-gamma activity dissociates attention from intention in premotor cortex. Although their main focus was on this dissociation and colocalization with their previous fMRI results, it is interesting that between 200 and 450 ms after stimulus onset, they found high frequency (60–200 Hz) gamma activity similar to the early latency stimulus-induced gamma responses we observed. In another study, Tallon-Baudry et al. (2005) compared gamma band activity during visual object processing under attended vs. unattended conditions in two visual areas known to play a role in visual object processing: lateral occipital cortex and fusiform gyrus. This study showed an increase in baseline gamma activity in lateral occipital cortex with attention but a subsequent decrease upon stimulus presentation, while there was an increase in stimulus-induced gamma oscillations with attention in fusiform gyrus. The reported responses occurred between 30 and 130 Hz, which overlaps the frequency range of the gamma responses we observed. However, this study did not report a significantly larger power increase in high-gamma frequencies than in lower gamma frequencies under attended conditions. Similarly, MEG studies have also shown event-related power increases in high-gamma frequencies during attention, but the most sensitive frequency range was reported to be 60–90 Hz (Bauer et al., 2006). MEG may be less sensitive to higher frequency activity than subdural ECoG due to the greater distance between its sensors and the cortical sources of activation.

Previous studies have demonstrated a number of effects from anticipation or expectancy in the pre-stimulus period: an increase in gamma frequency power (Gonzalez Andino et al., 2005), increase in synchronization (de Oliveira et al., 1997), increase in single unit firing rates (Luck et al., 1997) and an increase in the BOLD response (Kastner et al., 1999). In those studies, attention was required at the onset of a stimulus. In contrast, our experimental task did not critically require attention to the stimulus until 400 ms after stimulus onset. Similarly, Fries et al. (2001) computed spike-LFP synchronization from V4 during a task that required monkeys to detect a change in stimulus color at a random time after stimulus onset (500–5000 ms). They showed for the attended condition an increase in the firing rate after 450 ms of stimulus presentation, but an increase in synchronization that started even before the onset of the stimulus and continued until the color changed. In our study, we did not find statistically significant differences between the two attention conditions in gamma power before the anticipated change in stimulus intensity, either during baseline or during early post-stimulus (100–300 ms) time periods. This can be seen in the power versus time plots in Figs. 3, 4 and 7, where the high-gamma power in the baseline and early post-stimulus period was generally not statistically different for the tactile attend and auditory attend conditions. Our task required the subject to attend continuously to one of the two modalities, so some effect

of attention in this period was indeed expected. A potential explanation is that our human subjects learned to focus their attention after stimulus onset. Humans have been shown to be capable of quickly switching the locus of attention in time (the flexible-selection hypothesis, see Vogel et al., 2005 and references therein). This interpretation is supported by the lack of significant differences between the two attention conditions in the event-related potentials and early post-stimulus high-gamma responses recorded in our subjects. The absence of a statistically significant difference in high-gamma power during the baseline and early post-stimulus period does not affect the main results of the study, and further allows us to examine stimulus-induced vs. attention-related gamma power modulations.

Although our experiment was designed to temporally dissociate stimulus-induced gamma activity and attention-related gamma activity, it is possible that what appeared to be attention-related gamma was due to enhanced stimulus processing in the attended modality. In this case, high-gamma activity would only be a reflection of sensory processing, and enhanced gamma responses at longer latencies in the attended condition would be due to an increase in the duration of this processing. The long lasting sustained gamma activity might also reflect a comparison process of the current stimulus input with some internal representation of the target stimulus. Further studies would be needed to test this hypothesis. Nevertheless, as mentioned above, high-gamma responses have been observed in several studies due to anticipation/expectancy (Brovelli et al., 2005), suggesting that these responses are not limited to stimulus processing. Furthermore, in the present study the high-gamma responses observed in pre-frontal cortex occurred only at longer latencies (i.e. 500–700 ms, without any stimulus-related activity).

Since subjects had to continually attend to one of the two modalities (and the target appeared rarely), the degree of attention required during the task may be less than that during a task that requires focused attention for a shorter duration. For example, the effect of attention may be much larger for stimuli following a complex stimulus, since the subjects had to respond if the next trial was complex as well. We did not have enough trials to test this hypothesis (further, the responses during these trials could also have been affected by stimulus/memory/motor preparation effects). Nonetheless, a consistent increase in high-gamma activity with attention in an experimental paradigm where the attentional requirement is not maximal strengthens our conclusion that high-gamma activity is highly correlated with selective attention.

A potential limitation of our experimental design was that the subjects were only required to respond to a small subset of stimuli. Although measures were taken to select perceptual thresholds in the target (complex) stimuli that required the subjects to pay attention to the task (see Section 2.3), the limited behavioral response did not allow us to verify attention to all the stimuli. Nevertheless, the

positive results shown herein are difficult to explain otherwise. A pop-out effect (in which the target stimulus attracts attention and the subject simply waits for it to appear in the cued modality) is an unlikely explanation because the analysis was performed only for responses to simple stimuli that had no physical change in intensity. Similarly, a change in high-gamma power due to a change in stimulus grip or a change in the mental state of the subject (due to fatigue, effects of medicines, etc.) can be largely ruled out because the baseline power for the two attentional condition remained the same; only the relative change with respect to the baseline was used for analysis. In our experimental paradigm it was not possible to control the exact time at which attention was oriented towards the stimulus: we could only ensure that significant attention was required at ~400 ms after stimulus onset. Thus, difference in power (between the two attentional conditions) during the baseline period and during early post-stimulus latencies were also possible outcomes of this experiment. This would have been consistent with persistent attention on the attended modality or attentional orientation immediately after stimulus onset, respectively. As mentioned above, the results shown in the paper (power difference only after ~400 ms) can be explained by attentional orientation after ~400 ms of stimulus onset, which is consistent with the flexible selection hypothesis (Vogel et al., 2005) and is further substantiated by the event-related potential analysis.

Since the grip force of the subject on the stimulator was not quantitatively monitored, it may be possible that the subjects changed their grip after 300–400 ms in expectation of a possible change in the stimulus intensity. Although this possibility cannot be completely ruled out, it is unlikely to explain the results obtained in this paper. First, all the subjects were specifically instructed not to change their grip force and no obvious twitch in the hand was observed during the presentation of the tactile stimulus (the experimenters continuously monitored patient behavior during the experiment either directly or through a video surveillance camera). Furthermore, for Subjects 1 and 2, the attention effect was demonstrated with auditory stimuli (A^* vs A), since the tactile stimulus produced almost no activity in these electrodes. An analysis of ‘stimulus-induced’ vs. ‘attention-related’ gamma activity (Fig. 6) showed that even for Subject 3, the increase in high-gamma activity during the attention period was similar to Subject 1, suggesting a common attention-related mechanism.

It is not surprising that different electrodes in our study showed somewhat different behavior. For example, one electrode over auditory association cortex in Subject 2 had no early latency stimulus-induced gamma response but did have an attentionally modulated gamma response at longer latencies. The inter-electrode spacing of the subdural array was at least 1 cm for all subjects, and clinical circumstances did not allow for comprehensive sampling of homologous cortical regions across subjects.

Even though the coverage of prefrontal regions was limited, our results (Fig. 5) were consistent with the existing literature on the role of prefrontal cortex in attention. Anterior cingulate cortex, midline frontal cortex, and dorsolateral prefrontal cortex form the ‘anterior attention system’, known to be particularly involved in target detection (Posner and Peterson, 1990). This agrees with the results shown in Fig. 5, where we observed an increase in gamma activity when subjects were trying to detect a change in stimulus intensity.

Our results also support the hypothesis that a stimulus that is consciously perceived and processed is associated with activation of widespread cortical areas (manifesting as oscillations in the gamma band). Synchronization of gamma oscillations in distributed neural networks has been proposed to play an important role in conscious perception (Singer and Gray, 1995; Rodriguez et al., 1999; Varela et al., 2001; Meador et al., 2002). Theoretical work suggesting a role for neuronal synchronization in selective attention (Niebur et al., 1993; Niebur and Koch, 1994; Engel et al., 2001; Tiesinga and Sejnowski, 2004) has been supported by micro-electrode recordings in awake behaving primates that have demonstrated an increase in oscillatory neuronal activity when a stimulus is attended (Steinmetz et al., 2000; Fries et al., 2001). Although synchronization of individual neurons could not be measured with the ECoG macroelectrodes that were implanted for clinical purposes in our human subjects, the increases in ECoG gamma activity reported herein likely required the synchronization of membrane potentials in a significant proportion of the cortical neuronal populations that were recorded. Future studies with multiple micro- and macro-electrodes will be necessary to further characterize the relationship between neuronal synchronization and the high-gamma activity reported here and in previous ECoG studies (Crone et al., 2006).

Our results in the present study demonstrate for the first time a consistent, modality-specific augmentation of high-gamma (>60 Hz) activity in human somatosensory and auditory cortices during selective attention. This augmentation was also observed in frontal areas known to participate in attentional processing. The increase in gamma activity could not be attributed to stimulus onset or changes in stimulus intensity but appeared to depend only upon the attentional condition of the experimental task. The high-gamma activity associated with attention was observed between 60 and 150 Hz, with the greatest augmentation of signal energy occurring at 80–150 Hz. This frequency range was slightly different from stimulus-induced gamma modulations, which were also significant in low gamma frequencies (40–60 Hz). Previous studies with ECoG in humans have indicated that high-gamma activity is an electrophysiological signature of cortical activation that is useful for human brain mapping in a variety of functional-anatomic domains (Crone et al., 2006, and references therein). Our findings in this study indicate that selective attention to a sensory

stimulus is associated with activation of a cortical network that includes sensory cortex and frontal regions known to play a role in the regulation of attention. In this context, it appears that high-gamma activity can also serve as an electrophysiological signature of selective attention in humans.

Acknowledgements

This work was supported by NIH Grants R01-NS40596 (N.E.C., E.N.), NS43188-01A1 (E.N., S.S.H.), 5R01EY016281-02 (E.N.) and NS34086 (S.S.H.). We thank L. Gintis for 3-D image reconstruction, P. J. Franaszczuk for assistance with the MP algorithm and K.O. Johnson and T. Yoshioka for assistance in stimulus design. We also thank the patients for participating in the study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.clinph.2007.09.136](https://doi.org/10.1016/j.clinph.2007.09.136).

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