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Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis
II. Event-related synchronization in the gamma band

Nathan E. Crone,[1] Diana L. Miglioretti,[3] Barry Gordon[1,4,5] and Ronald P. Lesser[1,2,5]

Departments of [1]Neurology and [2]Neurosurgery, The Johns Hopkins University School of Medicine, and the Departments of [3]Biostatistics and [4]Cognitive Science, and [5]Zanvyl Krieger Mind/Brain Institute, The Johns Hopkins University, Baltimore, Maryland, USA

Correspondence to: Dr Nathan Crone, Department of Neurology, The Johns Hopkins Hospital, Meyer 2–147, 600 N. Wolfe St, Baltimore, MD 21287, USA.
E-mail: ncrone@jhmi.edu

Summary
It has been shown in animals that neuronal activity in the 'gamma band' (>30 Hz) is associated with cortical activation and may play a role in multi-regional and multi-modal integration of cortical processing. Studies of gamma activity in human scalp EEG have typically focused on event-related synchronization (ERS) in the 40 Hz band. To assess further the gamma band ERS further, as an index of cortical activation and as a tool for human functional brain mapping, we recorded subdural electrocorticographic (ECoG) signals in five clinical subjects while they performed visual–motor decision tasks designed to activate the representations of different body parts in sensorimotor cortex. ECoG spectral analysis utilized a mixed-effects analysis of variance model in which within-trial temporal dependencies were accounted for. Taking an exploratory approach, we studied gamma ERS in 10-Hz-wide bands (overlapping by 5 Hz) ranging from 30 to 100 Hz, and compared these findings with changes in the alpha (8–13 Hz) and beta (15–25 Hz) bands. Gamma ERS (observed in three out of subjects) occurred in two broad bands—'low gamma' included the 35–45 and 40–50 Hz bands, and 'high gamma' the 75–85, 80–90, 85–95 and 90–100 Hz bands. The temporal and spatial characteristics of low and high gamma ERS were distinct, suggesting relatively independent neurophysiological mechanisms. Low gamma ERS often began after onset of the motor response and was sustained through much of it, in parallel with event-related desynchronization (ERD) in the alpha band. High gamma ERS often began during, or slightly before, the motor response and was transient, ending well before completion of the motor response. These temporal differences in low and high gamma suggest different functional associations with motor performance. Compared with alpha and beta ERD, the topographical patterns of low and high gamma ERS were more discrete and somatotopically specific and only occurred over contralateral sensorimotor cortex during unilateral limb movements (alpha and beta ERD were also observed ipsilaterally). Maps of sensorimotor function inferred from gamma ERS were consistent with maps generated by cortical electrical stimulation for clinical purposes. In addition, different task conditions in one subject produced consistent differences in both motor response latencies and onset latency of gamma ERS, particularly high gamma ERS. Compared with alpha and beta ERD, the topography of gamma ERS is more consistent with traditional maps of sensorimotor functional anatomy. In addition, gamma ERS may provide complementary information about cortical neurophysiology that is useful for mapping brain function in humans.

Keywords: event-related synchronization; gamma band; electrocorticography; sensorimotor cortex; brain mapping

Abbreviations: ECoG = electrocorticography; ERD = event-related desynchronization; ERS = event-related synchronization; MEG = magnetoencephalography

Introduction
Frequency analysis of the human EEG has, until recently, focused on changes in the lower frequency ranges, especially in the alpha band (8–13 Hz) (Berger, 1930; Pfurtscheller and Aranibar, 1977) and the beta band (15–25 Hz) (Jasper and Andrews, 1938; Pfurtscheller, 1981). Event-related suppression of spectral power in these bands has come to be known as event-related desynchronization (ERD) and has been shown to be associated with cortical activation

(Pfurtscheller and Aranibar, 1977; Pfurtscheller, 1981). However, changes in higher frequencies, collectively known as the 'gamma band' (>30 Hz), have also been associated with cortical activation (Spydell *et al*., 1979; Pfurtscheller *et al*., 1993), with special attention being paid to changes in the 40 Hz band. These changes have typically consisted of an *increase*, or augmentation, of spectral power, which has been called event-related synchronization (ERS). Moreover, experiments in animals have suggested that neuronal activity in the gamma frequency range may play an important role in the neurophysiological mechanisms of both basic and complex functions of cerebral cortex (Gray *et al*., 1989; Singer, 1993; Basar-Eroglu *et al*., 1996).

We investigated gamma band activity in sensorimotor cortex using a method for functional brain mapping in humans, namely electrocorticographic (ECoG) spectral analysis, in which enhancements of the basic strategy of Pfurtscheller *et al*. (1993) are applied to ECoG signals recorded from the surface of the brain. Because the gamma band includes all frequencies >30 Hz, and because different frequency bands within this range have been studied by other investigators, we decided to pursue an exploratory approach, eschewing any assumptions about the frequencies most likely to bear fruit. We therefore analysed a series of 10-Hz-wide bands, overlapping by 5 Hz and ranging from 25 to 100 Hz, in order to determine which frequencies might yield the most useful indices of cortical activation. The details of our results using ECoG spectral analysis in the alpha (8–13.7 Hz) and beta (15–25 and 20–30 Hz) bands are presented in a companion paper (Crone *et al*., 1998).

For the purposes of recording high-frequency EEG activity, scalp-recorded EEGs have several technical limitations that are overcome by ECoG recordings from the surface of the brain. The scalp, skull and dura mater cause spatial blurring of cortically generated signals (Gevins *et al*., 1994) and also act to filter out high-frequency EEG activity (Pfurtscheller and Cooper, 1975). Scalp EEG is also plagued by noise from the membrane potentials of scalp muscles, whose frequency spectrum overlaps that of EEG gamma band activity. However, ECoG recordings are restricted to unique clinical situations in which patients require the implantation of subdural electrodes. These electrodes are necessary for functional mapping and/or seizure localization (Lesser *et al*., 1987) prior to surgical treatment of epilepsy or brain lesions near functionally important cortical regions. They also allow ECoG signals to be recorded while patients are awake and able to cooperate with experimental tasks, without exposing them to any risks beyond those already assumed for strictly clinical purposes. This paper describes, in detail, the results of recording gamma band activity in the sensorimotor cortex of five clinical subjects, one of whom is our major focus because he had the most comprehensive coverage of sensorimotor cortex by implanted subdural electrodes.

Because the clinical situations of our subjects required functional mapping in preparation for surgical resection, we were able to study the ability of gamma ERS to map cortical function by comparing it with that of a more established functional mapping technique: cortical electrical stimulation mapping. Expectations about functional neuroanatomy are most often derived from the literature and are for the most part based upon other individuals or groups, using different methods under different conditions. This literature-based knowledge does not typically take into account the individual variability of functional–anatomical organization. By providing information about the functional anatomy of the sensorimotor system in each of our subjects, cortical-stimulation mapping improved our ability to localize the cortical representations of different body parts. Because the seizure focus in one of our subjects could not be sufficiently defined with his first subdural electrode implantation, a second implantation was performed 6 months later. This unusual clinical situation allowed us to test the reproducibility of gamma ERS and the functional maps generated by cortical electrical stimulation mapping.

Methods

Subjects and clinical procedures

In a companion paper (Crone *et al*., 1998) we have provided details about the clinical characteristics of our subjects, the anatomical placement of their subdural electrodes and the procedures used for cortical electrical stimulation mapping. All subjects agreed to participate in this research study and gave their informed consent according to a protocol approved by the Joint Committee on Clinical Investigation of The Johns Hopkins Medical Institutions, in compliance with standards of the Declaration of Helsinki. Note that the clinical circumstances of Subject 1 required subdural grid implantation on two separate occasions (1A and B), and electrical stimulation mapping and ECoG were performed on both occasions.

Experimental procedures

A visual–motor decision task was designed to investigate the somatotopic distribution of cortical responses during sensorimotor performance. Details regarding our testing apparatus, as well as the rationale and procedures of this task are presented in a companion paper (Crone *et al*., 1998). In brief, we asked each subject to make a sustained voluntary muscle contraction in one of several body parts (tongue protrusion, eye-winking, fist-clenching or foot dorsiflexion) in response to a picture stimulus depicting one of these movements. Each of the pictured body parts was presented on a video monitor in a random sequence. The subject was instructed to begin the action depicted as quickly as possible and to sustain the muscle contraction until the visual stimulus disappeared—a fixed interval of 3 s after it appeared. When the visual stimulus disappeared, the subject relaxed and waited for the next stimulus (⩾3.8 s later) while maintaining gaze fixation on a black dot in the centre of the video screen.

Although tongue protrusion was always in the midline and involved bilateral tongue muscles, in all subjects the visual–motor decision task was performed separately for limb movements on the right (e.g. tongue, right face, right arm and right leg) and on the left (e.g. tongue, left face, left arm and left leg) sides. In Subject 4 all four body parts (25 trials for each body part and 100 trials in total) were tested on the right side only (contralateral to the grid). In two of the three subjects in whom ECoG electrodes were unilateral (1 and 5), both sides of the body were tested in order to study cortical activation associated with ipsilateral limb movements. In Subject 5 all four body parts were tested on both sides (25 trials for each body part on each side, 100 trials on each side and 200 trials in total). In order to maximize the number of trials recorded without exhausting the subject, three subjects (1A, 2 and 3) were presented with only the tongue and hand stimuli (50 trials for each body part on each side, 100 trials on each side and 200 trials in total), and one subject (1B, second implantation) was presented with only the tongue, arm and leg stimuli (50 trials for each body part on each side, 150 trials on each side and 300 trials in total).

A simple visual–motor task was also used in one of our subjects (1B) to investigate the effect of the decision component of our visual–motor decision task on somatotopic patterns of cortical activation. In this task our subject was tested with a series of 50 stimulus–response trials using only one body part. Instead of asking the subject to decide which body part to move in response to a randomized visual stimulus, the subject was asked to make the same movement for every trial, in response to a visual stimulus which was identical in every trial. This task condition, referred to as the simple condition, is contrasted in this paper with the decision condition described above.

ECoG spectral analysis

In a companion paper (Crone *et al*., 1998) we have described the details of ECoG signal acquisition and artefact rejection, as well as the rationale and procedures for ECoG signal analysis, including filtering, remontaging, segmentation and data reduction via the fast Fourier transform. For the studies described in this paper, power spectrum density measurements were calculated for 13 frequency bands, each covering 10 Hz and overlapping its neighbours by 5 Hz. These bands spanned the frequency range from 25 to 100 Hz, including 25–35, 30–40, 35–45, 40–50, 50–60, 55–65, 60–70, 65–75, 70–80, 75–85, 80–90, 85–95 and 90–100 Hz. Our choice of gamma frequency bands for analysis was, by choice, arbitrary and exploratory. Estimates of power in the alpha (8–13.7 Hz) and beta (15–25 Hz) bands were also calculated for comparisons with the gamma bands.

Statistical analyses were performed to determine whether the spectral density values in post-stimulus epochs were significantly different from those in pre-stimulus (baseline) epochs. Details of the rationale and design of our statistical procedures were identical to those described elsewhere (Crone *et al*., 1998). For each post-stimulus epoch the geometric-mean percentage change in power from baseline, as well as the 95% confidence limits, were plotted against time to illustrate the magnitude and statistical significance of ERD over time.

Neuroanatomical correlations of the ECoG spectral analysis and cortical stimulation results were made possible by co-registering post-implantation, pre-resection CT scans with preoperative MRI scans according to procedures described elsewhere (Crone *et al*., 1998).

Results

In order to investigate the utility of gamma ERS as a tool for functional mapping, we compared its topographical and temporal patterns during muscular contractions of different body parts in five different clinical subjects. Because coverage of sensorimotor cortex by subdural electrodes was most comprehensive in Subject 1B (second implantation of Subject 1), we report our results in this subject with the greatest detail.

Subject 1

Task performance

Motor responses were recorded with surface EMG (see Crone *et al*., 1998), and trials with ambiguous or incorrect motor responses were excluded from analysis in each subject. Ambiguous motor responses included: those in which a motor response was not sustained; those in which a motor response from a different or contralateral body part occurred simultaneously; and those in which a motor response from the previous trial continued into the baseline period of the current trial. The motor responses of Subject 1B were correct and unambiguous in 89% of trials in which a choice of body part had to be made (decision condition), and 80–100% correct when no choice had to be made (simple condition). The simple tongue task, for which Subject 1B's performance was not as good (80% correct), was the last task given in a series of seven tasks, and fatigue may have been responsible for the less accurate performance.

For each trial, the time between onset of the visual stimulus and onset of the EMG response (reaction time) was measured by visual inspection. In Subject 1B the reaction times for different body parts under different task conditions were compared by fitting an analysis of variance model with a random effect for session, which accounts for the correlation between repeated measurements within a testing session. Because the distribution of reaction times was skewed to the right, a natural logarithm ($\log_n$) transform was performed before fitting the analysis of variance model. In addition, statistical analyses were repeated after excluding two extreme outliers, defined as having a $\log_n$-transformed reaction time of >3 SD from the mean. Results did not change when these outliers were excluded.

The antilog of the mean log-transformed reaction time

Table 1 *Task performance in Subject 1B*

Task	Body part	Trials (*n*)*	Reaction time†
Decision right	Tongue	45	426
Decision right	Fist	44	659
Decision right	Foot	44	660
Decision left	Tongue	43	491
Decision left	Fist	38	618
Decision left	Foot	46	676
Simple	Tongue	41	291
Simple	Right fist	48	434
Simple	Left fist	50	423
Simple	Right foot	48	441
Simple	Left foot	44	382

Decision right = visual motor decision task with right fist-clenching, right foot dorsiflexion, and tongue protrusion in midline; Decision left = visual motor decision task with left fist-clenching, left foot dorsiflexion, and tongue protrusion in midline; *Number of trials after excluding those with incorrect or ambiguous responses. †Geometric mean of reaction times, determined from EMG-recorded motor responses.

(geometric mean) is illustrated for each body part under each task condition in Table 1. The visual–motor decision task, which required a choice of responses between different body parts, produced response latencies that were ~160 ms longer [$t(480) = 5.53$, $P < 0.0001$] than those for the simple motor response task, which required movement of only a single body part. In addition, the response latencies for tongue movements under both the decision and simple task conditions were ~140 ms shorter [$t(480) = 5.35$, $P < 0.0001$] than those for arm or leg movements on either side under the same task conditions. There was no significant difference between response latencies for tasks performed on the right versus left sides [$t(480) = 1.05$, $P = 0.40$].

Gamma ERS

In Subject 1B augmentation of power above baseline (ERS) occurred in a number of bands within a frequency range that has been referred to as the 'gamma band' (>30 Hz). Although gamma ERS often occurred in and around the widely recognized 40 Hz band (35–45 and 40–50 Hz in our analyses), it also occurred in even higher bands, specifically the 75–85, 80–90, 85–95 and 90–100 Hz bands (Fig. 1). Examination of these results showed a clear differentiation between what we herein term the 'low' (35–50 Hz) and 'high' (75–100 Hz) gamma bands. Power changes within these two groupings of bands typically occurred with spatial and temporal similarity amongst the bands comprising each grouping. This consistency suggested broad band responses that were being observed using smaller bands that were, by methodological necessity, arbitrarily defined. Although the similarity of power changes in the 35–45 and 40–50 Hz bands could have been due to overlap of the two bands at a critical frequency (40–45 Hz), the similarity of power changes in non-overlapping bands (e.g. 75–85 and 90–100 Hz), notwithstanding possible spectral leakage, provided more evidence for a broad-band response in the high gamma range. Both the cortical topography and temporal course of high gamma ERS were clearly distinct from those of low gamma ERS, suggesting that the two phenomena behaved with some degree of independence and might have different neurophysiological mechanisms.

Low gamma ERS, particularly in the 40–50 Hz band, occurred in a more discrete topographical pattern than alpha (or beta) ERD, and was somatotopically specific for different body parts (Fig. 2). In contrast, alpha and beta ERD occurred in a more diffuse pattern during early phases of the motor response and became somatotopically specific only during the late phases of the sustained motor response (Crone *et al*., 1998). Although onset of low gamma ERS occasionally appeared to coincide with onset of the EMG response (Table 1; under 'Tongue' in Fig. 1), it usually occurred late, e.g. 200–500 ms after the EMG response onset (under 'Arm' in Fig. 1). During the decision condition, for all body parts, low gamma ERS was sustained, in parallel with alpha ERD, through the end of the post-stimulus period of analysis, i.e. for ⩾2 s (Figs 1 and 3). During the simple condition, low gamma ERS began earlier and returned towards baseline more rapidly than during the decision condition (Fig. 3). The difference in onset of low gamma ERS during the decision and simple conditions appeared to be similar to motor latency differences under the same task conditions (Table 1).

High gamma ERS occurred in more discrete spatial and temporal patterns than power changes in the alpha, beta and, even, the low gamma bands. Although high gamma ERS was usually accompanied by alpha and beta ERD, as well as low gamma ERS, it occurred in fewer electrodes (Fig. 4). High gamma ERS did not coincide with the greatest magnitude of alpha ERD but, instead, occurred in electrodes flanking these regions (Fig. 2). High gamma ERS was not observed in the recording electrodes overlying parasagittal perirolandic cortex during foot dorsiflexion, perhaps because these electrodes were not directly covering cortex representing distal leg movements.

High gamma ERS occurred over a much briefer time frame than power changes in the alpha, beta and low gamma bands. Onset of high gamma ERS often appeared to coincide with, or slightly precede, the onset of the motor response (see Fig. 5 and Table 1), and it often preceded the onset of low gamma ERS (compare with Fig. 3). In addition, high gamma ERS was typically transient, lasting only 400–1000 ms, and it was never sustained (Figs 1 and 5). For each tested body part, the onset of high gamma ERS appeared to occur later under the decision condition than under the simple condition, and these latency differences seemed similar to motor latency differences under the same task conditions (see Table 1 and Fig. 5). In addition, high gamma ERS during tongue protrusion appeared to begin earlier than during fist-clenching, concordant with the different response latencies of these body parts. This close temporal correspondence between motor performance and onset of spectral change was more

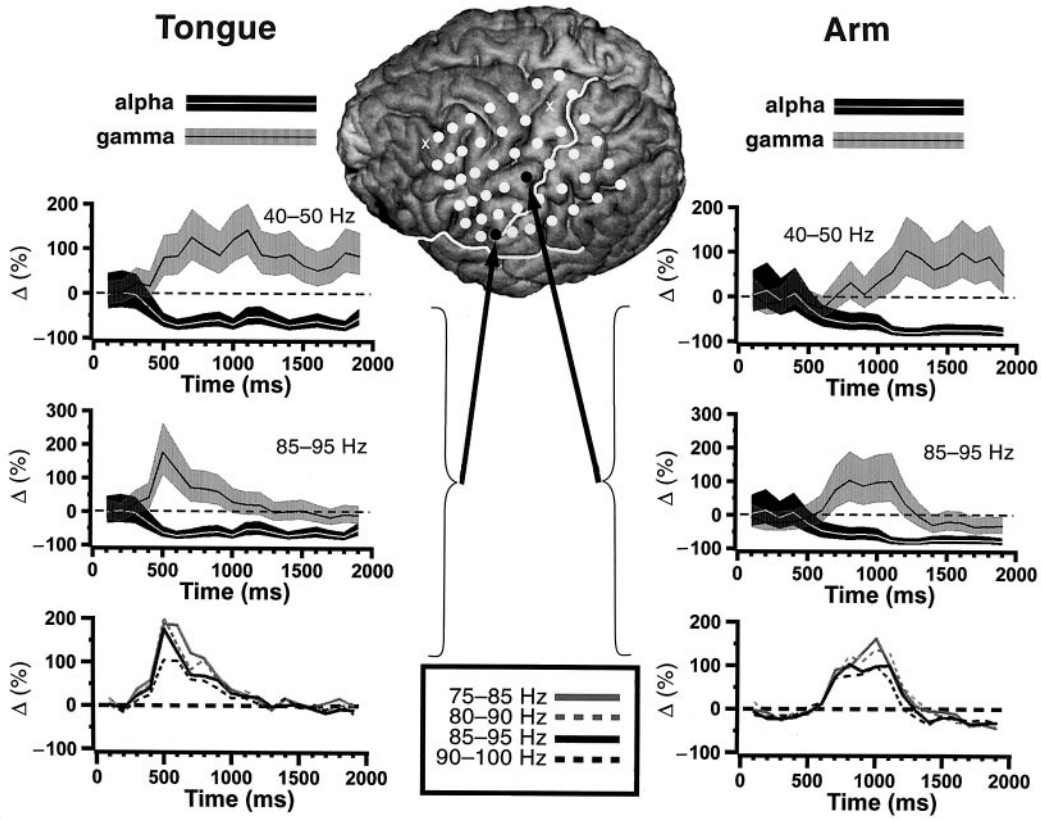

Fig. 1 Plots of alpha ERD, low gamma (40–50 Hz) ERS and high gamma (85–95 Hz) ERS, during tongue protrusion (left plots) and contralateral fist-clenching with the right arm (right plots) under the decision condition. Note similarity of plots for several bands in the high gamma range (75–100 Hz). Δ(%) = geometric mean percentage change in power from baseline (ERD or ERS). Upper two rows of plots also show 95% confidence intervals.

obvious for gamma ERS, particularly high gamma ERS, than it was for alpha or beta ERD.

Alpha and beta ERD may be observed during both contralateral and ipsilateral limb movements (Crone *et al*., 1998). However, we observed low and high gamma ERS only during contralateral limb movements, not during ipsilateral limb movements.

'Transitional' and 'auxiliary' frequency bands

Depending upon the electrode, power changes in the 25–35 and 30–40 Hz bands often occurred in temporal and spatial patterns which shared features with power changes in the 15–25 and 20–30 Hz (beta) bands and power changes in the 35–45 and 40–50 Hz (low gamma) bands. Beta power was typically suppressed (ERD) in association with putative cortical activation, whereas low gamma power was typically augmented (ERS). Power in the bands between these two broad frequency ranges sometimes increased and sometimes decreased in association with neighbouring frequency changes. We therefore refer to the behaviour of these bands as 'transitional' between their neighbouring bands.

Power in other frequency bands behaved in a manner we will term 'auxiliary', that is, power changes did not necessarily occur in these bands during putative activation of a cortical region, but whenever power changes in other frequency bands (i.e. alpha, beta and gamma) were particularly pronounced, power in these auxiliary bands would also change. The most consistent example of this was power augmentation in the 50–60 Hz band, which sometimes occurred when power augmentation in the low gamma bands was particularly robust. Another example of this category of spectral behaviour was the suppression of power in multiple gamma bands from 50 to 100 Hz during particularly robust power suppression in the alpha and beta bands. Still another example of this class of phenomena was low gamma ERS (Fig. 4) occurring in association with beta ERS. This was seen with both implantations of Subject 1. In this case, beta ERS occurred after a transient ERD over the putative representations of body parts that were not being moved. As noted in our companion paper (Crone *et al*., 1998), the beta ERS that we observed may be a modified analogue of the post-movement beta ERS described by Pfurtscheller *et al*. (1996).

Because the power changes in bands that we have termed transitional and auxiliary could have been caused by spectral leakage from neighbouring frequency bands, and because they were much less consistent across cortical regions,

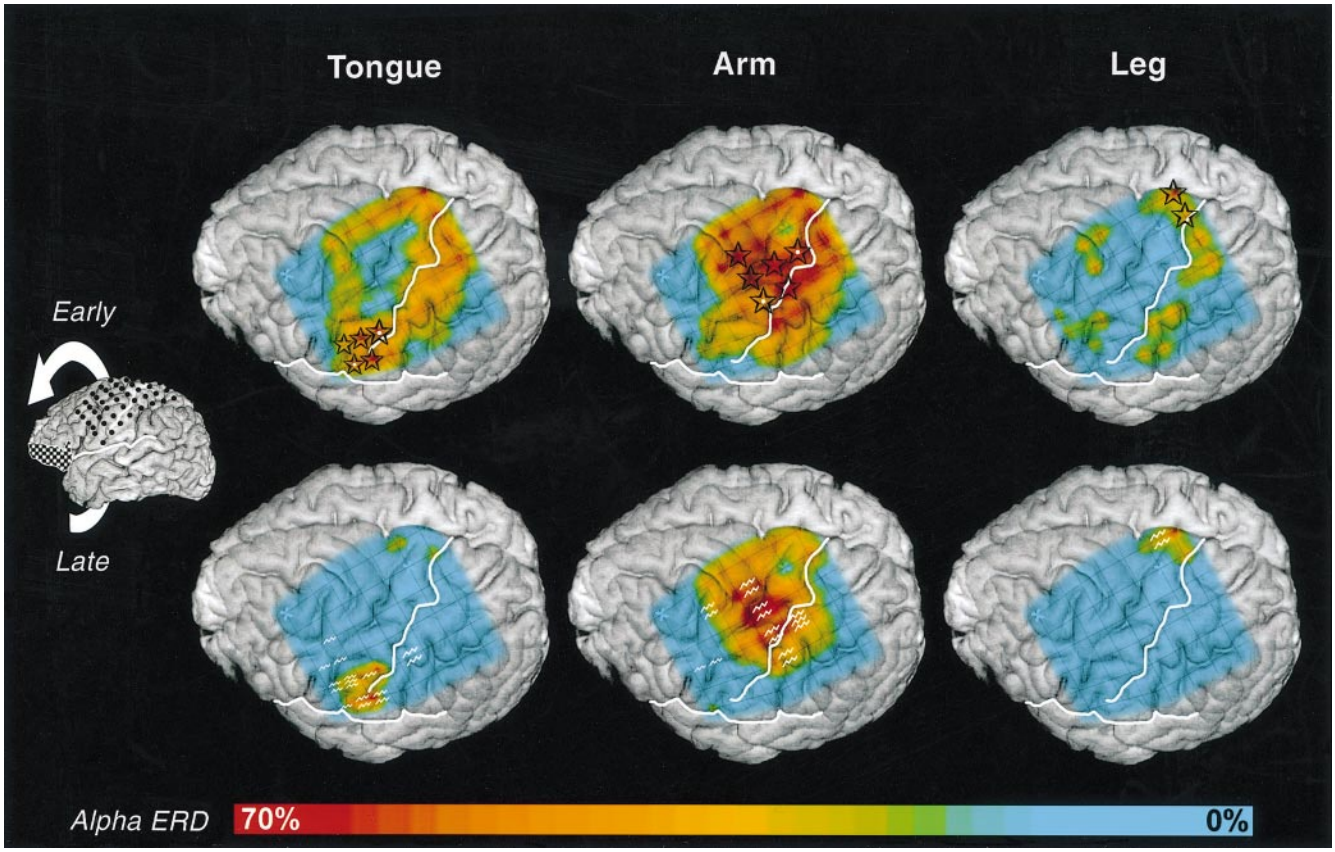

Fig. 2 Cortical topography of gamma ERS is compared with that of alpha ERD over left frontoparietal cortex. Separate plots are shown for each body part under the decision condition, i.e. during tongue protrusion, right (contralateral) fist-clenching and right foot dorsiflexion. Empty stars = low gamma ERS, and stars with white dots = high gamma ERS. Colour surface plots of alpha ERD illustrate the distinction between transient (early) and sustained (late) power changes. Early ERD was calculated by averaging the percentage (geometric mean) ERD for three 200-ms post-stimulus epochs centred at 600, 700 and 800 ms. Late ERD was calculated by averaging the percentage ERD in the 1700, 1800 and 1900-ms epochs. Late ERD corresponds to ERD that was sustained, i.e. after its onset, it continued through the end of the 2-s post-stimulus period of analysis (see Crone *et al*., 1998). Alpha ERD measures at each electrode (original values at thin line crossings) were interpolated using an inverse-distance weighting algorithm to produce a smooth colour map. Lightning-bolt icons denote electrical stimulation-induced disruption of motor function in the body part (tongue, right arm or right leg) indicated at the top of the column: one bolt = slowing or cessation of ongoing motor activity (wiggling tongue, fingers or toes); two bolts = involuntary motor response (e.g. posturing); and three bolts = clonic muscular contractions. The brain icon on the left illustrates rotational orientation of the brain and the location of the lesion in the left inferior frontal lobe (chequered area). The faded 'x's denote electrode sites in which ECoG could not be reliably recorded.

behavioural conditions and individual subjects, we did not examine them in any further detail in this paper.

Reproducibility of ECoG spectral analysis at different times

Subject 1 underwent two different implantations of subdural electrodes (noted herein as 1A and B), separated by 6 months, for invasive video/EEG monitoring and functional mapping with cortical electrical stimulation. Similar changes in the low and high gamma bands were observed with these two separate implantations. Comparison of the topographical patterns of gamma band activity revealed a match which was not perfect, but which was quite good overall, considering the difference in electrode placements (Fig. 4).

Comparison of ECoG spectral analysis and cortical electrical stimulation maps

Cortical electrical stimulation in, and adjacent to, paracentral cortex produced a variety of symptoms indicating disruption of motor function. The production of involuntary movements (positive responses), particularly clonic movements (not associated with afterdischarges), was considered more localizing than slowing or arrest of voluntary movements (negative responses), which have been found in previous studies to occur outside the primary sensorimotor cortices with a relatively non-specific distribution along the central sulcus (Nii *et al*., 1996). We therefore used a hierarchical categorization of the effects of cortical stimulation on motor function (Figs 2 and 4): no motor effect, motor dysfunction only (negative responses), motor responses (positive responses) without clonic contractions and motor responses

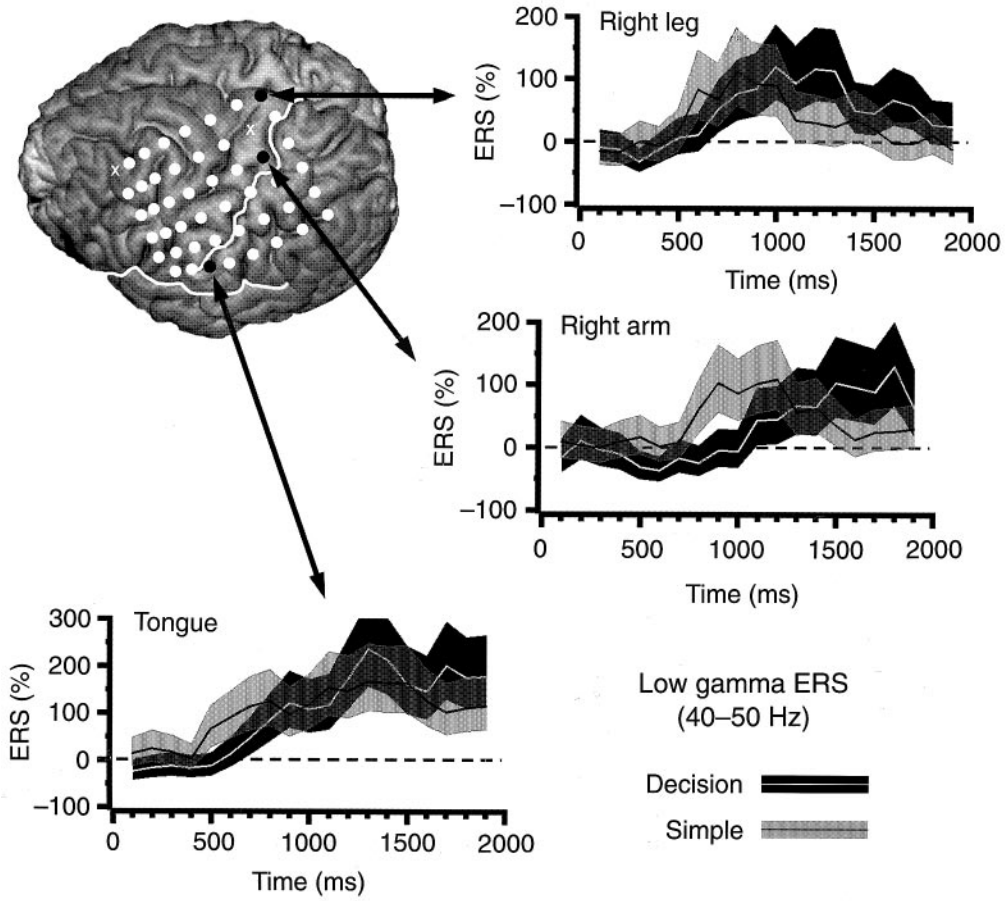

Fig. 3 Plots of low gamma (40–50 Hz) ERS over left frontoparietal cortex during tongue protrusion, right (contralateral) fist-clenching and right foot dorsiflexion under the decision (white line = geometric mean; black areas = 95% confidence intervals) and the simple (black line = geometric mean; grey areas = 95% confidence intervals) conditions. Note that low gamma ERS is delayed under the decision condition, the condition in which the response latencies are also delayed (see Table 1). Note also that the return to baseline is quicker under the simple condition.

with clonic contractions. Note that positive motor responses, with and without clonic contractions, were often accompanied by motor dysfunction (slowing or arrest of voluntary movements), but motor dysfunction alone (a negative response) was, by definition, not accompanied by any involuntary (positive) motor response.

The cortical-stimulation maps that were obtained from the two implantations of Subject 1 were very similar, although not identical, due in part to the different placement of electrodes (Fig. 4). Comparisons of the cortical-stimulation maps with the ECoG spectral analysis maps for different body parts, illustrated in Figs 2 and 4 (see also Crone *et al*., 1998), revealed a fair degree of congruence between these two methods of functional brain mapping.

Low gamma ERS and high gamma ERS were usually recorded from electrodes at which cortical stimulation produced disruption of motor function in the same body part. Whereas alpha ERD often occurred in regions where cortical stimulation produced no disruption or only inhibition of motor function (Fig. 2), low and high gamma ERS usually (though not always) occurred where stimulation produced positive motor responses of the involved body part.

Similar relationships between cortical stimulation, ECoG spectral analysis and somatotopy were also observed in the other subjects in whom we observed gamma ERS (see Figs 7 and 8 below).

Subjects 2–5

Subdural ECoG recordings were made in four other subjects during the same visual–motor task used for Subject 1. All these subjects were tested with the decision condition, but none were tested with the simple condition as described for Subject 1B.

Gamma ERS was observed in only three out of five of our subjects (1, 3 and 5). The electrode coverage in Subject 2 (Fig. 6) may have been too sparse to record gamma band activity, but in Subject 4 (Fig. 6) there was no obvious reason for the lack of gamma ERS. Although low gamma ERS was observed with foot dorsiflexion in Subject 1B (Fig. 2), high

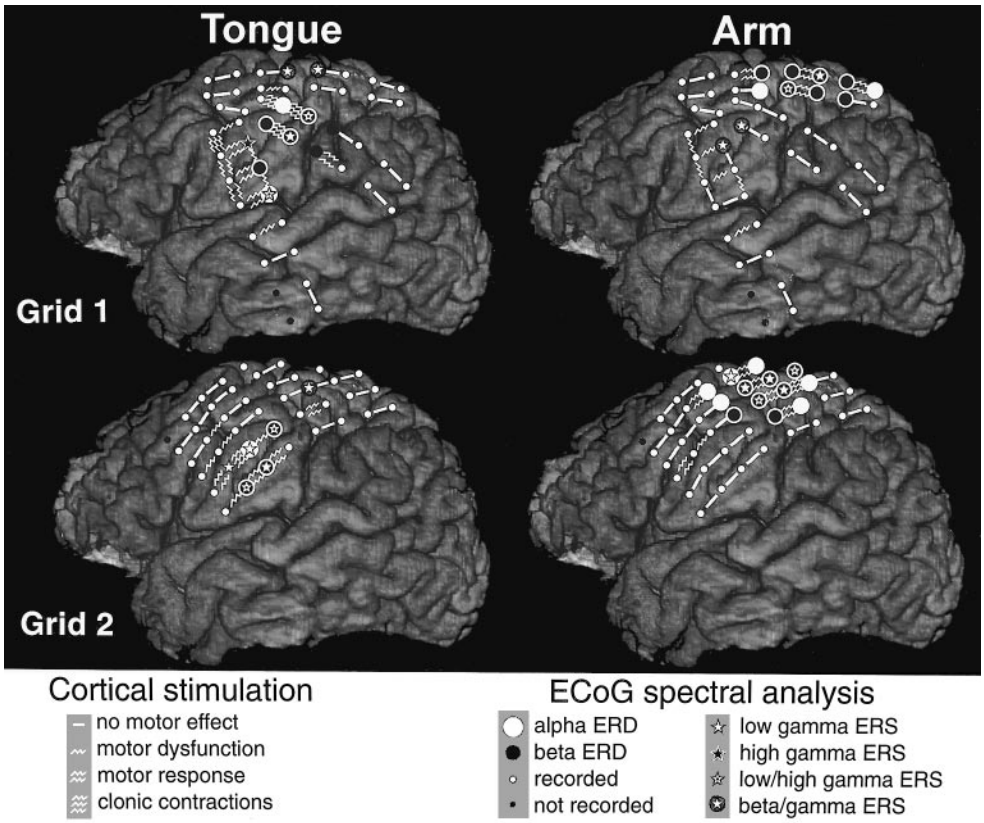

Fig. 4 Maps of ECoG spectral analysis and cortical stimulation results during two different implantations of grid electrodes. Both ECoG spectral analysis and cortical-stimulation maps of tongue (left column) and arm (right column) are similar between the first (top row) and second (bottom row) grid placements. Symbols denote alpha and/or beta ERD only if they were sustained (see Fig. 2 caption).

gamma ERS was not observed with foot dorsiflexion in any of our subjects, possibly due to inadequate coverage of interhemispheric sensorimotor cortex.

In all those subjects in whom gamma ERS was observed, it typically occurred in a more discrete spatial pattern than alpha or beta ERD (Figs 7 and 8). In Subjects 1 and 3, high gamma ERS occurred in only one or two electrodes during a particular task condition (Figs 4 and 8), indicating a more discrete spatial distribution than alpha ERD, beta ERD and, even, low gamma ERS. In Subject 5 low gamma ERS was not observed, but high gamma ERS was observed in four electrodes during tongue protrusion, in a spatial pattern similar to, but more discrete than alpha ERD (Fig. 7). We did not observe gamma ERS, low or high, in this subject during fist-clenching, but the subdural electrodes may not have covered this subject's cortical hand area well, as suggested by the lack of sustained alpha or beta ERD during the same task (Crone *et al*., 1998).

When it was observed, gamma ERS occurred in a more somatotopically specific spatial pattern than alpha or beta ERD. Alpha and beta ERD often occurred in a widespread distribution during early phases of the motor response and consistent somatotopy was demonstrated only during the late phases, i.e. near the end of the 2-s post-stimulus analysis period. This observation formed the basis for our distinction between transient and sustained alpha and beta ERD (see Crone *et al*., 1998). In contrast, regardless of its time course, gamma ERS always occurred in a somatotopic pattern (Figs 7 and 8) unless it was accompanied by beta ERS (Fig. 4). Even when sustained alpha ERD appeared to be insufficient for discerning a somatotopic pattern (Subject 3), gamma ERS did allow such a distinction to be made (Fig. 8).

Although unilateral fist-clenching produced at least transient alpha and beta ERD over both contralateral and ipsilateral sensorimotor cortices (Crone *et al*., 1998), gamma ERS was observed only over the contralateral sensorimotor cortex. Even in Subject 3, in whom fist-clenching produced sustained alpha ERD over the sensorimotor cortices bilaterally (Crone *et al*., 1998), only right fist-clenching produced gamma ERS over putative hand regions in the left hemisphere (Fig. 8). Although gamma ERS was not observed in this subject over the right hemisphere during left fist-clenching, this could have been due to inadequate electrode coverage of the arm area in this subject.

As with Subject 1, when high gamma ERS was observed in our other subjects, its temporal course was early and transient, typically beginning within 100 ms of the motor response onset, and lasting from 200 to 400 ms. Low gamma

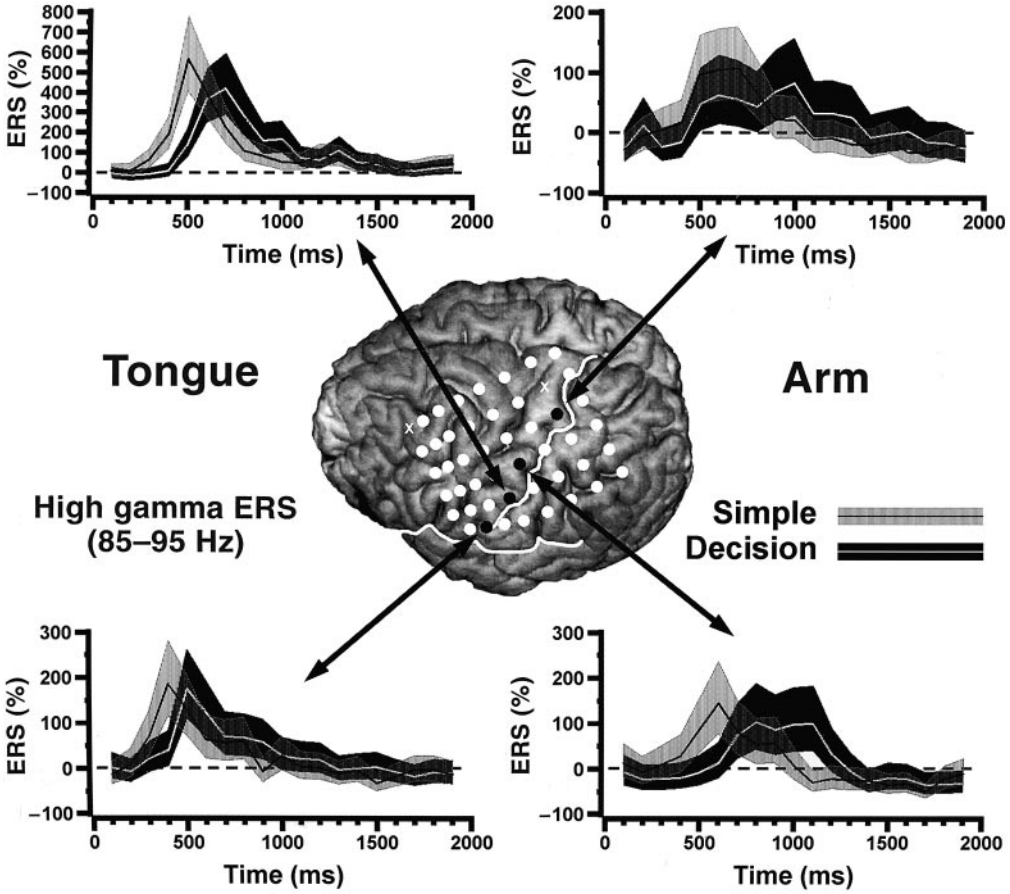

Fig. 5 Plots of high gamma (85–95 Hz) ERS, during tongue protrusion (left plots) and right (contralateral) fist-clenching (right plots) under the decision (white line = geometric mean; black areas = 95% confidence intervals) and simple (black line = geometric mean; grey areas = 95% confidence intervals) conditions. Note that the onset of high gamma ERS is later under the decision condition, the condition in which the response latencies (see Table 1) are also later.

ERS was observed in only two of our subjects (1 and 3). In both cases, its time course roughly paralleled that of alpha ERD, as in Fig. 1.

Discussion

Over the past 20 years neurophysiological investigations in animals have suggested the relevance of 40 Hz activity, as well as the more general concept of 'gamma band' activity, to cortical neurophysiology. Freeman's recordings from the olfactory cortex in the rabbit revealed inspiratory bursts of sinusoidal oscillations ranging from 40 to 80 Hz, occurring in odour-specific spatial patterns (Freeman, 1978). Similar studies in the cat and rat revealed oscillations with a similar frequency range (Bressler and Freeman, 1980). Bouyer *et al*. (1987) described 40 Hz activity in Brodmann areas 4, 5 and 6 of the cat during immobility and focused attention. However, this activity was postulated to be the homologue of the anterior beta rhythm described by Jasper and Penfield (1949). Local field recordings in the visual cortex of the cat have found that oscillatory neuronal firing in a frequency range of 40–60 Hz can become synchronized during visual stimulation: in spatially separate columns (Gray *et al*., 1989); between areas 17 and 18 (Eckhorn *et al*., 1988); and even between the two hemispheres, in area 17 (Engel *et al*., 1991), and that this synchronization is dependent upon global stimulus properties. In addition, Murthy and Fetz (1992) and Sanes and Donoghue (1993) demonstrated high-frequency local field activity (25–35 and 15–50 Hz, respectively) in the sensorimotor cortex of awake monkeys during hand movements. Bursts of single unit activity were commonly synchronized with local field potential oscillations, suggesting facilitation of neuronal firing.

These investigations and others have suggested that gamma band activity facilitates and/or is facilitated by the synchronization of neuronal firing between spatially segregated, but functionally related, neurons. This synchronization could form the temporal coding by which temporary assemblies of neurons represent higher-order, or global, stimulus properties. Such a mechanism has been proposed (von der Malsburg, 1995) as a potential solution to the binding problem associated with psychological

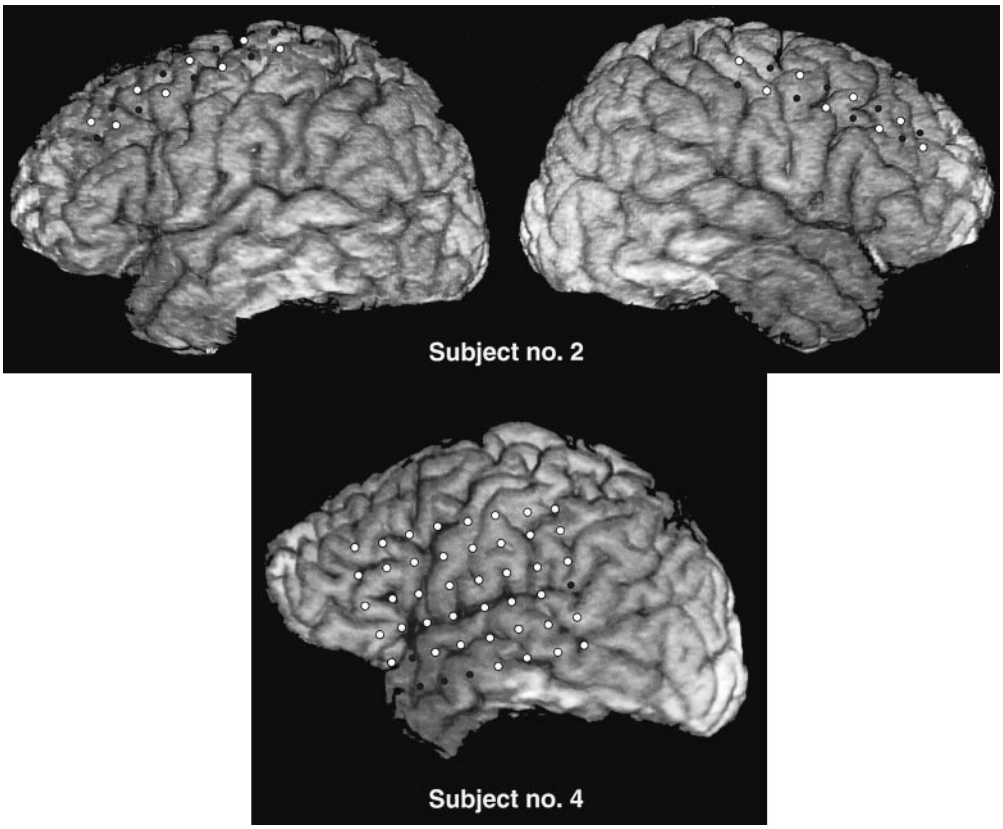

Fig. 6 Subdural electrode placements in Subjects 2 and 4. ECoG recordings were made with the white electrodes. Black electrodes were not used for ECoG recordings due to high impedance (Subject 4) or insufficient amplifier channels (Subject 2; the remainder of the subdural electrodes are not shown).

phenomena such as sensory segmentation, invariant object recognition and language parsing. In addition, gamma band activity has become the focus of theories of visual awareness and consciousness (Crick and Koch, 1990; Llinas and Pare, 1991).

Fewer studies of gamma band activity have been done in humans, and until recently these studies have been limited to scalp EEG recordings. Building upon his prior recordings of 40 Hz activity in cats, Sheer found an increase in 40 Hz EEG activity over the contralateral central scalp region in humans during both simple- and complex-choice reaction-time tasks (Sheer *et al*., 1966; DeFrance and Sheer, 1988). Pfurtscheller *et al*. (1993) demonstrated a lateralized increase in 40 Hz activity, which they termed 40 Hz ERS, during finger movements in three subjects, and in one of these subjects they showed a somatotopic pattern of gamma ERS during movements of the tongue, finger and toes. In a recent study using subdural electrode recordings, Menon *et al*. (1996) found no evidence, in two subjects, for task-related gamma band augmentation or spatially correlated gamma band activity during a somatosensory discrimination task with finger responses. Magnetoencephalographic (MEG) recordings have recently demonstrated evoked gamma band oscillations in response to auditory stimulation (Pantev *et al*., 1991; Ribary *et al*., 1991). However, there has been no report until now of gamma band activity in response to a sensorimotor task using either subdural ECoG or MEG.

During putative activation of sensorimotor cortex we found a significant augmentation of power in the 35–50 Hz range, which includes the widely studied 40 Hz band (35–45 Hz in our case). In addition, we observed augmentation of power in a higher frequency range (75–100 Hz), still within the broadly defined gamma band (>30 Hz). Whenever augmentation of either low or high gamma power was observed, it occurred in a spatial pattern that was somatotopically specific for different body parts. In particular, tongue protrusion was associated with gamma ERS over inferior-lateral perirolandic cortex, fist-clenching was associated with gamma ERS over more superior perirolandic cortex, and foot dorsiflexion was associated with gamma ERS over parasagittal perirolandic cortex (Fig. 2). This localization was further corroborated in each of our subjects by the results of cortical electrical stimulation using the same subdural electrodes.

Although alpha and beta ERD have been observed over bilateral sensorimotor cortices during unilateral limb movements (Pfurtscheller and Klimesch, 1991; Crone *et al*., 1998), gamma ERS has been observed only over contralateral sensorimotor cortex, a finding which is more consistent with the majority of lesion studies in both animals and humans. Our findings with gamma ERS were also more consistent with the results of PET and functional MRI (Grafton *et al*., 1991; Kim *et al*., 1993), in which activation of sensorimotor

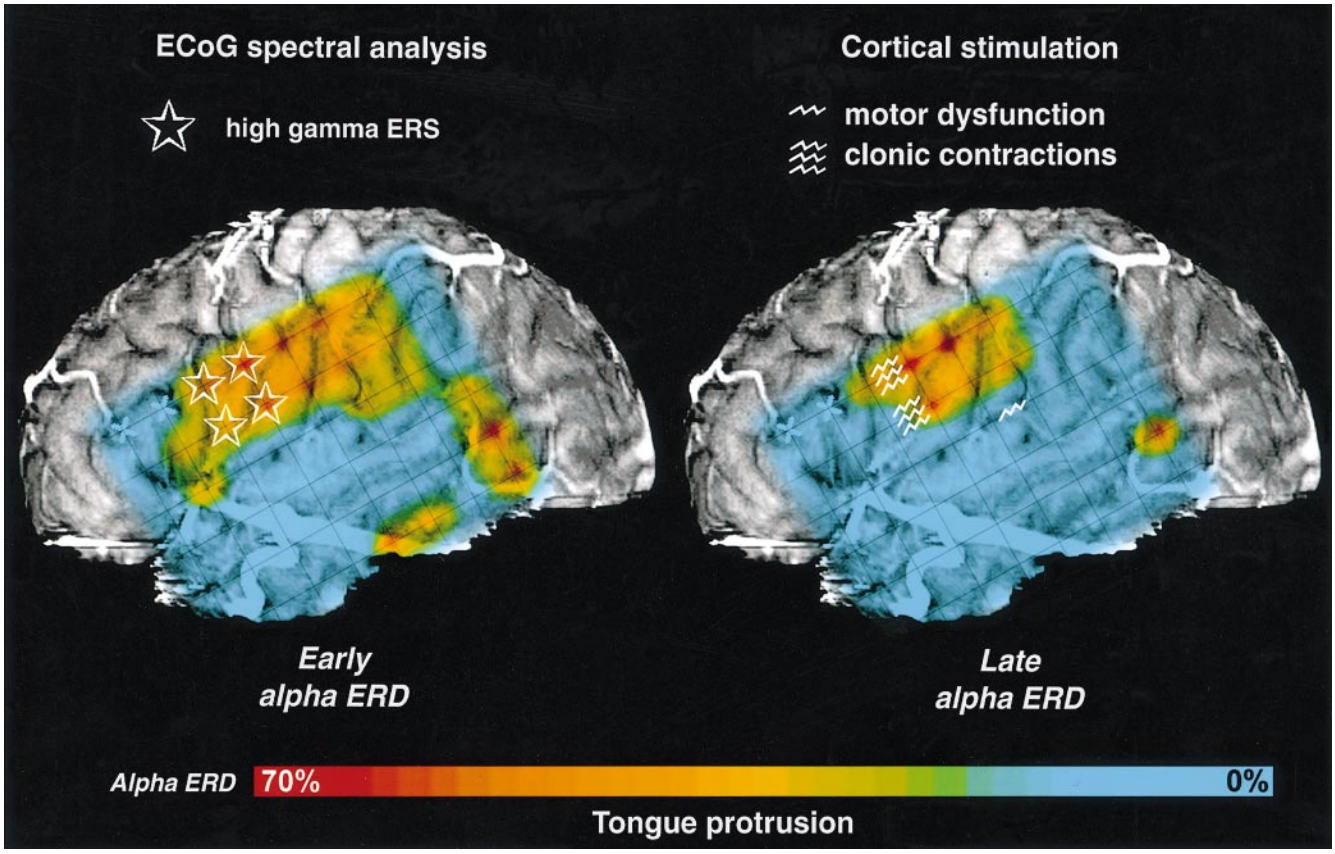

Fig. 7 Subject 5. Cortical topography of transient high gamma (85–95 Hz) ERS (white stars) during tongue protrusion is compared with that of alpha ERD during early and late epochs (colour surface plots as in Fig. 2) and with the results of cortical stimulation on tongue motor function. Lightning bolts represent motor responses with cortical stimulation (see Fig. 2 caption).

cortex has been more discrete and more consistently contralateral than that observed with alpha or beta ERD.

On the whole, compared with alpha and beta ERD, the topographical patterns of gamma ERS were more consistent with traditional ideas about the functional organization of sensorimotor cortex. In particular, gamma ERS occurred over contralateral, somatotopically defined regions of sensorimotor cortex. Previous studies have shown that lesions of these cortical regions often produce deficits in sensorimotor function. Considering our findings in conjunction with our discussion elsewhere (Crone *et al*., 1998) on the potential implications of the wide and bilateral distribution of alpha and beta suppression, it seems reasonable to speculate that gamma ERS may be an index of those cortical regions which are critical for cortical function at the time of recording. In contrast, alpha and/or beta ERD may also occur over regions that are only participating peripherally, but are nevertheless capable of supporting the same cortical function under different circumstances (e.g. lesions), perhaps through short-term and/or long-term mechanisms of synaptic plasticity.

The spatial patterns of gamma ERS were more discrete than those of alpha ERD in our ECoG recordings. This may have made it more difficult to detect gamma ERS reliably given our current methods, i.e. 1-cm electrode spacing. We observed gamma ERS in only three out of five of our subjects, yet we observed alpha and/or beta ERD in all subjects (Crone *et al*., 1998). This may be consistent with the findings by other investigators of 40 Hz activity in humans. To our knowledge phasic 40 Hz ERS has previously been recorded over sensorimotor cortex in only three human subjects (Pfurtscheller *et al*., 1993). It is difficult to compare our results directly with those of Sheer and others (Spydell *et al*., 1979; Spydell and Sheer, 1982) since they used very different tasks (e.g. mathematical problems, verbal analogies and facial discrimination) and made task-wise comparisons for a group of subjects. Auditory-evoked gamma band activity has been detected with MEG (Pantev *et al*., 1991), but until now there has been no report of MEG-recorded gamma band activity associated with activation of sensorimotor cortex. In two subjects with subdural electrode arrays, Menon *et al*. (1996) did not detect any increase in gamma power during a somatosensory discrimination task with a graded motor (finger) response. Although the discrepancy between their findings and ours could be due to differences in our sensorimotor tasks, or our methods of signal analysis, it is just as plausible that gamma band activity was generated in all of our subjects but we were unable to record it in some of them.

We can only speculate as to why gamma band activity might be recorded in some subjects and not in others.

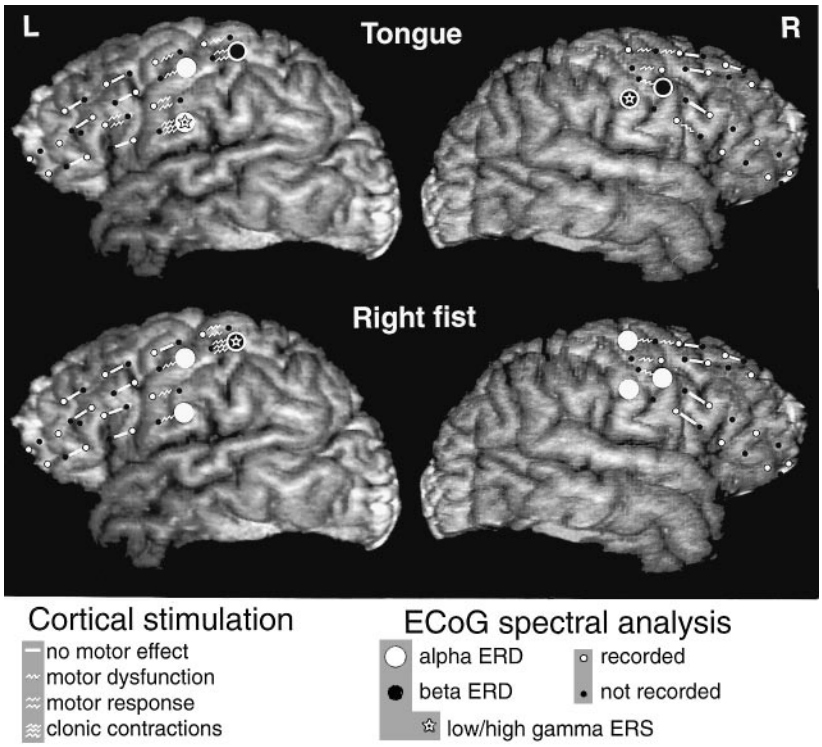

Fig. 8 Maps of ECoG spectral analysis and cortical stimulation results for Subject 3 during tongue protrusion and right fist-clenching. Only sustained alpha and beta ERD are illustrated (see Fig. 2 caption). Foot dorsiflexion was also performed but did not produce sustained alpha or beta ERD or transient gamma ERS in the visible electrodes. L = left hemisphere; R = right hemisphere.

Using these task conditions, in these brain regions, the generators for gamma band activity could be too small or orientated incorrectly, could be spatially distributed with insufficient density, or could be insufficiently coherent for summation and detection at the cortical surface in some subjects. Using similar subdural electrode arrays, Menon *et al*. (1996) did not detect spatially correlated gamma band activity at interelectrode distances >1.4 cm, and they suggested that 1-cm electrode spacing may be insufficient for capturing the spatial pattern of task-related gamma band activity. If this is true, subdural electrode arrays with interelectrode distances of $\leqslant 5$ mm may be necessary to consistently capture gamma band augmentation. In addition, gamma activity generated in the depths of the central sulcus might be invisible, even to subdural ECoG, given a weak tangential dipole. In this case MEG would be better suited to detect this activity.

To our knowledge, our finding of high gamma augmentation is the first of its kind in humans. Oscillatory EEG bursts recorded by Bressler and Freeman (1980) in the olfactory system of three different mammalian species occurred in a frequency range of 35–85 Hz. Later studies extended the estimate of the gamma band in mammals to the 30–100 Hz range (Eeckman and Freeman, 1990). The oscillatory neuronal firing described by Singer and others has generally been reported to occur in the frequency range of 40–60 Hz (Singer, 1993). Similar oscillatory activity was reported by Eckhorn *et al*. (1988) with a frequency range of 35–85 Hz. High gamma band augmentation in our subjects occurred in a broad band between ~75 and 100 Hz.

The time course of high gamma augmentation was very different from that of low gamma augmentation in our subjects. This is the best evidence we have to argue that high gamma activity is not simply a harmonic of low gamma activity. If high gamma ERS were caused by such an artefact, we would expect to see a similar, if not identical, time course for low gamma ERS. Nevertheless, further studies, perhaps using coherence measures, may be necessary to confirm the functional independence of low and high gamma bands.

In our subjects, the onset of low gamma band ERS, which includes the widely recognized 40 Hz band, generally overlapped or lagged behind the onset of the motor responses. In most cases it was also sustained during the subjects' motor responses. This time course paralleled those of alpha and beta ERD, suggesting that the neurophysiological mechanisms for these phenomena might be linked in some way. Given the stimulus–response paradigm of our task, the temporal profiles of these indices suggest that they are associated with execution of the motor task, with some possible degree of habituation, particularly in the case of beta ERD. Using a self-paced button-pushing task, Pfurtscheller *et al*. (1993, 1994) observed 40 Hz ERS just prior to their subjects' motor responses, and this suggested to them that this activity

reflected motor programming, i.e. planning of the motor output. Unlike the button-pushing task, which requires a brief and transient motor response, our visual–motor task required a continuous, sustained motor response. Since our statistical analyses used the visual stimulus, rather than the motor response, as an anchor for averaging, the variability of our subjects' motor responses, combined with the limitations of our methods, probably introduced sufficient temporal uncertainty that we cannot exclude the possibility that low gamma augmentation occurred slightly before the motor response, therefore reflecting motor programming. However, the persistence of low gamma ERS well beyond initiation of the motor response suggests that it also reflects motor output, sustained attention to the motor output and/or continued motor programming. In this way our results with the visual–motor task may have complemented those of Pfurtscheller *et al*. (1993, 1994).

High gamma ERS often appeared to coincide with, or slightly precede, the onset of our subjects' motor responses. In addition, when significant differences in motor response latencies were produced by different task conditions (i.e. decision versus simple or tongue versus fist), a similar difference was seen in the onset latency of high gamma ERS, providing evidence for the relevance of this phenomenon as an index of cortical activation and suggesting a tight link with initiation of the motor response. Such a close temporal correspondence with initiation of the motor response was not seen with alpha ERD, beta ERD or low gamma ERS. The temporal profile of high gamma ERS was also distinguishable from that of low gamma ERS because it was typically transient, usually lasting no more than a few hundred milliseconds. These findings suggest that the neurophysiological mechanisms of high gamma ERS may be functionally distinct from those of alpha and beta ERD and, even, low gamma ERS. In addition, high gamma ERS may be more specifically associated with planning or initiation of the motor response than with its continuous execution.

Gamma ERS, particularly in the high gamma band, occurred over a broad frequency range. To some extent the bandwidth of this response could have been an artefact of spectral leakage, but we doubt that this fully explains the phenomenon. We could not distinguish any distinct peaks within the power spectra we measured, and our frequency resolution (10 Hz) should have been sufficient to detect narrower band responses. In spite of the proximity of our macroelectrodes to the cortical surface, we probably could not have recorded gamma ERS unless the dendritic potentials of a large population of neurons were oscillating synchronously, producing recordable potentials through summation. The finding of gamma ERS across a broad frequency band implies the presence of multiple oscillatory populations or ensembles of neurons synchronized at different frequencies. If gamma ERS is in fact a broad band response, it might have interesting implications for the theories of temporal coding advanced by von der Malsburg (1995) and experimentally supported by Singer and others (see above). In particular, temporal coding through synchronization of neuronal firing might have a greater capacity for simultaneous, yet distinct, neuronal ensembles, or bindings, if it operates in conjunction with oscillatory firing at different frequencies. Although the causal relationships between synchronization and oscillatory activity, at the levels of action potentials and dendritic potentials, have not yet been elucidated (Singer, 1994), the added dimension of oscillatory frequency tuning might allow greater multitasking within and between cortical regions.

Conclusions

To identify event-related changes in the gamma band and verify their utility for functional mapping, we explored a series of 10-Hz-wide bands ranging from 30 to 100 Hz and studied each with respect to its temporal profile, cortical topography, reproducibility and correlation with other indices of cortical function, including alpha and beta ERD and cortical-stimulation mapping. Although both low (35–50 Hz) and high (75–100 Hz) gamma ERS appeared to produce more somatotopically specific patterns of cortical activation than alpha and beta ERD (Crone *et al*., 1998), they were not universally present and therefore could not be used as a sole marker for cortical activation. However, when either low or high gamma ERS were present, they appeared to complement alpha and beta ERD in the localization of cortical activity, both in time and in space. These findings suggest that changes in different regions of the ECoG power spectrum may have distinct neurophysiological mechanisms. If these mechanisms can be differentiated and understood, then ECoG spectral analysis, as well as frequency analysis of electromagnetic recordings in general, could offer added richness and detail to the enterprise of functional brain mapping and to our understanding of brain function.

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