Silence Is Golden: Transient Neural Deactivation in the Prefrontal Cortex during Attentive Reading

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It is becoming increasingly clear that attention-demanding tasks engage not only activation of specific cortical regions but also deactivation of other regions that could interfere with the task at hand. At the same time, electrophysiological studies in animals and humans have found that the participation of cortical regions to cognitive processes translates into local synchronization of rhythmic neural activity at frequencies above 40 Hz (so-called gamma-band synchronization). Such synchronization is seen as a potential facilitator of neural communication and synaptic plasticity. We found evidence that cognitive processes can also involve the disruption of gamma-band activity in high-order brain regions. Intracerebral electroencephalograms were recorded in 3 epileptic patients during 2 reading tasks. Visual presentation of words induced a strong deactivation in a broad (20–150 Hz) frequency range in the left ventral lateral prefrontal cortex, in parallel with gamma-band activations within the reading network, including Broca's area. The observed energy decrease in neural signals was reproducible across patients. It peaked around 500 ms after stimulus onset and appeared subject to attention-modulated amplification. Our results suggest that cognition might be mediated by a co-ordinated interaction between regional gamma-band synchronizations and desynchronizations, possibly reflecting enhanced versus reduced local neural communication.

Keywords: gamma band, intracerebral EEG, reading, task-induced deactivation, ventral lateral prefrontal cortex

Introduction

In interpreting task-induced metabolic decreases in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies, several authors have suggested that performing attention-demanding cognitive tasks requires not only regional activations but also deactivations, presumably reflecting decreases in neural activity in regions supporting processes unrelated or irrelevant to the task at hand (i.e., Gusnard and Raichle 2001; McKiernan et al. 2003; Fox et al. 2005; Lachaux et al. 2005).

In electrophysiological recordings, the active recruitment of a cortical region during a cognitive task translates into a local increase in fast oscillatory activity for frequencies above 40 Hz (the so-called gamma band) (Tallon-Baudry and Bertrand 1999). This phenomenon, called gamma-band response (GBR) is believed to reflect a synchronization mechanism facilitating communication within and between local neural networks (Fries 2005). This observation is quite general in scope and has been replicated in multiple brain regions and cognitive tasks, including language (Sinai et al. 2005; Tanji et al. 2005), visual attention and perception (Brovelli et al.

2005; Lachaux et al. 2005; Tallon-Baudry et al. 2005; Tanji et al. 2005), memory (Fell, Fernandez, et al. 2003; Fell, Klaver, et al. 2003; Howard et al. 2003; Sederberg et al. 2003; Jung et al. 2006; Mainy et al. 2007), and sensorimotor processes (Crone et al. 1998; Pfurtscheller et al. 2003; Szurhaj and Derambure 2006), especially by means of human intracranial recordings, which provide direct electrophysiological measurements from well-defined cerebral structures.

Thus far, however, there have yet been very few reports of local decreases in gamma activity in relation to cognitive processing. Negative GBRs, or gamma-band suppressions (GBS), have been reported in scalp magnetoencephalographic (MEG) recordings (Hirata et al. 2004); however, due to the limited spatial resolution of scalp MEG recordings, these observations could not be precisely linked with specific brain areas. In intracerebral recordings, though GBS has been reported in the periphery of the primary visual cortex in response to foveal presentation of visual stimuli (Lachaux et al. 2005), up until very recently, stimulus-induced energy decreases have been habitually and almost exclusively observed in the alpha and lower beta ranges (<20 Hz), these frequency bands known to be negatively correlated with cortical recruitment (Crone et al. 1998; Pfurtscheller et al. 2003). Such absence of reported GBS is surprising, as one might have predicted that local neural communication might decrease in cortical regions not relevant to ongoing cognitive processes, both in low-level sensory areas and high-level structures, particularly the frontal cortex.

This study reports a clear example of GBS in the prefrontal cortex during a high-level cognitive task. We analyzed intracranial electroencephalographic (EEG) signals from epileptic patients implanted on therapeutic grounds with depth electrodes while they performed reading tasks emphasizing visual, phonological, or semantic processes under different attention conditions. Time–frequency (TF) analysis of the cortical signals revealed a negative GBR in the ventral lateral prefrontal cortex.

Materials and Methods

Subjects

The 3 participants in the study (P1, P2, and P3) were women, right-handed, native French speakers and aged 25, 39, and 26 years. All 3 were candidates for surgery for their drug-resistant partial epilepsy. Magnetic resonance imaging was normal in P3 but showed a left hippocampal sclerosis with left posterior parietal atrophy in P1 and a left hippocampal sclerosis in P2.

As the location of the epileptic focus could not be identified using noninvasive methods, intracerebral recordings were made from these by means of stereotactically implanted multilead depth electrodes (SEEG), an example of which is shown in Figure 1. These recordings indicated that the epileptogenic foci were located in the left anteromesial
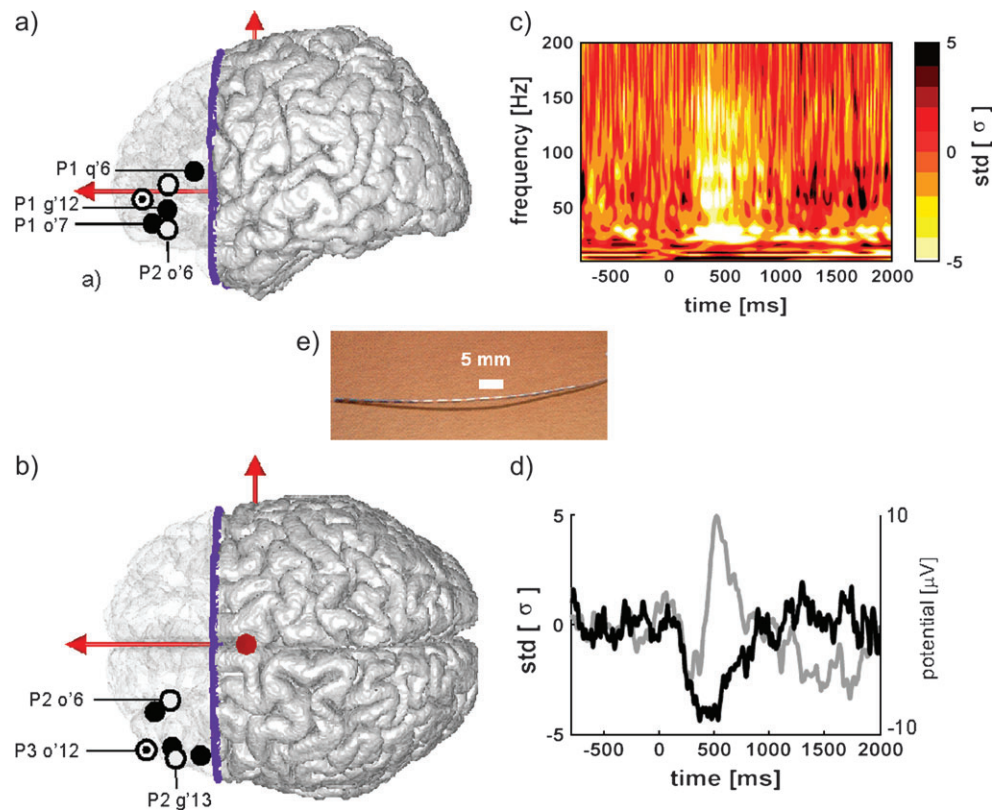
Figure 1. Transient deactivation in the ventral lateral prefrontal cortex during single word reading. Left panels show the localization of the 5 VLPFC sites showing stimulus-induced deactivations in the STRINGS experiment, projected onto the lateral and top view of a 3D reconstruction of the Montreal Neurological Institute single-subject magnetic resonance imaging. Patients are coded by colored symbols; the site names refer to Table 1. The figure also shows site q'6, in Broca area of patient P1, where a stimulus-induced activation was found. (*c*) TF representation of the energy modulation induced in site o'7 (P1) by words in the STRINGS experiment (semantic condition); for each frequency, the energy is expressed in units of the standard deviation of the (−200:−100 ms) prestimulus period. (*d*) Time course of the evoked potentials (in gray) and the energy modulation (in black) in the (20–150 Hz) frequency band (in standard deviation of the [−200:−100 ms] prestimulus period), same site and condition as in (*c*). Note that the deactivation can only be seen in the energy profile not in the evoked potential. (*e*) Multisites depth electrode.

temporal cortex for P1 and P2 and in left anterior temporal cortex for P3.

Selection of implanted sites was made on purely clinical grounds with no reference to the present experimental protocol. The patients had previously given their written informed consent to participate in the experiment.

Electrode Implantation

For each patient, 10–13 semirigid electrodes (see Fig. 1) were implanted in cortical areas suspected of being the origin of seizures. For each patient, these areas covered parts of the mesial and lateral temporal cortices as well as regions of prefrontal cortex. Each electrode had a diameter of 0.8 mm and comprised, depending on the target region, between 10 and 15 two-millimeter-long contacts, spaced 1.5 mm apart (Dixi, Besançon, France). Electrode contacts were identified on the patient's individual stereotactic scheme and then anatomically localized using the proportional atlas of Talairach and Tournoux (Talairach and Tournoux 1988).

Experimental Paradigms

The patients successively performed 2 experimental tasks. In the first task (STRINGS), the patients were presented with strings of characters that either formed words ("semantic" condition), pseudowords ("phonological" condition), or consonant strings ("orthographic" condition). Each string was presented for 2 s, before a 1.5-s (on average) period during which they had to indicate by means of a response button with their left index finger whether 1) the words were names of living or non-living entities (semantic condition), 2) the pseudowords ended with vowel sounds (e.g., gurdo) or consonant sounds (e.g., ziple) (phonological condition), and 3) the consonant strings contained the

same letter twice (orthographic condition). Each patient completed 13 blocks, each consisting of one series of each stimulus type with 20 consecutive stimuli per series (i.e., 60 per block).

The second task (STORIES) was designed to mimic more natural reading conditions and study the effect of attention on reading. The patients were presented with a succession of words, some printed in green type others in red (type color displayed in random order). Each color told a different story, and the patient had to attend to and remember only one of the 2, the green or the red. Each story was 200 word long. There was one attended story per block and 6 consecutive blocks. The attended color changed with each new block. The patient had to retell the experimenter the attended story at the end of each block. Word presentation subtended 2.1 degrees of eccentricity horizontally. On average, words were presented for 100 ms every 700 ms. This task was taken from an earlier evoked potential study (Nobre et al. 1998) and adapted to slightly longer interstimuli intervals.

Recordings and Stimulation

The SEEG studies were performed extraoperatively according to our routine procedure (Kahane et al. 2004). Intracerebral recordings during the experimental paradigm were obtained using an audio video EEG monitoring system (Micromed, Treviso, Italy), allowing for the simultaneous recording of 63 depth EEG channels sampled at 512 Hz [0.1–200 Hz bandwidth]. The experiment was conducted 4 days after electrode implantation. One of the contact sites in the white matter was chosen as reference.

TF and Evoked Potential Analysis

For each single trial showing no sign of epileptiform activity, bipolar derivations computed between adjacent electrode contacts were

analyzed 1) using the standard evoked potential procedure and 2) in the TF domain by convolution with complex Gaussian Morlet's wavelets (Tallon-Baudry et al. 1997). This convolution provided for each trial a TF power map $P(t,f)=|w(t,f)*s(t)|^2$, where $w(t,f)$ was for each time t and frequency f a complex Morlet's wavelet $w(t,f)=A\exp(-t^2/2\sigma_t^2)\exp(2i\pi ft)$, with $A=(\sigma_t\sqrt{\pi})^{-1/2}$ and $\sigma_t=1/(2\pi\sigma_f)$ and σ_f a function of the frequency f: $\sigma_f=f/7$. The investigated frequency range was 1–200 Hz. These TF maps were then averaged across all trials in a given experimental condition. In the figures, these maps are normalized for visualization purposes following procedures described in the legends.

TF maps were used to identify recording sites with negative GBRs (i.e., with a lower energy level in the gamma-band after vs. before stimulus presentation, when comparing spectral energy averaged across the trials) and for each such site to define a TF region of interest (TFROI) centered on the peak of this negative response. For reasons explained at the beginning of the Results, TFROI had a broad frequency extent (20–150 Hz) (adjusted to the frequency extent of negative responses), and their duration was set to 100 ms.

Statistical Analysis

For each site with a negative GBR, pre- and poststimulus energy levels were compared statistically with Wilcoxon tests in each experimental condition: the Wilcoxon test is a nonparametric equivalent of a paired t-test comparing in this case, across the trials, the average energy in the TFROI (frequency extent = [20–150 Hz], duration = 100 ms, centered on the peak of the negative GBR identified in TF maps), with the energy measured in a tile of similar frequency extent (20–150 Hz) over a 100-ms prestimulus baseline period (from –200 ms to –100 ms). To correct for multiple comparisons (Bonferroni correction, number of sites × number of experimental conditions [STRINGS {3} + STORIES {2}]), significant activations and deactivations were defined by a P value less than 0.002.

The effect of experimental condition in each TFROI (i.e., semantic vs. phonological condition in the STRINGS experiment) was investigated via a Kruskal–Wallis nonparametric analysis (in the text: KW) comparing the energy values measured in each trial of the 2 conditions in the TFROI (correction for multiple comparisons as for Wilcoxon tests).

EEG signals were evaluated with the software package for electrophysiological analysis (ELAN-Pack) developed at the INSERM U821 laboratory.

Results

Behavioral Responses

In the STRINGS experiment, the percentage of correct responses was generally high in all 3 tasks (semantic: P1, 89%; P2, 99%; P3, 99%; phonologic: P1, 91%; P2, 92%; P3, 88%; orthographic: P1, 92%; P2, 95%; P3, 95%). An analysis of reaction times showed that in general responses were faster in the semantic task [semantic: P1, mean reaction time = 1000(standard deviation = 260 ms); P2, 780(200); P3, 1000(230); phonologic: P1, 1210(290); P2, 990(320); P3, 1550(300); orthographic: P1, 1160(290); P2, 1450(310); P3, 1450(300)]. In the STORIES experiment, the debriefing sessions following each block clearly indicated that patients had read the target story, captured its global meaning, and were able to tell the correct sequence of events.

Electrophysiological Responses

STRINGS experiment: TF analysis and statistical comparison between pre- and poststimulus energy level in the gamma band revealed 5 sites with negative GBRs (P1, o′7, g′12; P2, o′6, g′13; P3, o′12, see Table 1). While, in each patient, electrodes sampled widely distributed portions of the frontal lobes, such deactivations were found exclusively in the anterior portion of the left ventral lateral prefrontal cortex, extending mostly

Table 1

Anatomical locations of each site of interest

| Patient	Site name	Talairach (mm)	Anatomical region	
P1	o′7	−30, +46, −11	Mid frontal gyrus (BA 10-11)	
P1	g′12	−47, +37, −5	Inf. frontal gyrus (BA 47-10)	[AQ9]
P1	q′6*	−50, +23, +11	Inf. frontal gyrus (BA 45) [Broca, pars triangularis]	
P2	o′6	−25, +39, −14	Inf. frontal gyrus (BA 47)	
P2	g′13	−51, +36, +6	Inf. frontal gyrus (BA 45–46)	
P3	o′12	−49, 49, 0	Mid frontal gyrus (BA 10-46)	

The time intervals specified correspond to the intervals during which the energy in the 20–150 Hz band was significantly lower (Wilcoxon, $P < 0.0001$) than in the 200 ms preceding the stimulus. The values are for the semantic condition in the STRINGS experiment and for the attention condition in the STORIES experiment. The * star sign indicates an activation, not a deactivation. [AQ10]

over Brodmann areas (BAs) 10, 47 and over portions of BAs 11, 46, and 45 (see Table 1 and Fig. 1). These negative responses occurred concurrently with positive GBRs (stimulus-induced energy increases) in frontal regions often associated with reading or attentional processes, such as Broca's area (see site q′6 [P1] and r′7 [P2]; see Fig. 2 and supplementary Fig. 1) and the dorsolateral prefrontal cortex (see site g′14 [P3] in supplementary Fig. 1). Overall, across the 3 conditions, there were 9 frontal lobe bipoles with significant positive GBRs (P1, 3; P2, 1; P3, 5), whereas 25 showed no significant response (positive or negative) (P1, 7; P2, 11; P3, 7).

These responses were easily characterized by their TF maps (Fig. 1, and supplementary Fig. 1): the presentation of the letter strings induced a significant energy decrease in a broad frequency range (>20 Hz), including, in addition to gamma, the high beta band. Although the beta and gamma ranges have been shown to be functionally dissociated in several studies, including studies from our group, the similarity of the effect in the 2 frequency bands did not allow us to consider them separately in the present case.

Figure 2 shows, for each site, the energy modulation induced in each condition of the experiment by letter strings in the 20–150 Hz range. For comparison purposes with a "neutral state," the energy has been normalized with respect to a 3-min period of rest that followed the experiment (Fig. 2) (through z-transform using mean and standard deviation of the energy measured during rest). This normalization aimed to determine whether stimulus-induced gamma suppression corresponded to 1) a return to rest level, that is, the transient interruption by stimulus onset of task-specific prestimulus (but not present at rest) neural activity—in which case the suppression should translate to a return to zero (rest level) in the graphs of Figure 2—or, rather, 2) an active suppression bringing energy level below rest value, that is, the interruption of a nontask-specific process, but which is simply part of the brain's general ongoing activity—in which case the suppression should translate in Figure 2 into a negative deviation from 0. As can be seen in the figure, the effect observed is not a return to rest level but an actual energy suppression relative to rest. The above normalization was also chosen to highlight possible baseline shifts in gamma-band energy relative to rest, that is, energy decreases (or increases) sustained throughout the task, relative to the level measured at rest, outside the context of the task. These should be differentiated from stimulus-induced responses, which are transient variations due to the stimulation. As can be seen in Figure 2, there were no baseline shifts in the present experiment, as prestimulus energy levels did not deviate from values measured at rest.
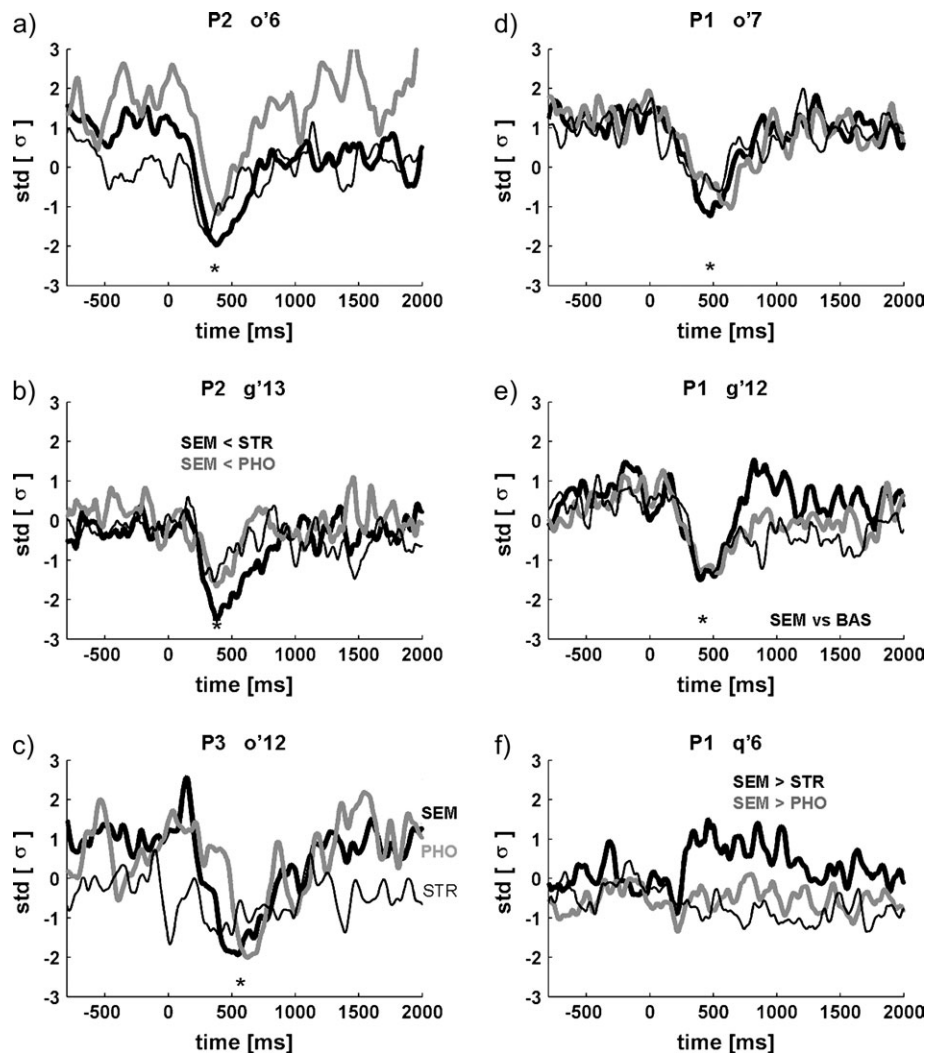
Figure 2. Deactivations in response to letter strings presentation in the STRINGS experiment. Each plot represents the time course of the energy recorded in the (20–150 Hz) frequency band in one of the 3 experimental conditions (bold black: semantic; black: orthographic; bold gray: phonological), the energy is expressed in standard deviations from the energy level recorded during a 3-min rest period that followed the experiment, and the zero value corresponds to the mean energy at rest. Stars signal significant negative peaks in the 3 conditions (Wilcoxon comparison with [−200 ms;−100 ms] prestimulus energy level). In graph (*b*), this negative peak was significantly stronger in the semantic condition than in the orthographic and phonologic conditions (standard error of mean (SEM) < STR, SEM < PHO, Kruskal–Wallis comparison). For comparison purpose with these deactivations, graph (*f*) shows a significant energy increase observed in the same frequency band in a slightly posterior site in the inferior frontal gyrus, in Broca's area pars triangularis (P1, q'6; [50, +23, +11]); this increase occurred only in the semantic condition.

As is evident from Figure 2, the deactivation time course was fairly reproducible across patients and recording sites, with a gradual energy decrease starting between 150 and 350 ms after stimulus onset and a negative peak at around 500 ms followed by a gradual return to baseline level at latencies ranging between 650 and 950 ms. In particular, the return to baseline was not faster in the semantic condition associated with faster reaction times. This "V"-shaped energy suppression curve was thus reproducible across the 3 experimental conditions, although, in one patient (P2, g'13), it was stronger in the semantic condition than in the phonological and orthographic conditions (Kruskal–Wallis comparison).

STORIES experiment: This second experiment tested whether negative GBRs were attention dependant. As expected from the previous results, negative stimulus-induced deactivations were also found in this second reading experiment, at least for attended words: in 3 sites (o'7 and g'12 in P1; g'13 in P2, see Table 1), all part of the group of 5 sites previously described

(Fig. 3). At these 3 sites, the deactivation frequency range and timing were similar in both the STORIES and STRINGS experiments. However, observed deactivation was function of the subjects' attention levels, as unattended words failed to trigger gamma-band energy suppression. In effect, we observed no significant difference between pre- and poststimulus gamma-band energy for unattended words.

As in the STRINGS experiment, the comparison with post-task rest level (Fig. 3) revealed that the observed GBS brought the energy value below its rest level, eliminating the possibility of it being due to the transient interruption of a prestimulus process specific to the task. We observed one exception (P1, g'12), where the gamma-band energy in the intratask baseline (recorded during the 100 ms preceding the stimulus) was itself above the level in the rest block.

The online supplementary data present results from 3 additional patients recorded during slightly similar tasks in the same brain structures. These results largely confirm the

observations presented above of a transient energy suppression in a broad gamma band in response to words stimuli during reading, dependant upon the subjects attention and localized in the ventral lateral prefrontal cortex (see supplementary Materials).

Discussion

Our results evidence a transient suppression of activity in the left ventral lateral prefrontal cortex (BA 47/11) during the active processing of letter strings, including words. This suppression peaked around 500 ms after stimulus presentation and occurred only for attended stimuli. These findings suggest a flexible mechanism to interrupt transiently local neural communication in cortical regions not relevant to the task-at-hand.
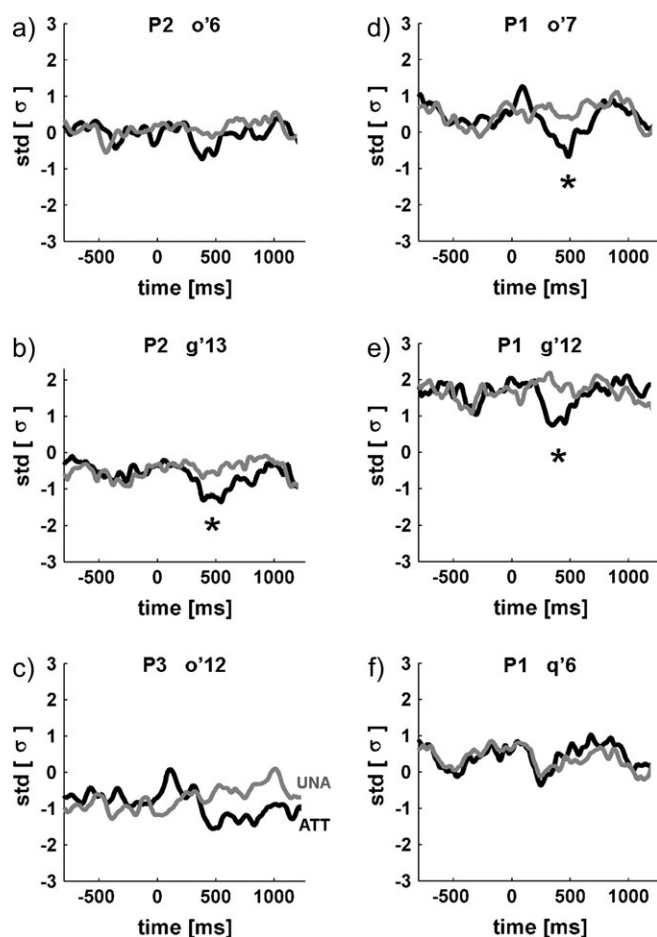
Energy recorded in the gamma range by intracranial EEG electrodes is extremely sensitive to the degree of local synchronization within the recorded neural population, indicating that energy decreases correspond to local desynchronization. En-

Figure 3. Effect of attention on the VLPFC responses in the STORIES experiment. Same presentation as in Figure 2 but for responses to attended (black) and unattended (gray) words in the STORY experiment. Each plot represents the time course of the energy recorded in the (20–150 Hz) frequency band. Stars signal significant peaks of deactivation relative to the (−200:−100 ms) prestimulus period (Wilcoxon test) for attended words. Unattended words induced no significant deactivation, and at all latencies indicated by star signs, energy was significantly lower for attended versus unattended words (Kruskal–Wallis comparison). Figure (f) shows the response to attended and unattended words in Broca's pars triangularis (P1, q'6), with no significant deactivation or difference between the 2 conditions.

hanced gamma-band synchronization has been proposed as a mechanism facilitating communication between neighboring neurons participating in the formation of transient neural networks (Fries 2005) and mediating the influence of a given local neural population on distant cortical regions (Varela et al. 2001). In particular, gamma-band synchronization has been proposed as a gain control mechanism contributing to attentional selection (Salinas and Sejnowski 2001). Conversely, transient interruption of gamma synchronization might be an efficient way of shutting down local neural communication, disassembling local neural networks, and reducing the influence of a given cortical region on the rest of the system. A prediction would be that this mechanism should be quite general and observed throughout the brain. However, to our knowledge and quite surprisingly, these results constitute the first direct observations of such high-frequency neural deactivations in a high-level human brain area. This might be partially explained by the fact that such effects can only be revealed through the rare conjunction of focal intracranial electrophysiological recordings in humans from high-level brain areas during cognitive tasks and EEG spectral energy quantifications. Although there have been numerous intracranial EEG studies in humans performing cognitive tasks (Lachaux et al. 2003), common analysis techniques focusing on the evoked potentials is not best suited to detecting decreases in neural activity relative to a baseline level, as evident from Figure 1. As more and more studies using the above-exposed conjunction, evidence of stimulus-induced GBSs might start accumulating.

There is an obvious parallel between the effects reported here and task-induced metabolic deactivations (TIDs) found in fMRI and PET studies, which refer to regional decreases in blood flow or oxygen consumption during an active task relative to a "resting" or "passive" baseline (Gusnard and Raichle 2001). Despite their possible importance for cerebral functional organization, relatively little is known about the neural phenomena underlying TIDs or about their dynamics. In particular, original studies of TIDs, which used block-design paradigms and compared metabolic activity during "task" versus "rest" blocks (e.g., Shulman et al. 1997; Mazoyer et al. 2001) have mostly emphasized sustained deactivations observed over an entire task. However, because the cognitive subprocesses associated with specific brain regions are usually transient and mediated by neural activations lasting a couple of hundreds of milliseconds or less, it is logical to infer that deactivations should also exist at this shorter timescale and play a major functional role in cognition.

Our knowledge about TID would be greatly augmented if a strong correspondence was established between TID and GBS. Considering recent evidence that gamma-band activations coincide spatially with regional blood oxygenation level–dependent (BOLD) increases (Niessing et al. 2005; Lachaux et al. 2007), one might assume that GBS should be associated with BOLD deactivations relative to rest. Still, this putative symmetry may be wrong if gamma suppression is an active mechanism associated with metabolic demands.

As we could not test this hypothesis directly with fMRI data from the same patients, or in the same task, we searched for reading-induced ventral lateral prefrontal cortex (VLPFC) deactivations in the fMRI/PET literature. We found that, in general, most fMRI studies have contrasted BOLD signals between active conditions, involving for instance semantic versus phonological processing (Pugh et al. 1996), and may thus have failed to detect deactivations relative to rest that do

not differ between visual, phonological, and semantic tasks. Nevertheless, there have been reports of fMRI deactivations in BA 47/11 during reading: Shulman et al. (1997) reviewed 9 PET studies to determine the consistency of blood flow decreases in active visual tasks relative to passive viewing and observed that reading tasks induced activation decreases in the VLPFC region described in the present study (and referred to as BA 47/10). Another meta-analysis study (Mazoyer et al. 2001) tried to summarize fMRI/PET deactivations induced by several tasks (including language tasks, visual discrimination, mental calculation, or mental imagery) relative to conscious resting state and revealed a network involving predominantly mesial frontal structures, precuneus, angular, and posterior cingulate gyrus—but also, if to a lesser extent, BA 47/11.

One should also emphasize that the short duration of the VLPFC gamma suppression might evoke only weak BOLD reductions. The phenomenon we describe is a transient negative response to the stimulus (an "event-related suppression"), which should be differentiated from a baseline shift, that is, a sustained suppression of activity throughout the task (task-induced deactivations). fMRI or PET task-induced deactivations have often been observed in block-design protocols comparing the overall BOLD signal at rest versus task, as in the 2 meta-analysis studies cited above; as such, they were necessarily more sensitive to baseline shifts than to transient stimulus-induced negative responses. The latter kind of deactivation can be detected using fMRI event-related paradigms, and 2 such studies have found evidence for transient, event-related suppressions (Slotnick et al. 2003; Deary et al. 2004). Such transient suppressions have been observed in visual tasks in the precuneus (Deary et al. 2004) and in visual cortex (Slotnick et al. 2003) in relation to inhibitory effects of visual attention on neural representation of unattended stimuli. These event-related TIDs extended over the course of seconds and could not be associated with precisely timed processes because of the limited time resolution of fMRI. However, we believe that fMRI counterparts of the suppression effects reported in this study are more likely to be identifiable in event-related fMRI paradigms than in block-design paradigms.

In summary, there are indications, but certainly no definitive evidence, that the GBS reported here in the VLPFC might correspond to TIDs found in PET and fMRI.

Why would BA 47/11 deactivate during reading? A first interpretation is that this region is involved in verbally mediated thought. This possibility was explicitly proposed by Shulman et al. (1997) in interpreting the stronger PET activation of this region during passive fixation relative to reading tasks. This was also suggested by Mazoyer et al. (2001), who emphasized that conscious rest episodes, during which they found enhanced VLPFC activity relative to tasks, are most frequently associated with inner speech (as reported by experiments' participants; Mazoyer et al. 2001). This is consistent with the immediate proximity of VLPFC to several language areas, including Broca's area. Further, BA 47/11 has been associated in several studies with semantic memory: it might be involved in accessing, maintaining, and manipulating semantic representations (Gabrieli et al. 1998; Poldrack et al. 1999; Fletcher and Henson 2001; Otten et al. 2001). A region subserving semantic storage might conceivably be recruited by verbally mediated thought. In this context, GBS would correspond to a transient interruption of the ongoing background thinking process, serving to maximize receptivity to new verbal information. Such interruption should bring gamma energy below rest level and would cease as subjects stop attending to stimuli and the internal monologue resumes. Clearly, numerous control experiments would be needed to confirm this hypothesis; in particular, the suppression of verbally mediated thought should not just occur during language tasks but possibly also during any attention-demanding task; this could be tested in subsequent, nonverbal, experiments.

This last point relates directly to the question of whether the deactivations we observed were task specific or nontask specific (Gusnard and Raichle 2001), which were difficult to test because both of our tasks engaged primarily language-related functions. Task-specific deactivations are assumed to be modality specific and most often found in sensory or motor cortices (McKiernan et al. 2003; Lachaux et al. 2005). In contrast, task-unspecific decreases are most often found in cortical areas involved in higher level cognitive processing (Gusnard and Raichle 2001; McKiernan et al. 2003). The fact that the deactivation also occurred in response to nonsemantic material, the consonant strings, may suggest that it was not specific of the task; however, this control task involved mental counting and therefore inner speech. Also, the deactivation was sometimes stronger in the semantic condition than in the phonological condition; however, it is not clear whether this could be attributed to a variation in the specific process at hand or to a difference in attentional load between the 2 conditions.

A further interpretation of the VLPFC deactivation is that it provides an unspecific emotional gating aimed at inhibiting adverse emotional signals to maximize the level of performance. This was proposed by Pochon et al. (2002) to explain the deactivation observed in fMRI during a *n*-back memory task, who motivated their interpretation by the proximity of the limbic system. Our data were not sufficient to support or invalidate this hypothesis. We expect further studies will test this possibility.

The timing of the observed GBS is in itself intriguing: despite the fact that the stimulus presentation duration (2000 vs. 100 ms) and interstimulus interval (700 vs. 3500 ms) were very different in the 2 experimental conditions, STRINGS and STORIES, the time course of the deactivation was similar, with a peak around 500 ms in all cases. Also, reaction times in the 3 tasks of the STRINGS experiment were different, faster for the semantic task, and, still, the timing of the deactivation did not change across tasks. This raises the question of why the deactivation would not last during the entire processing of the stimuli? The GBS seems like a reflex phenomenon with a fixed timing and a rapid, automatic return to baseline. What would happen if 2 words were presented in rapid succession? If there is a limit to how fast 2 GBS cycles can follow each other (a refractory period), then we would expect the second stimulus failed triggering suppression of gamma-band activity and therefore be processed as unattended words in the STORIES experiment. This might potentially translate in poor processing by the subject, as in the well-known attentional blink phenomenon (Raymond et al. 1992). Indeed, several authors have suggested that gamma synchrony may play a major role in this phenomenon (Fell et al. 2002; Kranczioch et al. 2005).

An additional question, which could not be answered here, is whether the VLPFC gamma suppression is necessary for words to be processed. At this point, we cannot think of an experiment that would demonstrate such a causal link. But, alternatively, it might be possible to induce an artificial transient suppression of activity in the VLPFC, with transcranial magnetic stimulation,

500 ms after word presentation and test the effect on memorization. Our results predict that words should be better memorized if followed by transcranial magnetic pulses.

Supplementary Material

Notes

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