Temporal Lobe Interictal Epileptic Discharges Affect Cerebral Activity in “Default Mode” Brain Regions

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Abstract: A cerebral network comprising precuneus, medial frontal, and temporoparietal cortices is less active both during goal-directed behavior and states of reduced consciousness than during conscious rest. We tested the hypothesis that the interictal epileptic discharges affect activity in these brain regions in patients with temporal lobe epilepsy who have complex partial seizures. At the group level, using electroencephalography-correlated functional magnetic resonance imaging in 19 consecutive patients with focal epilepsy, we found common decreases of resting state activity in 9 patients with temporal lobe epilepsy (TLE) but not in 10 patients with extra-TLE. We infer that the functional consequences of TLE interictal epileptic discharges are different from those in extra-TLE and affect ongoing brain function. Activity increases were detected in the ipsilateral hippocampus in patients with TLE, and in subthalamic, bilateral superior temporal and medial frontal brain regions in patients with extra-TLE, possibly indicating effects of different interictal epileptic discharge propagation.

Hum Brain Mapp 28:1023–1032, 2007. © 2006 Wiley-Liss, Inc.

Key words: temporal lobe; focal epilepsy; default mode; EEG; fMRI; consciousness; resting state

INTRODUCTION

Simultaneous electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) has been used in individual patients to map the brain areas involved in interictal epileptic discharges (IED) (Salek-Haddadi et al., 2003a) and in particular the area giving rise to the discharge—the “irritative zone” (Rosenow and Luders, 2001). In addition, however, EEG-fMRI allows the impact of epileptic discharges on ongoing brain function to be assessed (Gotman et al., 2005; Laufs et al., 2006) and the effects of epileptic activity across different patient groups to be studied (Hamandi et al., 2006).

Brain areas preferentially active on functional imaging during conscious rest include the precuneus and posterior cingulate, bilateral temporoparietal and medial prefrontal cortices (Mazoyer et al., 2001; Raichle et al., 2001; Shulman...
| Case | Number of IED during 35 min fMRI | Description of clinical EEG | Clinical localization | Seizure type | Structural MRI | Epilepsy syndrome |
|------|---------------------------------|----------------------------|----------------------|--------------|----------------|-------------------|
| 1    | 404                             | No lateralization          | L. Ant Temp Sp       | L. Temp      | SPS (epigastric), CPS | L-HS              | X                 |
| 2    | 638                             | No lateralization          | L. Ant Temp Sp       | L. Temp      | SPS, CPS, SGTCS     | L-HS              | X                 |
| 3    | 630                             | No clear change            | L. Ant Temp Sp       | L. Temp      | CPS, SGTCS          | L-HS              | xTLE              |
| 4    | 72                              | Independent R and L seizure onsets | L Ant mid-Temp SW | Temp, uncertain laterality | CPS | L-HS | xTLE |
| 5    | 45                              | Subdural electrodes: seizure onset outside of the resected areas, possibly contralateral | Widespread theta, frequent Temp shW, and redominantly L mid Temp Sp | L Temp | CPS, SGTCS | L Temp lobe resection | Post L Temp lobe resection for DNET, plus R-HS | X |
| 6    | 58                              | Initially bilateral theta, then left sided rhythmic shWs | L. Temp slow waves and Sp plus R Temp Sp during sleep | Temp | CPS, SGTCS | MRI negative | Cryptogenic | X |
| 7    | 190                             | –                            | L. Temp slowing with frequent L Ant Temp Sp | L Lateralised | SGTCS | MRI negative | Post-traumatic | X |
| 8    | 79                              | L hemisphere                | L. Temp slow and shWs | L Temp | CPS | L-HS | X |
| 9    | 166                             | No clear lateralisation     | L. slow activity, Bil SW, pSpW, L Temp Sp | Diffuse | CPS, SGTCS | Focal lesion L middle Temp gyrus, L Temp lobe smaller than R | DNET | X |
| 10   | 82                              | –                            | Widespread, R Sp, shW, and sharp and slow waves maximal frontocentral | R Lateralised | SPS (motor) | Diffuse cortical thickening R hemisphere, within Par and Occ lobes, extending to frontal region | MCD | X |
| 11   | 50                              | No clear changes            | Bil, Post Temp/Occ sharp and slow wave complexes with L Sp | Bilateral | CPS, SGTCS | Widespread band and subcortical nodular heterotopia, predominantly posterior | MCD | X |
| 12   | 230                             | –                            | L. slow activity with L Post Temp Sp | L Lateralised | CPS, SGTCS | L cystic encephalomalacia | Perinatal subarachnoid haemorrhage | X |
| 13   | 73                              | –                            | Over central region Bil SW | R Frontal | SPS (focal motor), SGTCS | R parietal open leptomicrogyria | MCD | X |
| 14   | 477                             | No change                   | Continuous L Par Sp  | L Parietal | SPS (sensory) | Thickened cortex in the L Ant-inferior Par region just extending into the inferior Front gyrus (FCD) | MCD | X |
| 15   | 97                              | –                            | L. Sp, shW, and slow waves, some Bil synchronous and occasionally R-sided | Diffuse | CPS, SGTCS | Extensive polymicrogyria involving both hemispheres, R > L | MCD | X |
This network expresses strong functional connectivity at rest (Greicius et al., 2003; Laufs et al., 2003) and has higher overall activity during resting wakefulness than in states of impaired consciousness such as sleep, anaesthesia, and coma (Laureys et al., 2004) or during generalized spike and wave discharges (GSW) (Archer et al., 2003; Gotman et al., 2005; Hamandi et al., 2006; Laufs et al., 2006). Activity in these regions also decreases during a wide range of cognitive tasks (Mazoyer et al., 2001; Raichle et al., 2001) and this observation of “task-independent deactivation” has led to the proposal that activity in these structures serves as a “default mode” of brain function that predominates whenever subjects are awake, but not performing any explicit task (Raichle et al., 2001).

Functional connectivity in the default mode network has been shown to be affected in patients with Alzheimer’s disease (Greicius et al., 2004), and temporal lobe connectivity in particular (Wang et al., 2006). Recently, spontaneous alteration of functional connectivity between language areas was also demonstrated in patients with temporal lobe epilepsy (TLE) (Waites et al., 2006).

We sought to test the hypothesis that IED occurring during the resting state would result in a relative BOLD signal decrease in default mode brain areas. In patients lying at rest with their eyes closed in the scanner we expect the default mode network to be active. Interruption of resting state activity as a direct consequence of IED should then result in a relative decrease in BOLD signal within the default mode areas. Aside from testing this hypothesis we also set out to explore any BOLD signal increases common to the group, as these may reveal underlying networks not detectable at the individual level. We investigate the effects of IED in two groups of patients with focal epilepsy, namely with TLE and extra-TLE.

**MATERIAL AND METHODS**

**Patients**

63 patients with focal epilepsy underwent EEG-fMRI (Salek-Haddadi et al., 2006). Of those, we selected all scanning sessions with a spiking rate of between one and twenty IED per minute during data acquisition, corresponding to the mid-range level of activity in the group. This selection was necessary to facilitate a balanced design for the purpose of group analysis (Friston et al., 2005). All patients gave written informed consent (Joint Ethics Committee of the National Hospital for Neurology and Neurosurgery and Institute of Neurology). Clinical and experimental details are listed in Table I.

**Simultaneous Acquisition of EEG and fMRI**

The methods and results pertaining to single-subject analyses are reported elsewhere (Salek-Haddadi et al., 2006). Briefly, using MR-compatible equipment, ten EEG channels were recorded at Fp1/Fp2, F7/F8, T3/T4, T5/T6, O1/O2, et al., 1997). This network expresses strong functional connectivity at rest (Greicius et al., 2003; Laufs et al., 2003) and has higher overall activity during resting wakefulness than in states of impaired consciousness such as sleep, anaesthesia, and coma (Laureys et al., 2004) or during generalized spike and wave discharges (GSW) (Archer et al., 2003; Gotman et al., 2005; Hamandi et al., 2006; Laufs et al., 2006). Activity in these regions also decreases during a wide range of cognitive tasks (Mazoyer et al., 2001; Raichle et al., 2001) and this observation of “task-independent deactivation” has led to the proposal that activity in these structures serves as a “default mode” of brain function that predominates whenever subjects are awake, but not performing any explicit task (Raichle et al., 2001).

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TABLE II. Blood oxygen level-dependent signal decreases in regions of interest in 9 patients with temporal lobe epilepsy (TLE) and respective findings in 10 patients with extra-TLE

| Brain region of interest | Brodmann area (BA) | Center of region of interest (mm) | X  | Y  | Z  | Z-score | P value |
|--------------------------|--------------------|-----------------------------------|----|----|----|---------|---------|
| 9 patients with TLE      |                    |                                   |    |    |    |         |         |
| Precuneus                | BA 7               |                                   | -5 | -49| 40 | 2.9     | 0.030   |
| Posterior Cingulate      | BA 31              |                                   | 1  | -35| 34 | 2.7     | 0.048   |
| Frontal Gyrus, left      | BA 8/9             |                                   | -11| 41 | 42 | 2.0     | 0.135   |
| Frontal Gyrus, right     | BA 8/9             |                                   | 5  | 49 | 36 | 2.7     | 0.043   |
| Inferior Parietal Lobule, left | BA 40 |                                   | -53| -39| 42 | 2.7     | 0.047   |
| Inferior Parietal Lobule, right | BA 40 |                                   | 45 | -57| 34 | 2.0     | 0.144(1) |
| (1)                      | BA 40              |                                   | 56 | -48| 40 | 2.7     | 0.049   |
| 10 patients with extra-TLE|                    |                                   |    |    |    |         |         |
|                          |                    | No deactivations found in regions of interest nor across the whole brain at P < 0.001 uncorrected for multiple comparisons |

Results of region of interest analyses (random effects group analyses). Z-scores are reported for activations within spherical search volumes (1 cm in diameter) centered at coordinates taken from (Shulman et al., 1997); P values are corrected for multiple comparisons within these volumes. Note that although the activation in the region of interest positioned in the right inferior parietal volume did not reach significance, a nearby area of activation did (indicated by (1)). All coordinates are given in Talairach space, converted from Montreal Neurological Institute space using mni2tal (http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach).

Fz (ground) and Pz as the reference (10–20 system), and bipolar electrocardiogram (Krakov et al., 2000). Seven hundred and four T2*-weighted single-shot gradient-echo echo-planar images (EPI; TE/TR: 40/3000, flip angle: 90°, 21 5 mm interleaved slices, FOV = 24 × 24 cm², 642 matrix) were acquired continuously over 35 min on a 1.5 Tesla Horizon EchoSpeed MRI scanner (General Electric, Milwaukee, WI). Patients were asked to rest with their eyes shut and to keep their head still. After gradient and pulse artifact reduction (Allen et al., 1998, 2000), IED were individually identified and the fMRI data were preprocessed and analyzed using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/). After discarding the first four image volumes, the EPI time series were realigned, normalized (MN305 space, SPM2) and the images spatially smoothed with a cubic Gaussian Kernel of 8 mm full width at half maximum.

**Statistical Parametric Mapping**

IED onsets were used to build a linear model of the effects of interest by convolution with a canonical hemodynamic response function (HRF, event-related design) and its temporal derivative to account for possible variations in the blood oxygen level-dependent (BOLD) response delay. Motion realignment parameters were modelled as a confound (Friston et al., 1996).

A single T-contrast image was generated per subject from the first (single-subject) level and the images used to inform a second level (group effect) analysis to test for any common patterns. Analyses were performed for both TLE and extra-TLE groups. A random effects model was used to identify any typical responses consistent across the patients (Friston et al., 1999). We used this approach to test the hypothesis that negative responses arose in one or more of the default mode areas: precuneus, posterior cingulate, frontal, and inferior parietal cortices bilaterally. For this purpose, regions of interest were defined as spheres with 1 cm diameter centered on coordinates given in Table II, taken from (Raichle et al., 2001; Shulman et al., 1997). The statistical images were thresholded at P < 0.05 (family wise error-corrected for multiple comparisons within the search volume). Any positive responses were further explored at a threshold of P < 0.001 (uncorrected at the single voxel level), and declared significant at P < 0.05 (corrected for multiple comparisons at the cluster level) as we were not testing a specific hypothesis.

**RESULTS**

**Common IED-Related Deactivations in Default Mode Areas in TLE but not in Extra-TLE**

On the basis of the inclusion criteria for group analysis, 19 scanning sessions were analyzed. They were divided into two groups: one group with TLE (n = 9) and one with extra-TLE (n = 10). The TLE group as a whole showed significant IED-related deactivation in the posterior cingulate, the precuneus, the left and right frontal and parietal lobes (Fig. 1, Table II, see supplementary web material for single subject maps). The extra-TLE group did not show any significant IED-related deactivations (Table II). There was no significant difference between the two groups in terms of the number of IED during fMRI (P = 0.1, T-test).

**Common IED-Related Activations Specific to TLE and Extra-TLE**

All 9 TLE patients had left-sided IED (some bilateral and one additional diffuse IED, see Table I). We looked for com-
Epileptic Spikes Affect Resting State

Random effects group analysis blood oxygen level-dependent signal decreases in temporal lobe epilepsy with focal interictal epileptic discharges (IED) in comparison with classic “default mode” brain regions. A: Brain areas where blood oxygen level-dependent signal is significantly negatively correlated with IED are projected onto axial slices (Z coordinates given below each slice) of a template average brain. B: Corresponding display of brain regions to which the term “default mode” was originally applied. Taken from Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. Proc Natl Acad Sci USA 2001;98:676-82; © 2001 National Academy of Sciences, USA. Note that despite spatial normalization there is slight anatomical discrepancy between slices displayed in panel A versus panel B. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Complex Versus Simple Partial Seizures

Activity in default-mode brain regions is correlated with consciousness (Laureys et al., 2004) and so we looked at the differences in habitual seizure-types between these groups. We found that simple partial seizures (SPS) were more frequent in the patients with extra-TLE (5/10 patients) and were the single focal seizure type in three of them. Only 3 of 9 patients with TLE had SPS, and these always occurred in addition to complex partial seizures (CPS).

Aetiology

Apart from localization, etiology was assessed as a possible explanatory variable accounting for the differing BOLD response patterns. We found hippocampal sclerosis to be the prevalent pathology in the TLE group (5 of 9 patients), while malformations of cortical development (MCD) were the prominent pathology in the extra-TLE group (5 of the 10 patients, Table I).
DISCUSSION

Principal Findings

In patients with TLE, IED were associated with significant deactivation in default mode brain areas and with significant activation in the ipsilateral medial temporal lobe. In the patients with extra-TLE no significant deactivations were found, and there were activations in the subthalamic nucleus, the superior aspects of both temporal and medial frontal lobes. The findings indicate that deactivations in default mode brain regions are characteristic of IED in TLE while not seen in extra-TLE, and that different common activation patterns were seen in the two groups.

Methodological Considerations

EEG-fMRI can be used to investigate the electrical and hemodynamic aspects of brain activity changes during task-free rest such as those associated with individual IED. To facilitate intersubject comparison we restricted our analyses to experiments with 1–20 IED per minute. This enabled us to make valid inferences at the group level using a two-stage procedure but restricted the group size to 19 patients (Friston et al., 2005).

Violations of homoscedasticity implicit in the loss of balance at the first level can make the second level inference less efficient, but would not bias or invalidate it. A full mixed-effect analysis could improve the power of the inference but this is not necessary because we already have significant results using the more conservative summary-statistic approach (Penny and Holmes, 2006).

The distributed and distinct areas of the brain involved in default mode activity were originally identified by positron emission tomography and fMRI meta analyses that included studies with block designs (Gusnard and Raichle, 2001). Stimulus-correlated motion and circulation or respiration effects are thus unlikely to cause the observed signal changes. Nevertheless we took the precaution of modelling realignment parameters reflecting motion as a potential confound. Likewise, the signal changes observed during resting state brain activity do not originate from the aliasing of physiological noise (De Luca et al., 2006).

A group analysis emphasizes features common to all group members while suppressing the individual variability at the same time. Such an approach will be less sensitive to

TABLE III. Common blood oxygen level-dependent signal increases in 9 patients with temporal lobe epilepsy (TLE) and respective findings in 10 patients with extra-TLE

| Brain region, cluster maxima (>8 mm apart) | Talairach coordinates (mm) | Z-score |
|-------------------------------------------|---------------------------|---------|
| Left Cerebrum Hippocampus                  | −26 −35 −1              | 3.7     |
| Left Cerebrum Parahippocampal gyrus       | −26 −11 −25             | 3.7     |
| Left Cerebrum Superior Temporal Gyrus     | −48 4 −6                 | 3.9     |
| Right Cerebrum Medial Frontal Gyrus Lobe  | 2 −8 52                 | 3.7     |
| Right Cerebrum Anterior Cingulate nucleus | 10 26 −6                | 3.4     |
| Left Cerebrum Subthalamic nucleus         | −2 −16 −6               | 3.3     |
| Right Cerebrum Superior Temporal Gyrus    | 64 −8 0                 | 3.4     |
| Right Cerebrum Middle Temporal Gyrus      | 56 −8 −6                | 3.2     |
| Right Cerebrum Postcentral Gyrus          | 8 −40 66                | 3.1     |

Results of explorative (P < 0.001 uncorrected for multiple comparisons) random effects group analyses. Main cluster grey matter coordinates are given as Talairach coordinates (compare Table II) and automatically labelled using Talairach Daemon V1.1 (Research Imaging Center, University of Texas Health Science Center at San Antonio). Z-scores are reported for local voxel maxima (extent threshold: 15 voxels).

*P < 0.05 corrected for multiple comparisons.
IED-correlated BOLD signal changes reflecting potentially different irritative zones but will rather indicate common pathways of IED propagation or their associated effects on ongoing brain function, that fail to reach statistical significance at the single subject level. A group analysis will therefore highlight common features (“typical effects”) for a group of patients investigated.

**Previous Work**

Deactivations in relation to IED were found in default mode brain areas in 10 of a series of 60 analyzed scanning sessions, mostly associated with bilateral or generalised bursts of spikes (Kobayashi et al., 2006). IED localization however was not further specified nor a group analysis performed. Meanwhile, the same group has recently also found ipsilateral medial temporal activation in a group of patients with temporal lobe IED (Grova et al., 2006).

Using Single Photon Emission Computed Tomography (SPECT), Van Paesschen and coworkers described significant ictal hypoperfusion in the superior frontal gyrus and the precuneus in 90% of TLE patients with complex partial seizures studied, plus hypoperfusion in temporal, occipital, and cerebellar regions (Van Paesschen et al., 2003). Bluemenfeld et al., using EEG-SPECT found that temporal lobe seizure-related loss of consciousness was associated with bilateral decreases in cerebral blood flow in the frontal and parietal association cortex and retrosplenium. In contrast, however, when consciousness was preserved, such widespread changes were not seen (Blumenfeld et al., 2004).

The distribution of these ictal perfusion decreases is consistent with our interictal findings in those with TLE who mainly had CPS. Although failure to detect deactivations in default mode brain areas in those with extra-TLE does not translate to their absence, it does suggest that IED do not influence brain function in this network to the degree IED do in TLE.

**IED Propagation Affects Default Mode Network in TLE**

In TLE, epileptic activity may spread from the temporal lobe into one or more functionally interconnected default mode brain regions and the effect of propagated activity can be measured by fMRI. Epileptic networks can lead to widespread secondary inhibition of nonseizing cortical regions via subcortical structures (Norden and Blumenfeld, 2002). It has previously been reported that—even very short (Laufs et al., 2006)—GSW were associated with deactivations in default mode brain regions (Gotman et al., 2005; Hamandi et al., 2006; Laufs et al., 2006; Salek-Haddadi et al., 2003b).

Alarcon and colleagues proposed that in TLE a lesion may affect remote, functionally coupled normal brain regions and that IED may originate from separate regions, resulting in propagation to and recruitment of other neuronal assemblies (Alarcon et al., 1997). Indeed Ebersole and colleagues suggested that scalp EEG changes in TLE principally reflect propagated epileptic activity (Pacia and Ebersole, 1997). The current study supports the notion that temporal lobe IED affect an epileptic network rather than a circumscribed focus. Further, it may be inferred that the medial anterior temporal lobe structures are a crucial part of such a network in this group of patients with TLE, who had a variety of underlying pathologies at varying locations within the temporal lobe.

**The (left) Temporal Lobe and the Default Mode Brain Network**

Functional connectivity studies have identified the temporal lobe (Fox et al., 2005; Fransson, 2005), and more specifically the hippocampus (Greicius and Menon, 2004), as another part of the default mode network. Activity changes in the default mode network could thus be a consequence of IED-effects on the functionally connected hippocampus, or—as was demonstrated in the case of Alzheimer’s disease...
(Wang et al., 2006)—the result of disturbed functional connectivity between the hippocampus and other default mode regions. In patients with left TLE, Waites and colleagues have recently demonstrated that functional connectivity in the “language network” was disturbed (Waites et al., 2006). As our subjects all had left-biased IED, we could not investigate laterality influences on default mode activity. This would be interesting especially since verb generation tasks, for example, lead to left-lateralized temporal lobe activations (Rowan et al., 2004) and classically deactivate default mode brain regions (Burton et al., 2004).

Our findings do not address the issue of causality, but indicate a correlation between IED in TLE and default mode network fluctuations. A hypothetical alternative explanation is that alteration of the default mode (e.g. by an external cause) facilitates IED. In the case of GSW, a link with sleep spindles and arousal has already been demonstrated (Steriade, 2005).

An Analogy between the Thalamus in GSW and the Hippocampus in TLE

The hippocampus plays a central role in propagation of epileptic activity in TLE, and hippocampal sclerosis often accompanies different pathologies in the temporal lobe (Duncan and Sagar, 1987; Thom et al., 2005). An analogy could be drawn between the role of the thalamus in the propagation of GSW and the role of the hippocampus in the propagation of IED in TLE, with both resulting in antidromic deactivation of default mode brain regions.

Similarly, the activations seen in association with IED in the extra-TLE group suggest a different “propagation network” consisting of subthalamic nuclei, superior temporal lobe and medial frontal structures (Figure 3, Table III). This group however was more heterogeneous and this possibility remains speculative until a higher number and more defined groups of epilepsy syndromes have been studied.

Lack of Default Mode Deactivation in Extratemporal Lobe Epilepsy

Possible reasons for the lack of deactivations associated with IED in extra-TLE need consideration. These include a lack of sensitivity and the failure of scalp EEG to detect deep IED. Extratemporal IED propagation to the default mode network might not occur so readily and so may not have distant effects: Blume at al. showed that interictal activity in extra-TLE mainly remains within the lobe of origin (Blume et al., 2001).

As much as propagation of IED might depend on the lobe of origin, it may also be a function of underlying pathology. In this series, MCD was the prominent pathology in the extra-TLE group, and their pathoneurophysiology will be different to that of hippocampal sclerosis, for example. Further EEG-fMRI studies of patients with MCD and those with acquired lesions in temporal and extratemporal lobes are needed to resolve this issue.

IED Location-Independent Deactivation of the Default Mode Brain Areas

Our data suggest that activation of an epileptic network associated with TLE-IED is associated with the deactivation of the cerebral areas that are active during conscious rest, in the same way as deactivation occurs consequent to a cognitive activation paradigm (Gusnard and Raichle, 2001). Our results indicate further that default mode brain areas deactivate irrespective of the IED location within the temporal lobe. Such decreases are therefore not epilepsy-specific, but may instead reflect an alteration of the mental state, in particular consciousness (Gotman et al., 2005; Laufs et al., 2006; Salek-Haddadi et al., 2003b). In focal epilepsy, fMRI deactivations have been found to correlate less with spike location and generally occur later than activations (Aghakhani et al., 2006; Bagshaw et al., 2004) and may thus reflect such “downstream” cognitive effects. In contrast, the activations we found in TLE are closer to the spike origin (Salek-Haddadi et al., 2006).

Possible Implications of Common (De-)activation of Brain Areas

Although generally considered a subclinical and purely an EEG event, TLE-IED have been shown to be associated with transient cognitive impairment and a decrease in reaction time (Binnie, 2003; Shewmon and Erwin, 1988). Our finding that IED in TLE were associated with an alteration of resting state brain function raises the possibility that IED might also affect activity in regions supporting specific cognitive functions during a task. In this study, when patients were at rest, no task was presented and only default mode activity remained irrespective of the IED location within the temporal lobe. Such decreases are therefore not epilepsy-specific, but may instead reflect an alteration of the mental state, in particular consciousness (Gotman et al., 2005; Laufs et al., 2006; Salek-Haddadi et al., 2003b). In focal epilepsy, fMRI deactivations have been found to correlate less with spike location and generally occur later than activations (Aghakhani et al., 2006; Bagshaw et al., 2004) and may thus reflect such “downstream” cognitive effects. In contrast, the activations we found in TLE are closer to the spike origin (Salek-Haddadi et al., 2006).

CONCLUSION

We found that brain areas that are active when a subject is in a state of relaxed wakefulness deactivate during IED of temporal lobe origin but not in extra-TLE. We show that EEG-fMRI group analysis can be used to explore networks associated with interictal discharges. Our data suggest that medial temporal lobe structures are central in generating or propagating IED in TLE, while superior temporal, subthalamic, and mesial frontal brain regions are involved in extratemporal lobe activation.
ACKNOWLEDGMENTS

We thank Karl Friston for advice in designing the study and during manuscript revision. Thanks to Mark Symms for MRI developments, Philippa Bartlett and Jane Burdett for MRI scanning, and our patients for participating. We used matlab routines (display_slices.m and mni2tal.m) written by Matthew Brett.

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