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SHORT REPORT

Lateralising value of experiential hallucinations in temporal lobe epilepsy

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ABSTRACT

Objectives Ever since John Hughlings Jackson first described the so-called 'dreamy state' during temporal lobe epilepsy, that is, the sense of an abnormal familiarity (déjà vu) or vivid memory-like hallucinations from the past (experiential hallucinations), these phenomena have been studied and repeatedly linked to mesial temporal lobe structures. However, little is known about the lateralising value of either déjà vu or experiential hallucinations.

Methods We analysed a sample of 28 patients with intractable focal epilepsy suffering from either déjà vu or experiential hallucinations. All the patients underwent thorough presurgical examination, including MRI, positron emission tomography, single-photon emission CT, EEG and neuropsychological examination.

Results While déjà vu was due to right or left mesial temporal lobe epilepsy, experiential hallucinations were strongly lateralised to the left mesial temporal lobe. Moreover, there was a significant effect for interictal language deficits being more frequent in patients suffering from experiential hallucinations.

Conclusions These results suggest a lateralising value for experiential hallucinations to the left temporal lobe.

INTRODUCTION

'Dreamy states' or 'intellectual aura' has been associated with temporal lobe seizures since their first description in the late 19th century by John Hughlings Jackson.[1] They encompass vivid, memory-like hallucinations from the past (ie, experiential hallucinations, EH) and the sense of an abnormal familiarity (ie, déjà vu or déjà vecu, DV). Penfield and coworker[2 3] suggested an exclusive temporal neocortical origin and classified the so-called 'psychical seizures' as either interpretive illusions of present experience (DV) or as experiential visual or auditory hallucinations from the past (EH), whereas others have stressed the involvement of the mesial temporal lobe and limbic structures, in particular the amygdala, the hippocampus[4 5] and the rhinal cortex.[6] Although a predominance of the non-dominant hemisphere for the sensation of DV has been suggested,[2 5 7] others did not find a significant lateralisation for DV or EH.[4 6 8 9]

In order to determine the lateralising value of both DV and EH, we systematically compared the epileptogenic or putative epileptogenic zone in 28 patients with temporal lobe epilepsy presenting with DV and EH. These patients underwent thorough presurgical epilepsy evaluation using a multimodality imaging approach[10] and intracranial depth electrodes, as well as a comprehensive neurological, neuropsychological (interictal and postictal) and psychiatric examination.

MATERIAL AND METHODS

Patient characteristics and clinical workup

From a population of patients suffering from intractable epilepsy who underwent presurgical evaluation in the Epilepsy Unit at the University Hospital of Geneva between 1996 and 2009, patients reporting either DV or EH were retrospectively selected. Patients with primary generalised seizures and/or bilateral pathology were excluded from the analysis. Ethical approval was obtained from the Ethical committee at the University Hospital of Geneva.

Basic patient characteristics (age, sex, handedness, seizure frequency, seizure duration, psychiatric comorbidities), surgical therapy and postsurgical outcome as well as the results of neurological examination and postictal (in the immediate postictal period) and interictal neuropsychological evaluation were compared in the two groups. We used a χ^2 test for independent samples, or the Fisher's exact test if the total number of expected observations in the contingency table was less than 20, all expected cell frequencies were <5, or any expected cell had fewer than 1 observation.

Multimodality imaging of the epileptogenic zone and overlap analysis

In order to determine the epileptogenic zone, a non-invasive multimodality imaging approach was first applied (phase I evaluation) in each of the patients as described previously.[10] It was only if the non-invasive approach could not unequivocally determine the epileptogenic zone that invasive evaluation using intracranial depth and subdural electrodes was used in a second step (phase II evaluation). As results from direct cortical stimulation were only available in a minority of patients, this information was not included in the analysis. Anatomical structures were labelled according to the Automated Anatomical Labelling (AAL) atlas implemented in MRIcron[11] and compared using a χ^2 test, or the Fisher's exact test, if the expected contingency table frequencies were low.

In order to illustrate the neuroanatomical correlates underlying DV and EH, we subsequently traced the epileptogenic zone as suggested by the multimodality imaging for each patient on the T1 template using MRIcron.[10] This allowed us to perform a simple voxel-based lesion overlap analysis establishing the anatomical subregions of maximal overlap for

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each group. For further details, please refer to the online supplementary material.

RESULTS

Demographics and clinical characteristics

Twenty-eight patients undergoing presurgical evaluation fulfilled the aforementioned criteria and were selected from a total of 450 patients (6%): 16 suffered from DV and 12 from EH. Demographic and clinical parameters did not significantly differ between the two groups (all $p>0.05$). Surgical therapy was performed in 22 of 28 patients (78%). A favourable outcome (seizure-free or seizure control within 3 months) was achieved in 17 patients (77%). Two patients did not benefit from the surgical procedure and the outcome was unknown in one patient due to an incomplete follow-up. For further details, refer to table 1 and the online supplementary material.

Neuropsychological testing

Interictal neuropsychological testing was available in 95% of the patients and postictal neuropsychological testing was available in 73% of the patients. There was a significant effect for interictal language deficits being more frequent in patients suffering from EH (8/12 or 67%), as compared with DV (3/16 or 13%, $\chi^2=6.6$, $p=0.01$) as well as for postictal language deficits (11/12 or 90% in EH vs 7/16 or 46% in DV, $\chi^2=6.8$, $p=0.008$). None of the other neuropsychological tests (interictal and postictal) showed a significant difference between the two patient groups (see online supplementary material).

The epileptogenic zone as suggested by multimodality imaging

DV (N=16) was associated with a seizure onset in the dominant hemisphere in 5 patients (32%), whereas EH (N=12) were associated with a seizure onset in the dominant hemisphere in 11 patients (92%, $\chi^2=10.22$, $p<0.01$). All patients with DV and EH suffered from temporal lobe epilepsy with a strong predominance of mesial onset ($p<0.01$): 13 (81%) of the patients with DV and 10 (83%) patients with EH had mesial temporal lobe epilepsy; a neocortical focus was found in only 3 patients with DV and 2 patients with EH (not significant). In two patients with EH, multimodality imaging suggested further involvement of the frontal lobe and the occipital lobe.

Maximal overlap of the epileptogenic zone

Figure 1 shows the results of the voxel-based overlap analysis of the epileptogenic zone. In the DV group, the right medial temporal lobe, notably the hippocampus and parahippocampus, is maximally implicated in 10 of 16 patients (centred at approximately Montreal Neurological Institute (MNI) x=28, y=−14, z=−19). In the EH group, the left medial temporal lobe, notably the left amygdala and the left parahippocampus, was the overlap region in 8 of 12 patients (MNI x=−24, y=−5, z=−26).

DISCUSSION

In the present study, we investigated the neural correlates of DV and EH due to temporal lobe epilepsy. We found that both DV and EH were associated with medial temporal lobe epilepsy, with a significant predominance of the language-dominant hemisphere in patients with EH as compared with DV. We conclude that psychic phenomena indicate temporal lobe onset, mainly mesial temporal, and that EH, but not DV, conveys lateralising information to the language-dominant hemisphere.

The finding that the sensation of DV, for example, the experience of abnormal familiarity and EH, for example, vivid memory-like hallucinations from the past, is linked to the mesial temporal lobe is in accordance with most of the recent literature on these phenomena. Penfield and coworker[2] were already able to induce DV or what they called "illusions of comparative interpretation" by electrical stimulation predominantly of the right, non-dominant temporal lobe. Later, Halgren *et al*[9] were able to reproduce these findings by stimulation of the hippocampal formation bilaterally with the use of depth electrodes. Gloor *et al*[4] suggested an exclusive role of the limbic system, that is, hippocampus, parahippocampus and amygdala, in the generation of experiential phenomena, such as illusions of familiarity, emotions and complex visual and auditory hallucinations. They proposed that limbic coactivation during neocortical seizure discharge may add an affective dimension and thus give rise to the experiential immediacy. However, they did not find evidence in favour of hemispheric dominance in the generation of experiential phenomena. These findings have recently been supported by both Weinand *et al*[7] and Vignal *et al*,[5] who were able to induce the sensation of abnormal familiarity by electric stimulation of the mesial temporal lobe. Finally, Bartolomei *et al*[6] showed a dissociation of DV and EH by either stimulation of the entorhinal or the perirhinal cortex, respectively, as compared with stimulation of the hippocampus and the amygdala.

Table 1 Patient characteristics

	Déjà vu N=16	Experiential phenomena N=12	p Value
Male/female	7/9	8/4	>0.05
Age at evaluation (y)	32.0 (SD 11.5)	32.4 (SD 7.9)	>0.05
Handedness (right/left/ambidextrous)	14/1/1	11/0/1	>0.05
Duration of epilepsy (y)	12.6 (SD 12.5)	11.4 (SD 9.4)	>0.05
Seizure frequency (p.a.)	238 (SD 519)	153 (SD 292)	>0.05
Neurological examination (normal/pathological)	12/4	9/3	>0.05
Family history (positive/negative)*	1/13	1/9	>0.05
Psychiatric comorbidity (yes/no)*	3/5	4/2	>0.05
Surgical therapy (yes/no)	13/3	9/3	>0.05
Favourable outcome after surgery (yes/no/unknown)†	13/0	6/2/1	>0.05

*Information could not be retrieved retrospectively for all patients; therefore, N differs from the total N.
†Refers only to operated patients (N=22).
p.a., per annum; y, year.

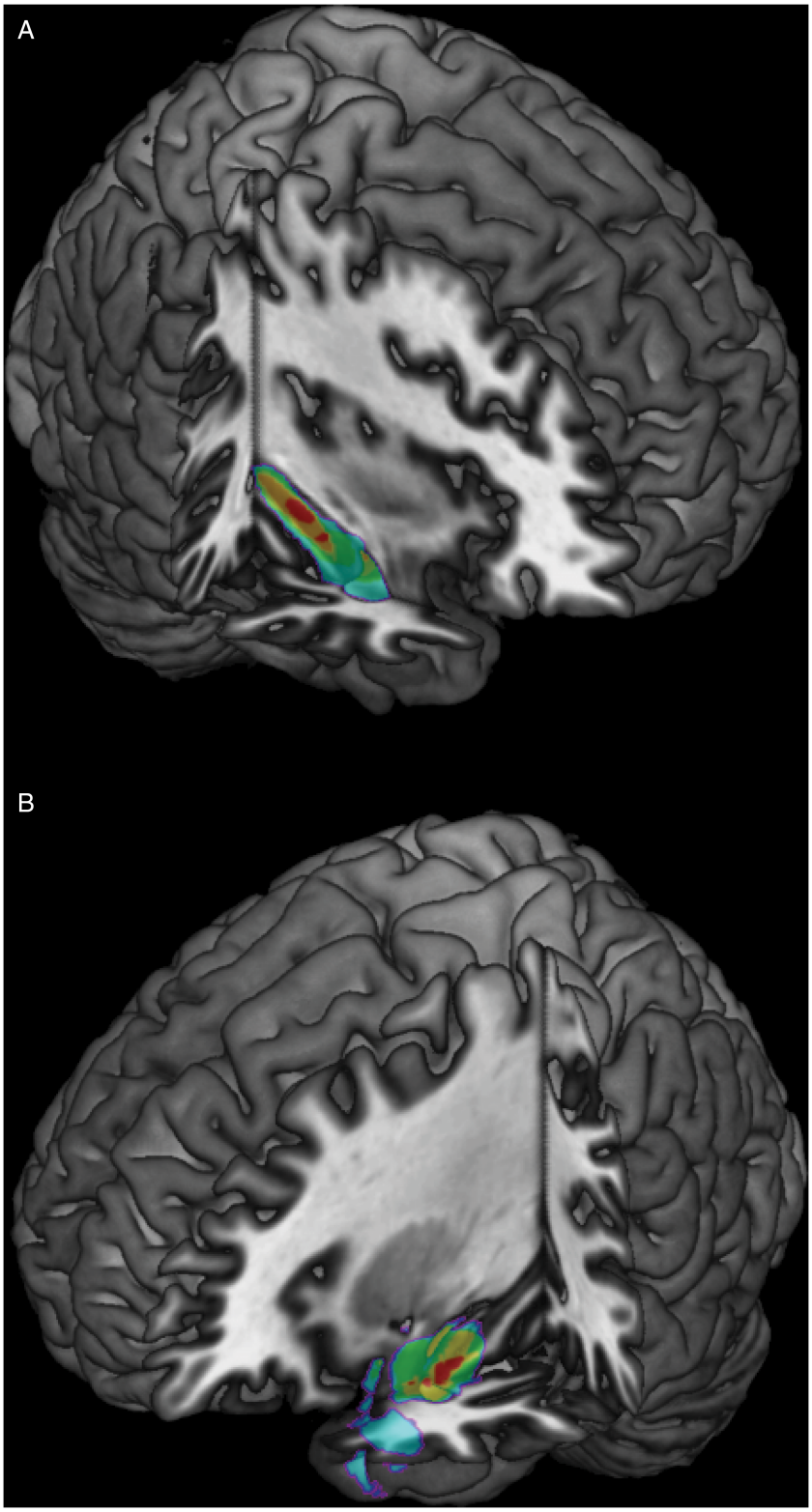

Figure 1 (A) Maximal overlap of the epileptogenic zone in patients suffering from déjà vu or déjà vecu in the right medial temporal lobe. The degree of overlap is indicated by change of colour from blue (n=7) to red (maximal overlap, n=10). (B) Maximal overlap of the epileptogenic zone in patients suffering from experiential hallucination in the left medial temporal lobe. The degree of overlap is indicated by change of colour from blue (n=5) to red (maximal overlap, n=8).

In contrast to previous studies,[2 4–6 9 12] we found that the mesial temporal lobe of the dominant hemisphere was more often implicated in the generation of EH due to epilepsy as compared with DV. This discrepancy could be related to the fact that these studies were mostly based on direct intracranial cortical stimulation using depth electrodes, that is, EH was induced even if the habitual seizures of the patient were not characterised by EH. In fact, cortical stimulation may recruit a network, including contralateral structures, and not necessarily interfere solely with the underlying cortical functions.[13]

The lateralisation in favour of the dominant hemisphere was further corroborated by the frequent observation of postictal language deficits in patients with EH. Furthermore, EH were often associated with auditory and, more specifically, verbal hallucinations; for example, patients stated that they heard a familiar voice or a familiar melody. Moreover, it has been shown that

episodic memory as well as visuospatial imagery in autobiographical memory is linked to a left-lateralised neural network including the left mesial temporal lobe and the left temporoparietal junction.[14] Other evidence for the importance of the left-sided temporal structure for autobiographic memory is provided by functional MRI[15] and positron emission tomography studies.[16] Careful examination of patients with temporal lobe epilepsy also showed lower scores in autobiographic memory tests in those who had left temporal lobe epilepsy,[17] pointing to a crucial role of the left mesial temporal lobe for remote personal memory, which is retrieved and relived on electrical activation as it occurs during a seizure under the form of EH. Accordingly, our patients with EH mostly report seeing and reliving scenes from their past, often in combination with auditory (familiar voices or sounds) or olfactory hallucinations (see online supplementary table S1 for details).

In conclusion, our findings confirm the association of both DV and EH with an epileptic focus in the mesial temporal lobe. Moreover, in contrast to previous work,[4–6] we demonstrate for the first time a lateralising value for EH in the context of epileptic seizures in the language-dominant mesial temporal lobe as compared with DV. This finding is in accordance with the crucial role of this brain region in the generation of autobiographical memory.

Contributors LH was responsible for the data collection, performed the overlap analysis and wrote the manuscript. GM helped with the image processing and overlap analysis. NE helped with the statistical analysis and writing of the manuscript. OB and MS helped with the writing of the manuscript and supervision of the research.

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Competing interests None.

Ethics approval Ethical Committee at the University Hospital of Geneva.

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Notes