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Case Report

Somatosensory phenomena elicited by electrical stimulation of hippocampus: Insight into the ictal network

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ABSTRACT

Up to 11% of patients with mesial temporal lobe epilepsy experience somatosensory auras, although these structures do not have any somatosensory physiological representation. We present the case of a patient with left mesial temporal lobe epilepsy who had somatosensory auras on the right side of the body. Stereo-EEG recording demonstrated seizure onset in the left mesial temporal structures, with propagation to the sensory cortices, when the patient experienced the somatosensory aura. Direct electrical stimulation of both the left amygdala and the hippocampus elicited the patient's habitual, somatosensory aura, with afterdischarges propagating to sensory cortices. These unusual responses to cortical stimulation suggest that in patients with epilepsy, aberrant neural networks are established, which have an essential role in ictogenesis.

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1. Introduction

Direct electrical stimulation (DES) of the healthy cortex elicits responses according to the physiology of the stimulated area. In patients with drug resistant epilepsy evaluated for surgical therapy, this method is used for mapping the eloquent cortex and for triggering the patients' habitual seizures, using intracerebral electrodes [1]. DES can elicit abnormal responses due to specific configurations of epileptic networks [2]. Up to 11% of patients with mesial temporal lobe epilepsy may experience somatosensory auras at the start of their habitual seizures [3,4], although these structures do not have any somatosensory physiological representation. The underlying mechanism is not yet fully understood. It is hypothesised that pathological networks contributing to ictogenesis, constitute the basis of rapid propagation of the activity to the somatosensory cortex.

2. Case report

We present the case of a 38-year-old male patient with drug-resistant left mesial temporal lobe epilepsy, reporting right-sided somatosensory auras. The patient has suffered from epilepsy since nine months of age and he has never achieved seizure freedom in spite of adequate trials of 10 anti-seizure medications. The patient did not have febrile seizures and the family history was negative for epilepsy. The patient had vagal nerve stimulator implanted to alleviate the seizures. However, this was deactivated due to side effects of facial spasms. The patient had an estimate of ten focal impaired awareness seizures per month, and rare focal to bilateral tonic–clonic seizures. He was eventually referred to our centre for presurgical evaluation.

During long-term video-EEG monitoring, 14 focal aware and four focal impaired awareness seizures were recorded. The seizures started with a somatosensory aura, consisting of a tingling sensation in the right lower limb, extending to the upper limb and then to the right side of the face (duration up to: 373 s). Focal impaired awareness seizures continued then with oroalimentary automatisms, motionless staring, bimanual or left-hand automatisms, ictal and postictal aphasia (duration: 78 s–7 min). Scalp EEG recordings, using the standard 25-electrode array of the

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International Federation of Clinical Neurophysiology [5] showed build-up of rhythmic 4–5 Hz ictal activity in the basal temporal area, 8–37 s after the clinical onset. Both interictal and ictal EEG source imaging, using the methodology previously validated in a large prospective study [6] localised to the left antero-mesial temporal area (Fig. 1A).

MRI showed slight atrophy of the left hippocampus and FDG-PET showed hypometabolism, anterior-inferior and mesial in the left temporal lobe (Supplementary Figs. 2 and 3). Due to the seemingly discordant semiology (somatosensory aura) we implanted stereotactic EEG depth electrodes into the left temporal lobe, parietal lobe and insula involving primary and secondary somatosensory cortices. A total of nine depth electrodes were implanted, corresponding to 90 contact points. After implantation, the CT scan was co-registered with the preimplantation-MRI, to visualize the depth electrodes (Fig. 1B).

We found continuous interictal spiking in the left amygdala and anterior hippocampus. Seizure onset was in the left amygdala and anterior hippocampus (Fig. 2) preceding the clinical start of the somatosensory aura. Occasionally, the ictal activity propagated to the lateral temporal regions, parietal contacts, posterior cingulate cortex and to the insula. Once the patient notified his somatosensory aura, the ictal activity propagated to the somatosensory and posterior cingulate cortices.

We performed electrical stimulation using the contact points of the depth electrodes (biphasic stimuli with a pulse duration of 2 ms; train duration of 4 s; stimulus intensity of 0.5–1 mA). Stimulation in the left amygdala and anterior hippocampus, with 50 Hz and 1 mA provoked the patient's habitual somatosensory aura, with a long train of afterdischarges in the hippocampus, amygdala, propagating to insula and posterior cingulate contacts. Five electroclinical seizures were recorded during stimulation. The network involved at 50 Hz stimulation was the same as the one recorded in seizures with spontaneous aura. Other sensory phenomena, not recognised by the patient as his aura, were evoked from all stimulated insular contacts: whole body- or throat tingling, as well as a localised right-sided headache.

The patient underwent left anterior temporal lobectomy. The histopathology showed hippocampal sclerosis type 1. The patient was completely seizure free at 12 months postoperative follow-up (before the submission of the manuscript).

3. Discussion

In a patient with focal seizures starting with somatosensory aura, we found the seizure onset zone localised in the left amygdala and hippocampus, preceding the aura. Propagation of the seizure activity to the sensory cortices coincided with the aura. Stimulation of the amygdala and anterior

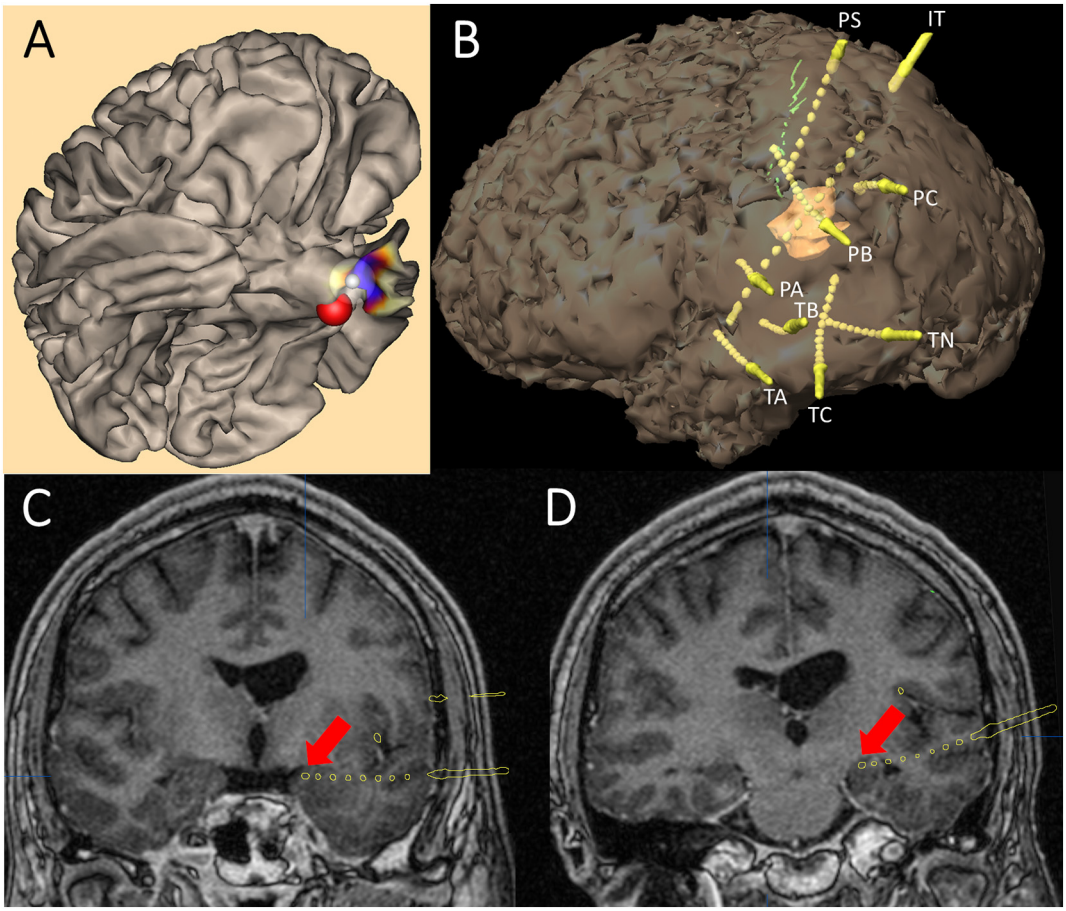

Fig. 1. Presurgical evaluation of the patient. A: Interictal and ictal EEG source image localised the activity to the left antero-mesial temporal area (equivalent current dipole and distributed source model). B: Post-implantation CT co-registered with the pre-implantation MRI to visualise the position of the depth electrodes. Temporal electrodes: TA (T2-gyrus ➔ amygdala), TB (T2-gyrus ➔ anterior hippocampus), TC (T2-gyrus ➔ posterior hippocampus), TN (posterior temporal cortex ➔ gyrus parahippocampalis). Parietal electrodes: PA (operculum ➔ insula), PB, PC and PS (parietal cortex ➔ posterior cingulate cortex), IT (parietal cortex ➔ insula). The green line shows the central sulcus and the orange model is the cystic enlargement of the left lateral ventricle at the level of trigone. C and D: Coronal images of SEEG electrode contact placement of TA (C) and TB (D) electrodes; red arrows show the contacts where seizure onset was recorded and where stimulation elicited the patient's habitual somatosensory aura. Further electrode contacts are shown in the Supplementary Fig. 5. Reconstruction was done with a post-implantation CT with automatic detection of metal, and fused to preoperative MRI, using BrainLab iPLan system.

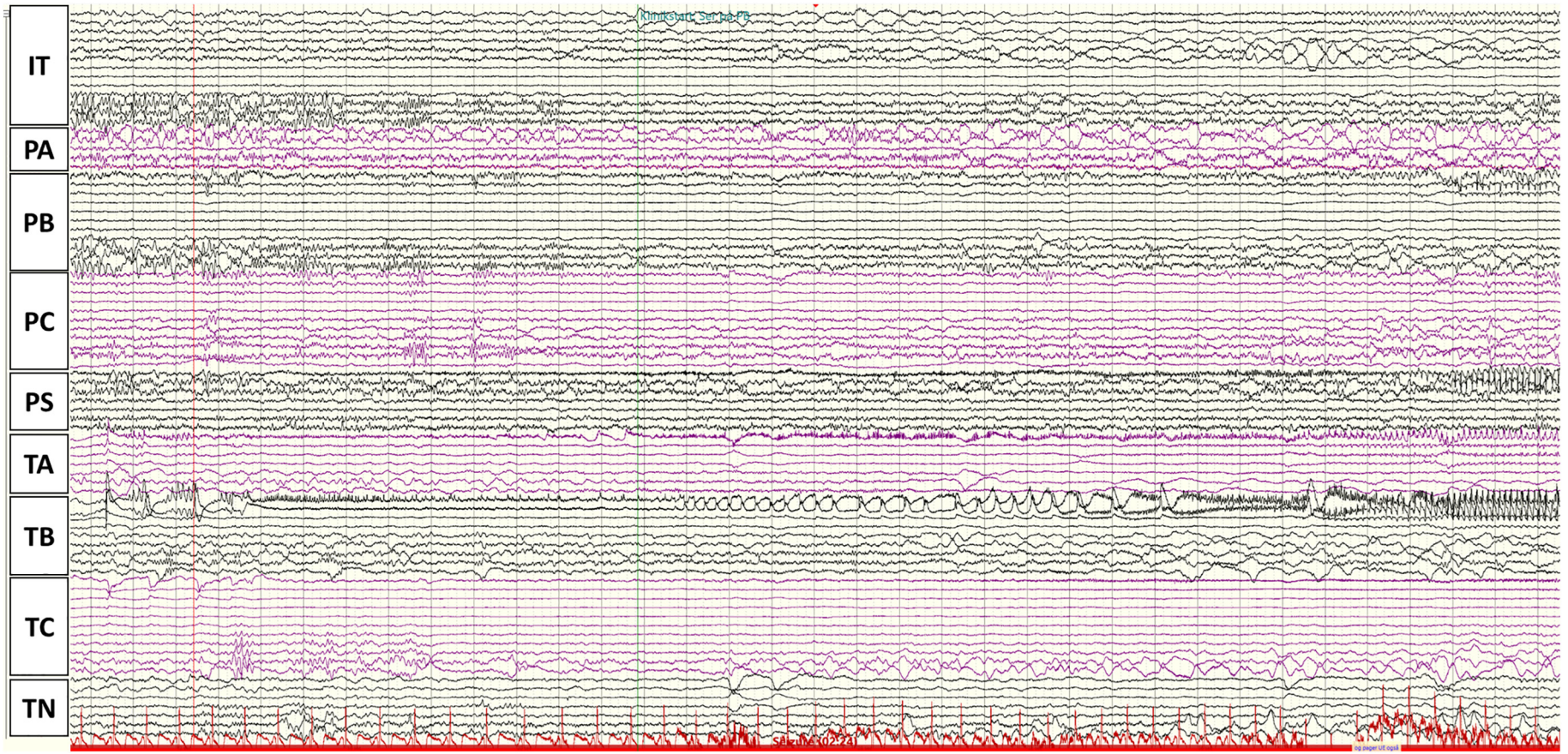

Fig. 2. Intracranial EEG recording showing seizure onset in the left hippocampus (contacts TB1–2) propagating to amygdala (contacts TA1–2) and then to the parietal contacts (PS1–2) at the time of the clinical start (aura) marked by the green vertical line. (Electrode names are listed in the legend to Fig. 1).

hippocampus elicited afterdischarges propagated to the sensory cortices, and provoked the patient's habitual somatosensory aura.

Previous studies found that patients with mesial temporal lobe epilepsy experiencing somatosensory aura, had a higher rate of breakthrough seizures and recommended a more detailed presurgical evaluation, including invasive EEG recordings, to investigate a possible extratemporal onset [4]. In our patient, the sequence of sensations in the aura were not typical for the somatosensory homunculus in the primary somatosensory cortex, and raised the possibility of a symptomatogenic zone in the secondary somatosensory cortex or insula, also taking into account the ipsilateral atrophy.

Up to 11% of patients with mesial temporal lobe epilepsy may experience somatosensory auras [3,4]. However, the pathological mechanisms have not been elucidated. We did a systematic literature search for publications somatosensory phenomena elicited by electrical stimulation of the mesial temporal structures. We used the search string: "(((((Intracranial OR Invasive)) AND Epilepsy) AND Stimulation) AND (Aura OR Sensation))". Other sources were identified via references in found records. A total of 1159 records were screened after removing duplicates (Supplementary Fig. 1). We used the PRISMA methodology [7] and we identified a single study relevant for our topic [8]. The study included 53 patients who underwent intracranial stimulation using either depth or subdural electrodes. Stimulation of the mesial temporal structures with depth electrodes elicited sensory responses in 39 cases. The authors did not specify whether these were somatosensory or viscerosensory (epigastric aura) and it was not possible to obtain this additional information by contacting the corresponding author. However, given the high prevalence of sensory responses (74%), it seems likely that the authors included viscerosensory phenomena (i.e., epigastric aura). Previous studies documenting somatosensory aura in patients with mesial temporal lobe epilepsy did not map the ictal network associated with the sensory phenomena.

4. Conclusion

In this study we documented that propagation of the ictal activity from the mesial temporal structures to the somatosensory structures and posterior cingulate cortex generated the somatosensory aura. Physiologically, the mesial temporal structures do not have somatosensory representation. Yet, development of atypical neuronal networks, as part of the ictogenesis, explains the somatosensory aura in patients with mesial temporal epilepsy. In some of these patients such as ours, resection of the mesial temporal seizure-onset zone can lead to complete seizure-free outcome.

Ethical statement

We confirm that this work has been carried out in accordance with the Declaration of Helsinki.

Declaration of competing interest

The authors do not report conflict of interest related to this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2020.100387.

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