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Subjective Distinguishability of Seizure and Non-seizure Déjà Vu: A Case Report, Brief Literature Review, and Research Prospects

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Abstract

Roughly two-thirds of all people report having experienced déjà vu—the odd feeling that a current experience is both novel and a repeat or replay of a previous, unrecalled experience. Reports of an association between déjà vu and seizure aura symptomatology have accumulated for over a century, and frequent déjà vu is also now known to be associated with focal seizures, particularly

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None.

Declaration of interests

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those of a medial temporal lobe (MTL) origin. A longstanding question is whether seizure-related déjà vu has the same basis and is the same subjective experience as non-seizure déjà vu. Survey research suggests that people who experience both seizure-related and non-seizure déjà vu can often subjectively distinguish between the two. We present a case of a person with a history of focal MTL seizures who reports having experienced both seizure-related and non-seizure *common* déjà vu, though the non-seizure type was more frequent during this person's youth than it is currently. The patient was studied with a virtual tour paradigm that has previously been shown to elicit déjà vu among non-clinical, young adult participants. The patient reported experiencing déjà vu of the common non-seizure type during the virtual tour paradigm, without associated abnormalities of the intracranial EEG. We situate this work in the context of broader ongoing projects examining the subjective correlates of seizures. The importance for memory research of virtual scenes, spatial tasks, virtual reality and this paradigm for isolating familiarity in the context of recall failure are discussed.

Keywords

Déjà vu; Subjective experience; Focal seizures; Seizure aura; Stereo-electroencephalography (SEEG); Consciousness

1. Introduction

Déjà vu—the feeling of having experienced the current situation before despite that seeming impossible—has a long-appreciated link to some forms of epilepsy (reviewed by Brown, 2004, Cleary & Brown, 2022) [1–2]. Medical descriptions and this link were provided by John Hughlings Jackson over a century ago [3–4]. Today, it is widely recognized that déjà vu that occurs with high frequency can indicate an underlying seizure, most often from focal seizures involving the medial temporal lobe (MTL) [5–31]. Nonetheless, there are some differences between what is commonly referred to as déjà vu in the context of seizures and epilepsy, or 'epileptic' déjà vu, and 'common' or 'non-seizure' déjà vu [2].

The clearest evidence for a distinction between epileptic and common déjà vu is the ability for some patients with epilepsy, who experience both, to readily make this distinction [5]. Seizure-related déjà vu tends to be longer and has other features that are not directly related to the experience of déjà vu: Feelings of depersonalization, fear, or the presence of vivid memories or olfactory hallucinations. This finding is in line with other reports in the literature, such as comparisons between people who experience ictal déjà vu and people with no history of epilepsy who report experiencing déjà vu [18,31]. Despite these differences, the similarities and unique nature of déjà vu have led to speculation that common déjà vu may also be due to focal seizures [32]. *Prima facie*, this seems unlikely given the pervasiveness of the phenomenon and the absence of seizures and EEG abnormalities in most of the human population; however, the idea cannot be completely ruled out given the possibility of benign MTL epilepsy [16] or that focal seizures underlying the aura might not be detectable with scalp EEG. Moreover, people who have experienced common déjà vu have been shown to have reduced gray matter volume in components of the limbic network, which correlates with the frequency of these experiences [33]. A subsequent study using

similar methods and a larger sample size found only a volumetric difference involving the insula [17]. Of note, in both cases of common déjà vu, abnormalities were left hemispheric, whereas the right hemisphere has been more often implicated in epileptic déjà vu [34–35]. Finally, it seems unlikely that patients with both sorts of déjà vu - with a proven predilection for epileptogenesis - would show stable or low rates of common déjà vu that is unrelated to seizures and has decreasing frequency with age [5].

A potentially useful approach for examining this issue is a recently developed method for increasing reports of déjà vu among non-clinical participants in the laboratory [36–38]. In this method, based on early theories of déjà vu mechanisms [1], participants view a series of simulated virtual tours through various scenes. Later, they view a series of virtual tours with new scenes, some of which have the same spatial layout as earlier-viewed scenes despite otherwise being novel scenes (see Figure 1). For example, a virtual lodge scene might have the same layout as a previously toured virtual shopping mall, and the movement through the virtual lodge scene follows the same series of turns through the scene as was taken during the shopping mall tour. The primary interest in this method is in familiarity-detection with novel scenes that have familiar layouts during instances of recall failure (when participants fail to recall the spatially similar scene that was presented earlier). Non-clinical, college student participants are more likely to report experiencing déjà vu in these instances than when touring novel scenes that do not share a spatial layout with earlier toured scenes; they also find those scenes to be more familiar [37–38]. This paradigm provides a key opportunity to study familiarity, including when isolated from recall.

As the virtual tour method presents a means of eliciting déjà vu through characteristics in the virtual environment, and in non-clinical participants, it can potentially shed light on whether there are similar neural circuits underlying these two distinguishable types of déjà vu among people who experience seizure-related déjà vu. The aim of the present case report is to show the feasibility of this method, ask whether this experimental paradigm can work in patients who report common and epileptic déjà vu, and finally, to examine our hypothesis that common déjà vu is not due to focal seizures.

2. Case report

2.1 Patient History

A 30-year-old left-handed man with a 5-year history of medically refractory epilepsy, without risk factors or pertinent additional medical history, was admitted to Emory University Hospital Intracranial Monitoring Unit for stereoelectroencephalography (SEEG). Seizures consisted of behavioral arrest followed soon after by unresponsiveness, fumbling with his hands, oral automatisms, sometimes with drooling and rare progression to bilateral tonic clonic seizure. Seizures were often accompanied by an aura and subjective phenomena that had changed during the course of his epilepsy: Initially, an aura was often present that consisted of a chill running up his spine, dysphoria and a vivid recollection. The recollection consisted of reliving an experience from his late childhood or early teens of visiting the local gas station on a Friday evening to choose a video to watch with his family. He was consciously aware that this should have been a happy memory for him, and that it seemed incongruous with his experienced dysphoria. This vivid reliving experience

has faded over the five-year course of his epilepsy. This original aura was a strong sense of déjà vu (or perhaps déjà vecu 'already experienced', intense and not merely visual; see [2]) during this event. Long-term video EEG monitoring revealed sleep-potentiated left anterior temporal spikes and occasional colocalized theta slowing. Three seizures were captured with behavioral arrest, staring, then later right arm dystonic posturing and spread to the face as generalization ensued, each with correlated left anterior temporal EEG onset. MRI revealed questionable fluid attenuation inversion recovery (FLAIR) hyperintensity of the left hippocampus, with normal architecture. fMRI revealed predominantly left-hemispheric activation during language tasks. Positron emission tomography (PET) revealed left temporal hypometabolism. Neuropsychological testing revealed high functioning across most domains with a WAIS-IV General Ability Index of 122 (92nd percentile), but with variable memory performance and slow and poorer performance for visual confrontation naming. Based on these data, and the variable presence of his aura, implantation hypotheses were left medial temporal, versus left neocortical temporal and cingulate. SEEG was considered given the possible wider than hippocampal involvement of the left and language-dominant temporal lobe for the purpose of deciding between tailored resection or ablation, versus neuromodulation. Implanted electrodes sampled the medial and lateral temporal structures (including the superior temporal gyrus, perirhinal area, entorhinal cortex, hippocampus, temporal pole, parahippocampal gyrus), anterior and posterior cingulate cortices and the orbitofrontal cortex with right amygdala, hippocampus, middle temporal and fusiform gyri. SEEG revealed left greater than right lateral and medial temporal interictal epileptiform abnormalities with after-discharges elicited by low-frequency electrical stimulation the left lateral temporal cortex, supramarginal, orbitofrontal, and mesial temporal areas. Neither déjà vu nor déjà vecu was elicited by stimulation, but at the time of admission this aura was not present. No seizures were captured during the admission, but given presumed wide bitemporal involvement, deep brain stimulation of the anterior nucleus of the thalamus was chosen by the patient and the treatment team in preference to an irreversible destructive procedure on the dominant hemisphere. During this SEEG hospitalization he consented to participate in the computerized virtual tour program, at which time he was off all anti-seizure medications.

2.2 Virtual Tour Paradigm

A computer system containing a variant of the Virtual Tour Paradigm [37] was moved into the patient's room on a mobile cart so that the patient could participate in the tour from his hospital bed. The video clips of each virtual tour were presented using ePrime software (v3, Psychology Software Tools, Sharpsburg, PA) using a Windows 10 computer (Intel i7 Processor, GeForce GTX 1080Ti graphics card) on a 27" monitor (P2715Q, Dell, Round Rock, TX) about 60 cm from the participant, with the monitor, mouse, keyboard and response buttons placed on a table over the bed and in front of the patient. The patient was instructed to press a button on a short-latency response box (Chronos, Psychology Software Tools, Sharpsburg, PA) next to the keyboard any time a déjà vu experience occurred during any of the tours. Briefly, and as described in more detail in Cleary and Claxton (2018) [37], the paradigm is divided into 'training scenes' and 'test scenes'. Training scenes consisted of a recorded voice describing the title of the scene (e.g., "This is a locker room. Locker room."), with the participant then being passively moved through a specific path in the

virtual scene. Half of the subsequently presented test scenes were different in theme and content, but spatially similar to a training scene; the other half were entirely novel. During the test phase the patient responded to prompts using the keyboard. In test scenes, movement through the predetermined path was stopped near its completion and immediately prior to a turn. In the case of test scenes having a similar training scene, this path was spatially identical. The first prompt asked if déjà vu had occurred during the tour, with the instruction to press “Y” for “yes” or “N” for “no.” The next prompt asked if, upon stopping, the person experienced a feeling of prediction regarding what the direction of the next turn should be (with the instruction to press “Y” for “yes” or “N” for “no). The participant was then requested to guess the direction of subsequent movement (“L” for “left” or “R” for “right”) and then asked to provide a familiarity rating on a scale of 0 (very unfamiliar) to 10 (very familiar). Finally, the participant was asked to indicate if successful recall of an earlier-viewed similar scene had occurred; here, the person was asked to type the name of any earlier-viewed scene that came to mind in response to the test tour and to press “Enter” if none came to mind. SEEG was reviewed, with a standard clinical approach, for any electrographic abnormalities during the testing paradigm.

2.2.1 Patient Experience of the Virtual Tour Paradigm—In our standard interview immediately following the virtual tour, the patient described having previously experienced both common and epileptic déjà vu. The patient described his experience of common déjà vu as being much more frequent for him when he was a teenager than currently. Interestingly, the epileptic déjà vu is also rare at present. He described the epileptic type of déjà vu as differing from common déjà vu in having an associated sense of worry or fear and feelings of dread as part of the seizure warning. He also described epileptic déjà vu experiences as feeling as if he can predict what happens next, whereas he does not have that feeling of prediction with common déjà vu. With epileptic déjà vu, the situation “feels so familiar” that he can “see what the next step is.” When asked how he would describe the difference between familiarity and déjà vu, his response was, “I would say that the difference is that déjà vu is a sensation and familiarity is just a feeling. Déjà vu is something hard to put your finger on. Déjà vu is a more intense sense of familiarity.”

2.2.2 The Virtual Tour Paradigm Elicited Subjective Familiarity and Déjà Vu in the Absence of Focal Seizures—Following completion of the computer simulations of virtual tours, the patient described his impressions of the paradigm and his subjective experiences. He stated that a lot of the scenes seemed familiar to him. He expressed that he did not have any sense of epileptic déjà vu during any of the tours. However, he stated that he did have “a sort of regular sense of déjà vu”. He went on to say that déjà vu in this case is a “confused familiarity”. Importantly, no seizures were observed during the patient’s participation in the virtual tour paradigm, despite good sampling of structures that are thought to be necessary for epileptic déjà vu - the perirhinal area, entorhinal and parahippocampal cortices, the hippocampus and portions of the lateral temporal lobe.

2.2.3 Spatially Similar Scenes Elicited Déjà Vu in the Context of Recall Failure—The patient successfully recalled 14 of the virtual training scenes from among the 32 test scenes that had the same spatial layout as a training scene, for a cued recall rate

of .44. Among the 18 test scenes that failed to elicit recall of their identically configured studied scenes, the patient reported experiencing déjà vu for three of the virtual scenes (a rate of .17), whereas among the 32 test scenes that did not have the same spatial layout as any earlier-toured scene, the patient reported experiencing déjà vu for none of them (a rate of 0). A Fisher's Exact test revealed these frequency differences to be significant ($p = .04$). The patient also reported déjà vu for four of the 14 test scenes that elicited successful recall of earlier identically configured scenes (a rate of 0.29); it is unclear if the sensation of déjà vu preceded the recall in these instances, as the temporal dynamics of responses were not recorded.

2.2.4 Feelings of Prediction Accompanied Familiarity but not Déjà Vu—

During recall failure, the participant's reported feeling of prediction rates were zero during reported déjà vu and .16 during non-déjà vu, and .17 among scenes identically configured to earlier viewed scenes and .16 among scenes not spatially similar to an earlier viewed scene. Reported feelings of familiarity during recall failure occurred at a rate of 1.0 during déjà vu (all three déjà vu reports were accompanied by a report of familiarity), of .45 during non-déjà vu, and at a rate of .56 among scenes identically configured to earlier viewed scenes, and .44 among scenes not spatially similar to an earlier viewed scene. None of the frequencies in these comparisons were significant. Although past research has suggested an association between déjà vu reports during recall failure in this paradigm and feelings of prediction, the patient exhibited no such association; zero of the three instances of reported déjà vu during recall failure were accompanied by reported feelings of prediction. However, although not during déjà vu, the patient did report a feeling of prediction a total of 8 times during the absence of recall. These 8 instances occurred for scenes that were deemed familiar but for which déjà vu was not reported. Among the total of 50 scenes for which recall was absent, 24 altogether were judged to be familiar; among these, 8 elicited reported feelings of prediction while 16 did not. In contrast, among the 26 of the scenes that were judged to be unfamiliar, none elicited a report of a feeling of prediction. A Fisher's Exact test revealed these frequency differences to be significant (p = .001). Finally, among scenes that spatially mapped onto earlier viewed scenes, there was no actual above-chance (chance = .50) predictive ability regarding the direction of the next turn during déjà vu (p Correct = .44) or during instances of recall failure more generally (p Correct = .33). No seizures were detected during tasks.

3. Discussion

Whether and how seizure-related déjà vu differs from common déjà vu remains an important question for researchers and clinicians. By capitalizing on the rare opportunity to have a person familiar with both epileptic and common déjà vu participate in the virtual tour paradigm that has been used to examine déjà vu in non-clinical participants [37], the present case report documents, in a novel way, that seizure-related déjà vu is subjectively distinguishable from an induced experience thought to be similar to the common déjà vu observed in non-clinical participants. Until now, qualitative evidence for this distinction was limited to survey and interview data, relying on long-past memory for the common form of déjà vu. This case study represents the first time the phenomenological distinction between

types of déjà vu experience has been directly observed in a clinical setting. Common déjà vu can be induced using the virtual tour paradigm, paving the way for SEEG studies that can help distinguish whether this common déjà vu-like experience has the same anatomical substrate as déjà vu produced by electrical stimulation in patients with epilepsy. This is important given the possibility that déjà vu may only be elicitable by stimulation and in the temporal lobe given hyper-excitability and involvement of these structures in the epileptic network. The present case report points toward the idea that déjà vu that is elicited by external factors, such as familiar visual or spatial aspects of the environment, is subjectively of the common type. The relative role of external phenomena or some internal state in driving spontaneous common déjà vu is unresolved. Regarding the occasionally posited ictal etiology for common déjà vu, seen in its most extreme form as the hypothesis that déjà vu represents environmentally-elicited seizures [39], this patient was off medications in the epilepsy monitoring unit and the experience of elicited déjà vu did not trigger, nor was it associated with, a seizure or epileptiform activity.

Studying common déjà vu and epileptic déjà vu together is a notable methodological advance for several reasons. First, it allows direct investigation of the long-held suspicion that déjà vu has multiple subtypes - common and epileptic - with the neural basis being cognitive and environmentally inducible in the former case, and related to seizures or after-discharges in the latter instance. Our hunch, however, is that “déjà vu” refers to a larger cluster of different but mechanistically related phenomena that likely all arise from the same (or overlapping) neurocognitive systems. Based on clinical evidence, these are rooted in the temporal lobe, and largely the medial temporal lobe. The central question is whether the described neural circuitry underlying epileptic déjà vu is the same as that of common déjà vu and familiarity-detection. We will address this empirically with our ongoing work using this paradigm, but cannot make robust claims regarding the neural correlates of real-world spontaneously occurring déjà vu with one participant and three episodes of common déjà vu that were induced by the controlled environment of our task (a controlled form of environmentally-induced déjà vu).

While our work holds promise for future studies with additional participants to better understand familiarity, memory mechanisms and déjà vu, there are some limitations. Firstly, participants in the virtual tour paradigm report déjà vu, but it is unclear that déjà vu as captured using this method is the same as that which occurs spontaneously in day-to-day life. Although some research suggests that sensitivity to spatial resemblance between scenes is correlated with real-life déjà vu frequency [40], the extent to which detection of spatial resemblance contributes to spontaneous, naturally occurring common déjà vu is unknown. Second, while a core hypothesis of our work is that environmentally induced déjà vu, using our virtual tour task, and epileptic déjà vu share a common neural substrate, based on prior work with epilepsy patients and based on lesion studies involving the perirhinal area and the network of which it is part [41–42], the fact that seizure and non-seizure déjà vu are subjectively distinguishable raises the possibility that different circuitry is involved in each. Given the additional features of the epileptic déjà vu phenomenon [31], it may mean that the same core network is responsible for déjà vu, but in the case of seizures, additional brain regions are activated giving rise to more complex phenomenology. Finally, another limitation of intracranial EEG studies is sparse sampling, but we often have

electrode contacts in several implicated temporal lobe structures, some structures that are not implicated (potentially functioning as a control), and occasionally in the same patient, frontal cortical regions that are important for attentional mechanisms. Furthermore, parallel studies may be performed with functional imaging covering the whole brain, albeit at a different timescale.

Two other major areas of investigation are relevant to this paradigm, and its development in the setting of human intracranial electrophysiology. Firstly, this affords the opportunity to study an aberration in conscious experience. Conscious experiences are often meta-cognitive - where the participant can appreciate the nature of an ongoing mental process. Déjà vu is such a metacognitive and conscious phenomenon [43], where there is an annotation concerning whether an episode is novel or familiar. In the case of déjà vu, both subjectively and based on typical characterizations of this phenomenon, this 'annotation' of experience appears to be both novel and familiar. In the setting of recall failure, as in our paradigm, we can examine the neural correlates of the meta-cognitive and conscious appreciation of familiarity. Ultimately, research on the forms of déjà vu could also help reveal the role of these systems in the animal's achievement of a first-person perspective, i.e. a structured experiential frame that provides us with a sense of where we are both in space and time [44–46]. The study of déjà vu and its varieties, then, may be a key point of entry into the investigation of subjectivity.

Relatedly, there is a fruitful and continuing body of literature that pertains to the subjective elements of conscious experience and how this is affected by focal seizures. While early commentary on this topic suggested taking a behavioral approach that carefully parses amnesia and behavioral arrest from impairments of consciousness [47], more recent work has confidently entered into the study of subjective consciousness and its neural correlates. Starting in the 2000s, key contributions include fruitfully conducted qualitative research that showed that attention is forced and that subjective experience is lost in a progressive manner as the seizure ensues [48], the use of consciousness scales that include the contents of consciousness [15], development of an Ictal Consciousness Inventory [49], and providing schemas for approaching this new area of knowledge [50–51]. This work builds on the older distinction of Plum and Posner between the level of arousal and content of consciousness that has been a useful framework [52], but not without limitations [53]. Our patient, as has been described in this important body of work, had a shift of attention ('forced attention') inward, with reminiscences that overall have been argued to represent an expansion of the content of consciousness, as his awareness was subsequently fractionally lost. In this sense, déjà vu fits into a broader conceptualization of seizure aura and subjective experience that includes other ways in which there can be a superadding of additional layers of distortions of subjective experience that can include hallucinations, reminiscences, and dissociative phenomena [54]. Studying specific subjective phenomena, as is exemplified and proposed here, has the potential to help us not only understand specific cognitive phenomena, but also the complex relationship between the content of consciousness, level of awareness, and attention. Using this framework, an interesting similarity between epileptic and common déjà vu is revealed: Attention seems forced in common déjà vu, and one can conceive of there being an expansion of self-reflective consciousness - the subject feels strongly that ongoing experience is strongly familiar, but juxtaposed with a sense of not previously

seeing (déjà vu) or immersively having (déjà vecu) the experience. The setting of obtaining intracranial electrophysiological data will enable us, at least in suitably implanted patients, to examine attentional mechanisms, as well as the circuitry of familiarity, in the setting of epileptic and both electrical-stimulation- and task-induced déjà vu.

Secondly, this work touches on the domain of virtual reality (VR) and its uses in human neuroscience [55–57]. To aid this line of research, we are developing an immersive VR-based version of this task that uses a head-mounted display (HMD). The purpose is to create a more intensely immersive version of the task and develop the tools and framework for further manipulations of conscious experience. Presently, the virtual tours are set up so that the user does not control the movement through the scene but instead follows a predefined movement path. As participants progress though the virtual tour, especially in the setting of immersive VR, they run the risk of experiencing cybersickness generated by sudden unexpected direction change within the scene. Cybersickness is best defined as a visually induced illness with common symptoms such as nausea, vomiting, dizziness, and fatigue [58]. Participants are seated during the virtual tour to aid in eliminating the feeling of cybersickness. Reducing the risk of cybersickness also requires special consideration during the development of the virtual tours to make sure the movement through scenes maintains an appropriate speed as well as does not perform any drastic camera rotations. These issues have been tackled extensively, but we will need to be sensitive to this in clinical populations. So not only will this work contribute to the use of VR in studies of human subjectivity but will also contribute toward making VR more generally useful in clinical studies.

4. Conclusions

Déjà vu has a well-documented association with epilepsy going back over a century. Whether or not the experience of déjà vu is always associated with some type of seizure activity has been unclear [32]. The present case report adds to a growing body of work suggesting that déjà vu can occur in the absence of detectable seizure activity and that one way in which this can occur is through environmental circumstances that trigger the experience. Although previous researchers have suggested that déjà vu can occur in the absence of detectable seizure activity and that when it does, it involves a different neural signature [59–60], this prior research has used scalp EEG, which is not suitable for detecting highly focal MTL seizure activity. Our case provides stronger evidence than prior scalp EEG studies by recording directly from pertinent brain regions. Thus, with SEEG, the present case study was able to more definitively rule out underlying seizure activity during the virtual tours or during the reported déjà vu experiences. These findings also fit with a previous case report of a patient who experienced déjà vu as a seizure symptom; that patient was unable to stop the seizure from progressing by refocusing attention onto another environmental stimulus (and away from the stimulus that seemed to prompt the onset of déjà vu), which suggests that the seizure-related déjà vu was emerging from internal, rather than external, factors [24]. Our findings suggest that in the present case, the patient’s feelings of déjà vu during the virtual tours were elicited by external factors, and these externally related déjà vu experiences did not feel to him like the seizure-related déjà vu.

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Highlights

1. Déjà vu-like experiences can be elicited experimentally
2. Induced Déjà vu is not associated with epileptiform abnormalities in intracranial EEG
3. Induced familiarity during recall failure is an important opportunity for memory research
4. Virtual reality has promise for human intracranial and memory studies
5. Subjective experiences during seizures are an opportunity for consciousness research

Figure 1. Images of spatially mapped virtual stimuli used in the virtual tour paradigm.

On the left is a bedroom scene, one of many possibly toured in the encoding phase. The right panel shows a clothing store, toured in the test phase, that has the same spatial configuration but is otherwise novel within the context of the experiment.

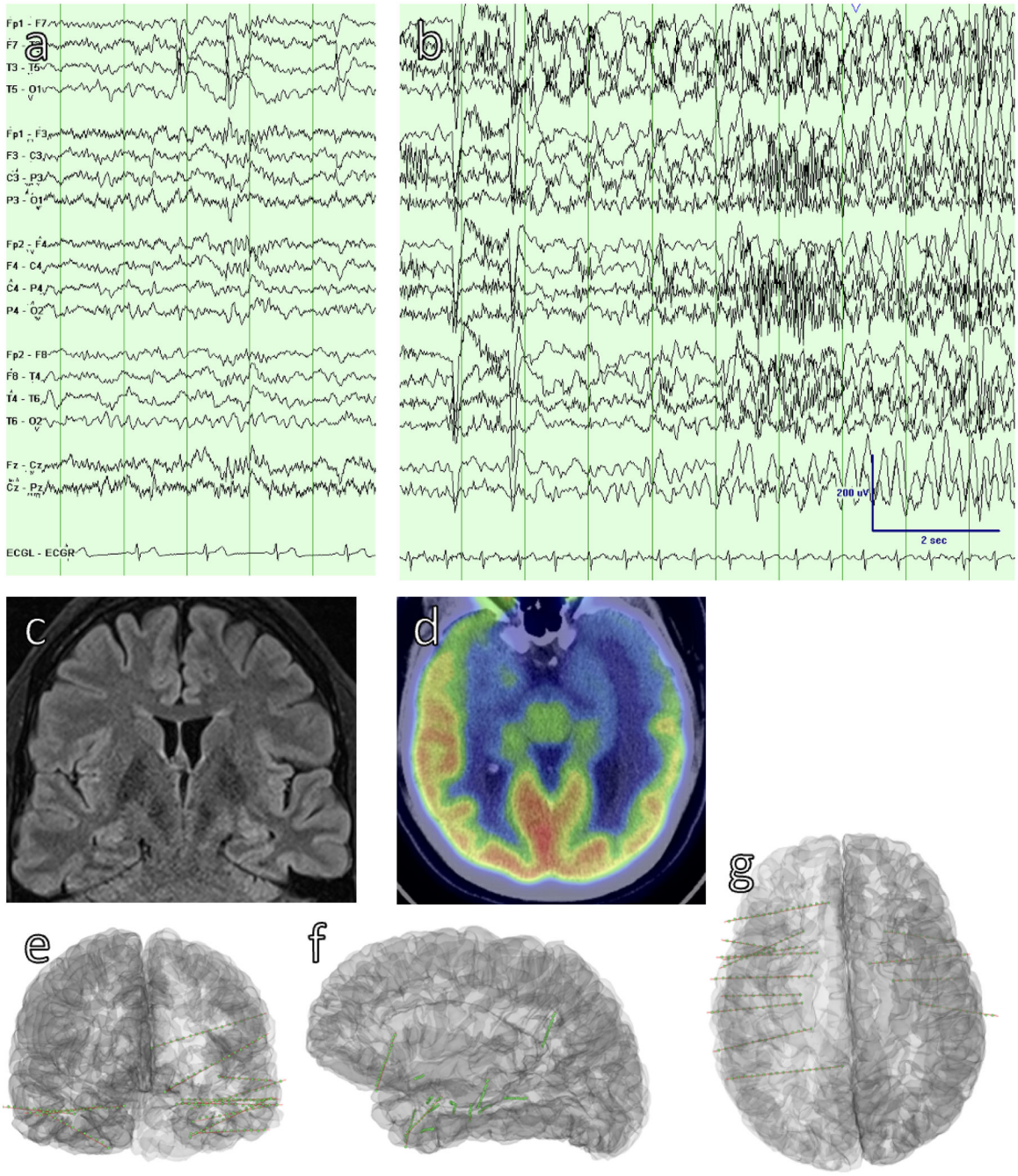

Figure 2. EEG, Imaging, and Electrode Placement Reconstruction.

(a) Sleep-activated left anterior temporal spikes. (b) Seizure onset over the same anterior temporal region. (c) MRI shows questionable hyperintensity of the left hippocampus on FLAIR. (d) PET reveals widespread hypometabolism in the left temporal lobe. Panels e-f show the pial surface segmentation with SEEG electrodes superimposed in coronal, sagittal and horizontal views, respectively.