Epilepsy & Behavior Reports 25 (2024) 100649

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr

"Amity Seizures": A previously unreported semiology localizing to a circuit between the right hippocampus and orbitofrontal area

Alexander Hedaya [a], Lawrence Ver Hoef [a,b,*]

[a] Department of Neurology, University of Alabama at Birmingham, Birmingham, AL 25233, USA
[b] Birmingham VA Medical Center, Neurology Service, Birmingham, AL 35233, USA

ARTICLE INFO

Keywords:
Frontal lobe seizure
Semiology
Emotion
Network engagement
SEEG

ABSTRACT

We describe a case of focal epilepsy with a semiology consisting of behaviors indicating an enthusiastic desire for those around him to get along and engage in friendly relations, which we refer to as "amity seizures". The patient was a 41-year-old right-handed male with seizures since age 26. Semiology consisted of stereotyped enthusiastic behaviors such as expressing "Peace! Peace!… Come on, we all on the same team, right?!", and giving hugs, kisses, and high-fives to those around him. On SEEG evaluation, 2 independent areas of seizure onset were identified, the right hippocampus and right posterior orbitofrontal area. Locally confined seizures had bland manifestation. However, spread from right hippocampus to right orbitofrontal area, or vice versa, elicited his typical amity seizure semiology. To our knowledge this is the first report of the seizure semiology we have coined "Amity seizures". While emotions were once thought to localize to discrete brain regions, they are now accepted to arise from networks across multiple brain regions. The fact that this behavior only occurred when seizures spread from either of 2 onset zones to the other suggests that this semiology results from network engagement between, and likely beyond, either onset zone.

1. Introduction

Amity is defined as the quality of goodwill and friendly relationship between people or entities. It is derived from the Latin "amicus", meaning friend, which is also the derivation of the word "amicable". Herein, we describe a case of a patient with focal epilepsy with a semiology consisting of behaviors indicating an enthusiastic desire for those around him to get along and engage in friendly relations, which we refer to as "amity seizures".

Earlier debate regarding the neurophysiology of emotion has surrounded whether discrete brain regions are responsible for emotions or whether emotions result from more widespread network engagement [1,2]. While fMRI studies have shown some discrete areas of emotional localization [3], more recent consensus falls of the side of dimensional theory, positing that network engagement and interplay between multiple brain regions generates emotional experience [4]. For example, acute psychologic stressors have been shown on fMRI to activate wide ranging network interactions [5]. The amygdala, orbitofrontal cortex, and hippocampus are structurally connected and implicated in generating emotion through widespread, distributive activation [6].

We report a case of SEEG-proven multifocal epilepsy producing a semiology of amity arising with conduction, in either direction, between 2 independent seizure-onset zones, specifically the right hippocampus and the right posterior orbitofrontal area.

2. Methods

Patient history, workup, and outcomes were obtained by review of electronic medical record. EEG and SEEG recordings were reviewed from archived studies. Figures with photographs involving patients, family, and staff, were deidentified by accepted standards [7]. All patients admitted to our epilepsy monitoring unite (EMU) sign a release that allows the use of data and images for teaching and research purposes. In addition to this, prior to article submission, informed consent was obtained from the patient for the use of photographs for publication.

Visualization of SEEG implantation for evaluation and making figures were performed with MRIcroGL (version 14.2.1 (Build 23C71), developed by Christ Rorden, Columbia, South Carolina, USA, https://www.nitrc.org/projects/mricrogl). Videos of his events were prepared with Apple iMovie (version 10.3, Apple Inc, Cupertino, California, USA) for compression, trimming, and basic audio/video enhancement. Initial facial blurring was performed with Gallio Pro (version 2.12.0,

* Corresponding author at: Department of Neurology, University of Alabama at Birmingham, Birmingham, AL 25233, USA.
E-mail addresses: aahedaya@uabmc.edu (A. Hedaya), lverhoef@uabmc.edu (L. Ver Hoef).

https://doi.org/10.1016/j.ebr.2024.100649
Received 8 November 2023; Received in revised form 17 January 2024; Accepted 21 January 2024
Available online 24 January 2024

developed by Trasee sp. z o.o., Poland). Davinci Resolve was used for final editing, blurring, post-processing, and audio editing (version 18.6.4, build 6, Blackmagic Design Pty. Ltd., Victoria, Australia).

3. Case report

The patient was a left-handed (made to write with right hand) 35 year-old male referred initially to the epilepsy clinic for evaluation for generalized tonic-clonic seizures. Seizures began at age 29. 5 years prior to seizure onset, he was in a car accident and sustained a closed skull base fracture. He went on to develop a sphenoid mucocele and underwent sinus surgery to remove this, leaving him with a skull defect. A year after mucocele repair, he had his first focal to bilateral tonic-clonic seizure and was subsequently found to have herniated a small piece of his temporal lobe (encephalocele) through this defect. He underwent another surgery to remove the herniated tissue, which was necrotic. This took place at an outside hospital and imaging was not available to us from this time-period. He had a second focal to bilateral tonic-clonic seizure, was placed on levetiracetam, and was seizure-free for the next 5 years. He continued to be highly functioning and working as a lawyer. Five years after his encephalocele resection, he developed focal impaired awareness seizures of the type described below.

The patient's family reported that his seizures included nonsense talk, saying "peace, peace", shaking hands, and not being himself. He would typically, but not always, have an aura of an indescribable but stereotypical "weird feeling". Seizures lasted 1–2 min and occurred 2–4 times per month. While he remained interactive during events, he had no memory of them. He felt generally fatigued after his seizures. Psychological stress was triggering to his events. At the time of evaluation, he was on levetiracetam 500 mg twice daily, oxcarbazepine extended release 1800 mg daily, and lamotrigine 50 mg twice daily.

He underwent pre-surgical evaluation with scalp video-EEG, stereo-EEG, MRI, PET, SPECT, MEG, and Wada testing. MRI showed a prior limited right mesial temporal lobe focal resection, loculated cystic replacement of much of the clivus and right skull base, but bilaterally normal-appearing hippocampi (Fig. 1). MEG showed four spike sources localizing to the right lateral and basal temporal regions. PET scan showed a metabolic defect in the right inferior medial temporal region, corresponding to known postsurgical changes. Subtraction ictal SPECT was nonlocalizing and only showed hypoperfusion of the area of the posterior superior sagittal sinus.

Neuropsychiatric testing demonstrated intact learning and above average recall of visual information, with isolated cognitive weaknesses across aspects of language including generative phonemic fluency and confrontational naming. Given that these findings were somewhat atypical for presumed non-dominant hemisphere dysfunction, some concern was raised for right-hemispheric language contribution. To clarify, fMRI was obtained and confirmed left-hemispheric language dominance. He also underwent WADA testing which showed strong left hemispheric support for speech and language. However, Wada recognition memory testing demonstrated good memory performance for both hemispheres (75 % score for right-sided injection versus 69 % score for left-sided injection). He was deemed to have a high likelihood of suffering at least some memory decline if he were to undergo resective epilepsy surgery, which he felt would impair him as a high functioning professional.

During EMU stay, scalp EEG captured focal seizures and interictal discharges that appeared to arise from the right temporal region. SEEG evaluation involved implantation of 10 right hemispheric electrodes targeting the amygdala, anterior hippocampus, posterior hippocampus, basal temporal lobe, anterior orbitofrontal area, posterior orbitofrontal area, anterior cingulate, posterior cingulate, thalamus, and frontal polar

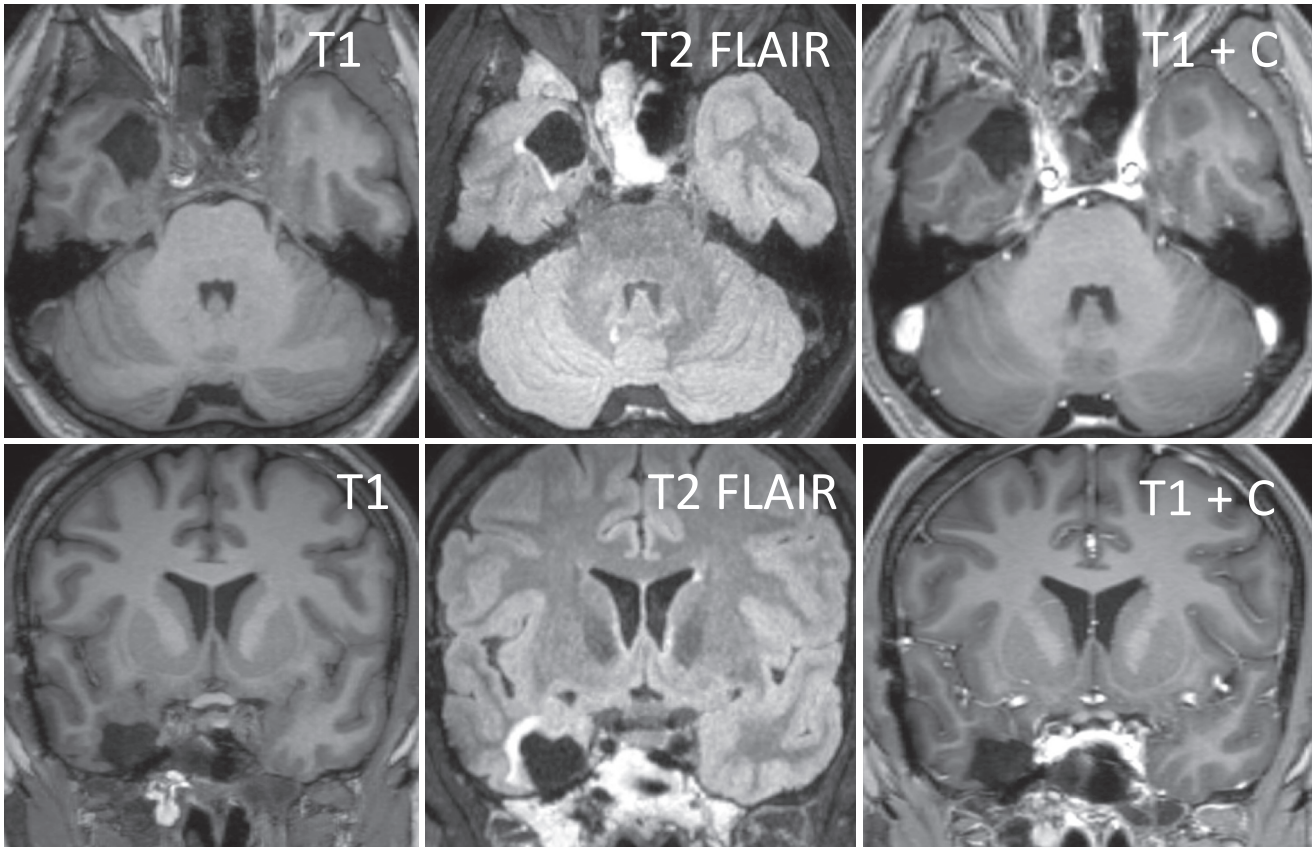

Fig. 1. MRI obtained for presurgical workup, prior to the placement of RNS to the right hippocampus and right orbitofrontal area. Shown are axial and coronal T1, T2 FLAIR, and T1 post-contrast images demonstrated R temporal cavity consistent with prior right focal encephalocele resection.

areas (Fig. 4). Six seizures were captured, and revealed two independent seizure onset zones, specifically the right hippocampus (RH) and right mesial posterior orbitofrontal (RMPOF) area. Of the 6 seizures, 3 arose from RMPOF, and 2 of those spread to the RH. 3 arose from the RH, of which 1 spread to the RMPOF (Table 1). Locally-confined seizures without spread outside either zone of onset had relatively bland manifestations, without characteristic amity semiology. Seizures confined to RH consisted of only a few gibberish words and a feeling like he may have a focal seizure. The single seizure confined to the RMPOF area consisted of a few gibberish words and few statements of "peace, peace" (dramatically less than typical event). However, seizure spread from RH to the RMPOF, or vice versa, manifested his typical amity seizure semiology. This conduction was temporally correlated to spread of the seizure from one site to the other (Figs. 2 and 3, Supplementary videos 1 and 2). The semiology consisted of stereotyped enthusiastic behaviors such as expressing "Peace! Peace!… Come on, we are all on the same team, right?!". He would give hugs and kisses to his wife, as well as EMU staff members, saying pleasantly, "Give me a hug, alright?". He would elicit handshakes and high-fives from those around him, often in quick succession, saying "handshake! Peace! OK, give me hug!" (Figs. 2 and 3, Supplementary videos 1 and 2). Despite clearly socially interacting with others, he had no recollection of these events whatsoever. Interictally, frequent epileptiform discharges were noted in the right hippocampus and right orbitofrontal area independently.

The anterior insula was penetrated by 3 electrodes. Specifically, the posterior superior portion was captured by the thalamus electrode (RT), the anterior inferior portion by the amygdala electrode (RA), and the anterior middle by the posterior orbitofrontal electrode (RPOF) (Fig. 4). These leads showed no seizure spread to the anterior insula. The frontal pole electrode showed no spread to the frontal pole.

Electrical stimulation (50 Hz, 1–8 mA) of seizure-onset zones failed to reproduce his characteristic semiology. However, stimulation of the right amygdala gave a vague, incomplete feeling reminiscent of his seizure aura. Stimulation of his amygdala and hippocampus demonstrated time-locked, low amplitude cortico-cortical evoked rhythmic activity in the RMPOF area, indicating strong effective connectivity, but stimulation of the RMPOF did not elicit an electrographic response in the mesial temporal structures.

Due to his estimated high risk of memory deficit after resective surgery, he elected to undergo responsive neurostimulation (RNS). Two RNS electrodes were placed, one in the right hippocampus, and a second in the right posterior orbitofrontal area (corresponding to SEEG electrode RPOF 1–4; Fig. 4).

At 4-year follow up, he had approximately unchanged seizure frequency on a regimen of levetiracetam, cenobamate, and oxcarbazepine. He continued to have rare GTCs. He reported subjective short-term memory difficulties, otherwise without complaint of altered social interaction, heightened spiritual experience, or other psychiatric complaint.

4. Discussion

To our knowledge this is the first report of the specific seizure semiology we have coined "Amity seizures". The fact that this behavior only occurred when seizures spread from either of 2 onset zones to the other suggests that this semiology results from network engagement between, and likely beyond, the right posterior orbitofrontal area, right hippocampus, and right amygdala.

As previously mentioned, the neurophysiology of emotions is now thought to originate in network engagement between different brain regions [4,8], rather than in discrete locations. For example, a widely distributed network between the amygdala, hippocampus, prefrontal cortex, and other structures is now thought to form the basis of fear and anxiety generation [9]. Similarly, connectivity between the amygdala and orbitofrontal cortex has been shown to mediate emotional regulation [10]. The differences in connections between limbic regions has

Table 1
Table summarizing SEEG findings as well as clinical semiology and total seizure times.

Seizure number	SEEG	Semiology	Total time (min: sec)
1	Hippocampus -> amygdala -> posterior orbitofrontal	Amity Semiology. Had a feeling like he was ill and sick to his stomach. He was not sure if it was a focal seizure or not. He then developed amity semiology when the seizure spread to his posterior orbitofrontal. He was able to read a sign during his seizure, but appeared somewhat inattentive. (Fig. 2 and Supplementary Video 1)	1:38
2	Posterior orbitofrontal	A few gibberish words, said the phrase "we all get along". No loss of awareness. Responded appropriately to nurse during ictal phase.	0:55
3	Hippocampus	Aura only. He felt like he may have a seizure. No loss of awareness.	0:51
4	Posterior orbitofrontal -> hippocampus and amygdala. (semiology ongoing despite termination of orbitofrontal seizure)	Amity Semiology. The seizure started with a posterior orbitofrontal seizure during sleep, which was noticed by staff who then woke him up. He felt completely normal. Ictal exam performed 40 s after electrographic seizure onset. He was conversant, able to remember a phrase, read with ease, and was alert and oriented. The exam was interrupted when he had a spread of seizure to his hippocampus that resulted in the development of amity semiology.	2:16
5	Right hippocampus	Aura only. Hippocampal seizure. He awoke suddenly and spoke unintelligible words, then mentioned that it felt like he was going to have a seizure. Exam was performed just as seizure ended, but was normal.	0:53
6	Posterior orbitofrontal -> hippocampus	Amity Semiology. He was working on his computer when he developed an orbitofrontal seizure that was noticed by staff. When they arrived at bedside he demonstrated no appreciable change in behavior. Then his seizure spread to his hippocampus at which point he developed amity semiology and an exam was not performed. Ictal exam was not attempted as he became	2:40

(continued on next page)

Table 1 (*continued*)

Seizure number	SEEG	Semiology	Total time (min: sec)
		inattentive. (Fig. 3 and Supplementary Video 2).	

been associated with psychiatric illness. The uncinate fasciculus, which connects the orbitofrontal cortex to the amygdala and anterior hippocampal gyrus, has been shown on diffusion tensor tractography to be disrupted in patients with psychogenic non-epileptic spells (PNES) compared to healthy controls [11]. Modulation to sites in this network have also been investigated as targets for the treatment of psychiatric illness [12,13]. Moreover, the orbitofrontal area plays a role in hedonic experience [14] and reward-driven learning behavior [15], and direct electrical stimulation to the area has improved mood in patients with epilepsy[16]. Dysfunction of the orbitofrontal are well-established to correlate with antisocial behavior [17,18,19].

In brief, Rolls et al has identified the orbitofrontal cortex as a primary driver of emotional experience within a larger network, recognizing the amygdala as a mediator of cortical and autonomic arousal, but not subjective emotion [6]. This hypothesis is remarkably compatible with our patient's case. When seizures were confined to only the right orbitofrontal area, he developed a mild expression of his typical semiology, consisting of mostly gibberish words with a statement of "we all get along", likely representing mild engagement of the network supporting his typical semiology. However, when seizures started in the right orbitofrontal and subsequently spread to the hippocampus and amygdala, he developed his complete, typical semiology. Comparatively, when seizures originating in the right hippocampus and amygdala resulted in his typical aura of "weird feeling", with subsequent spread leading to the onset of his robust semiology. While network engagement probably occurred to some degree beyond these areas, we suspect that amity seizures, and this patient's two seizure foci, are illustrations of the interaction between the known function of the orbitofrontal area in generating emotion and the amygdala in modulating arousal. By the ILAE semiological glossary, this semiology would be classified as a mimic automatism [20].

Regarding prior descriptions of semiologies with similar features, in a series of 42 patients undergoing SEEG for prefrontal seizures, Singh, et al described 2 patients with ictal semiology consisting of humming/singing, thigh-slapping, prosociality, and rhythmic body movement

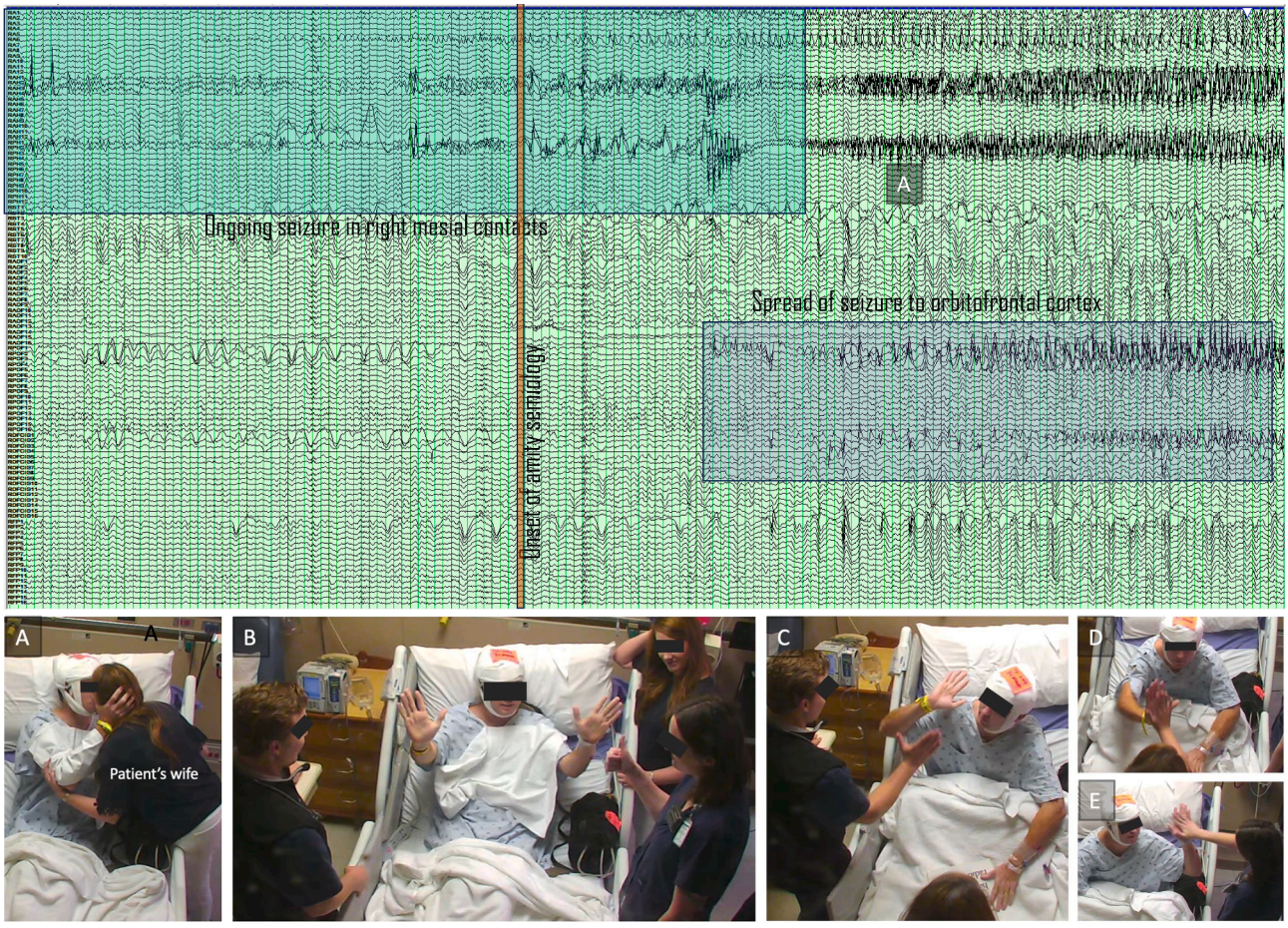

Fig. 2. Example of amity seizure on spread from right amygdala/hippocampus to right posterior orbitofrontal region, recorded on SEEG monitoring. Sensitivity 150uV/mm, timebase 15 mm/sec. Referential montage. Showing electrode RA (entry superior temporal gyrus, target amygdala), RAH (entry superior temporal gyrus, target anterior hippocampus), RPH (entry middle temporal gyrus, target posterior hippocampus), RBT (entry middle temporal gyrus, target basal temporal), RAOF (entry inferior frontal gyrus, target anterior orbitofrontal), RPOF (entry inferior frontal gyrus, target posterior orbitofrontal), ROFCing (entry superior frontal gyrus, target orbitofrontal), RFP (entry inferior frontal gyrus, target frontal pole). RCing (entry superior frontal gyrus, target posterior cingulate) and RT (entry frontal operculum, target thalamus) were omitted from this figure due to space limitations. Neither electrode showed seizure involvement. Herald spike at RAH 1–4 and RPH 1–3. RPOF changes are noted at this stage without clear ictal pattern. Ictal pattern starts in in RA 5–7 with rapid spread to RAH 1–3 and RPH 1–3. Subsequent spread to RPOF 1–3 and ROFCing 1–3. Onset of typical semiology noted on recording. Letters placed on the EEG tracing indicate the time at which a behavior occurred. If not listed, then the behavior occurred at some point after this segment of EEG.

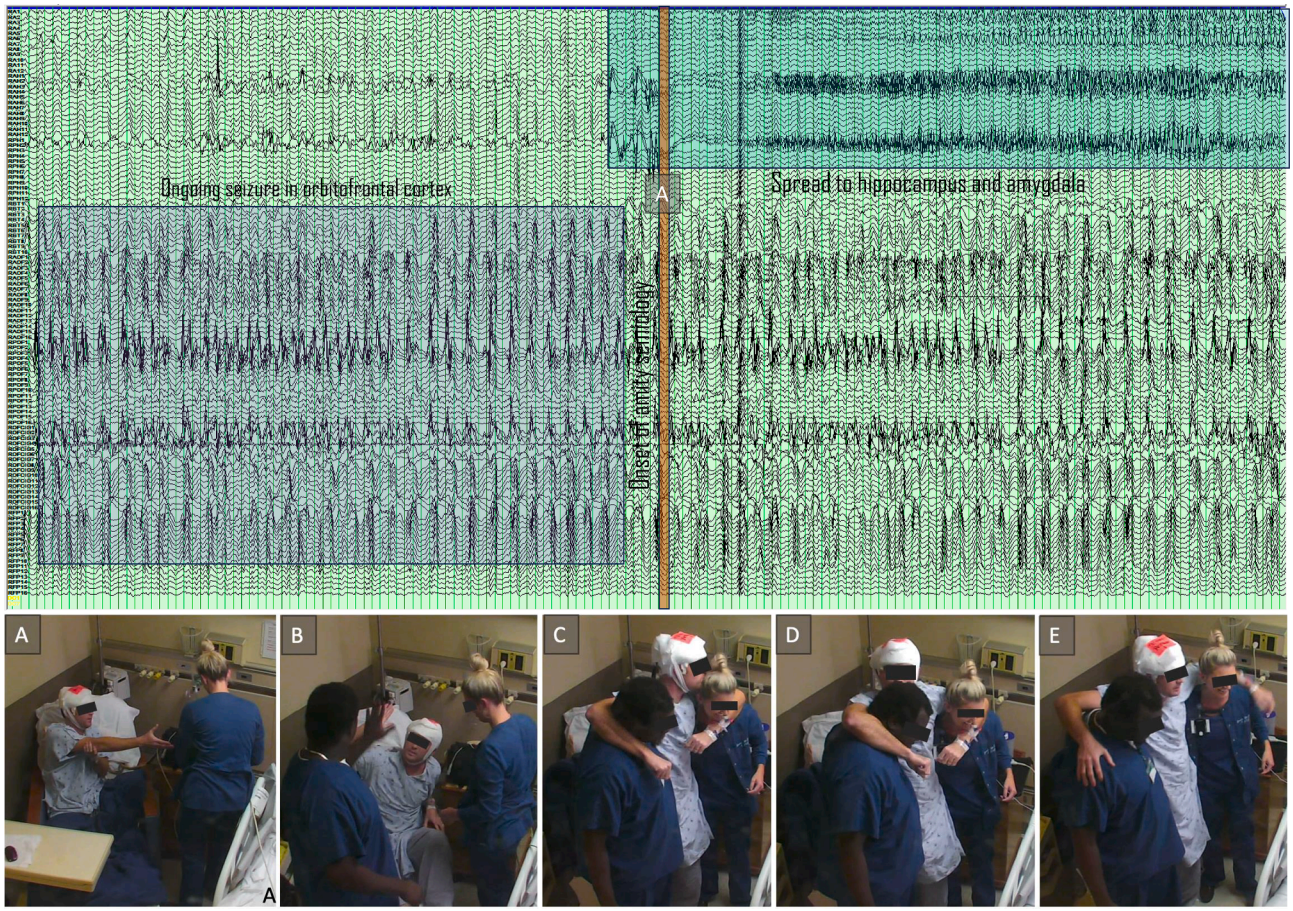

Fig. 3. Example of amity seizure on spread from right posterior orbitofrontal region to right amygdala/hippocampus, recorded on SEEG monitoring. See Fig. 2 for implantation scheme. RCing and RT omitted due to space limitation and no seizure involvement. Sensitivity 150uV/mm, timebase 15 mm/sec. Referential montage. The recording shows an ongoing seizure in RPOF 1–5 and ROFCing 3–5, with spread to RAH 1–3 and RPH 1–3 and subsequent involvement of RA. Onset of typical semiology noted on recording. Letters placed on the EEG tracing indicate the time at which a behavior occurred. If not listed, then the behavior occurred at some point after this segment of EEG.

[21]. In these cases, seizure-onset occurred in the frontopolar region with spread to anterior orbitofrontal cortex and pre-supplementary motor area, whereas seizure of the posterior orbitofrontal area was correlated with negative emotions such as fear. Lack of detailed, fully-elaborated description of these semiologies limits full comparison. Of note, our patient's seizures would be classified as mimic automatism [20].

Cortical stimulation studies have yielded inconclusive results in revealing the pathways associated with pleasant emotions. Both positive and negative emotions have been inconsistently generated by stimulation to a variety of locations, including the anterior cingulate gyrus, amygdala, temporal pole, and insula, among others [22,23,24]. In our case, stimulation did not produce typical semiology, although stimulation to his right amygdala elicited a vague, incomplete sense of his seizure aura. Likewise, ecstatic seizures, a rare but distinctly different semiology than what is described herein, are thought to localize to the anterior insula [25,26] despite the fact that direct stimulation of the anterior insula rarely produces ecstatic aura [27]. As a simple explanation, high frequency stimulation may unintentionally disrupt the native function of a complex network. More importantly, when compared to stimulation, seizures have more geographically widespread activity and likely simultaneously activate and deactivate brain networks. As another explanation, amity semiology may represent a release phenomenon generated by a loss of inhibitory control. His semiology included ictal kissing, a behavior thought to represent a release phenomenon, partly on the basis of its inability to be elicited by cortical stimulation [28]. Regardless, the failure of stimulation to produce any symptom resembling amity semiology points to the importance of network engagement in generating these unusual behavioral symptoms.

While ecstatic seizures are similar to this patient's amity seizures in that both demonstrate the presence of intense positive feelings, there are several features that we think makes amity seizures a distinct clinical entity. Ecstatic seizures are characterized by an individual, *internal* sensation of intense positive emotion and wellbeing [27], while amity semiology is notably relational and interpersonal. Furthermore, at least for the duration of their ecstatic experience, patients have preserved awareness, whereas our patient had no recollection of his event. However, in the case of both amity and ecstatic seizures, these regions likely produce such semiology via interaction with diverse areas of connection.

5. Conclusion

Overall, this case demonstrates the importance of network engagement in generating emotion, in our case amity. His seizures highlight the connection between the amygdala, hippocampus, and orbitofrontal cortex. RNS placement to the right amygdala and right posterior orbitofrontal area resulted in a reduction in his seizure frequency. The structure, function, and network organization of both regions remain complex and uncertain. Further studies are needed to determine their role in seizure semiology and emotional generation.

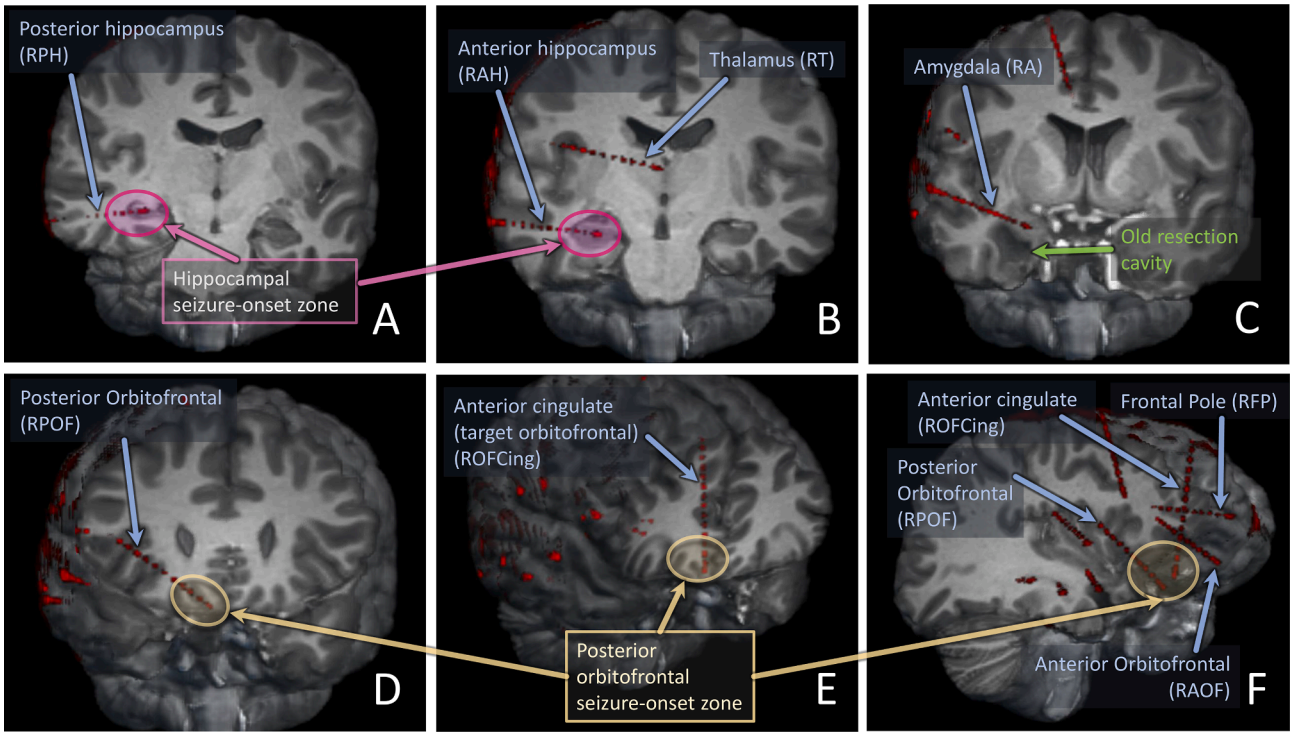

Fig. 4. This figure shows our SEEG implantation scheme in relation to this patient's two independent seizure-onset zones the right hippocampus and posterior orbitofrontal region. Of note, seizure spread occurred in either direction between these two areas. Locally confined seizures were also recorded for both onset-zones. A. Coronal slice showing right posterior hippocampus electrode (RPH) and the corresponding hippocampal seizure onset zone. B. The right anterior hippocampus (RAH) is shown, along with the seizure-onset zone in the hippocampus. The thalamic electrode (RT) is identified, although it did not detect any epileptiform activity during SEEG evaluation. C. The amygdala electrode (RA) is shown. Note the old, right temporal resection cavity (green arrow). The trajectory of the amygdala electrode was slightly modified from our usual protocol to avoid this cavity. Rapid spread to the amygdala often occurred when seizures affected the hippocampus. D. The posterior orbitofrontal electrode (RPOF) is shown with its terminus in the posterior orbitofrontal lobe. A second seizure onset-zone was noted in this region, marked on figure. E. Oblique cut showing the anterior cingulate electrode (ROFCing), with a target of the orbitofrontal lobe and corresponding seizure onset zone. F. Sagittal view demonstrating the course of the posterior orbitofrontal and anterior cingulate electrodes. The posterior orbitofrontal electrode is seen traversing the anterior insula (no spread to the insula was recorded for any seizure) and nearing the anterior cingulate electrode at the posterior orbitofrontal area, where these two electrodes recorded multiple seizures. The frontal pole (RFP) and anterior orbitofrontal (RAOF) electrodes are also identified. The frontal pole electrode recorded no seizure activity during SEEG monitoring. The anterior orbitofrontal electrode recorded some seizure spread. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Ethical statement

All patients admitted to our epilepsy monitoring unite (EMU) sign a release that allows the use of data and images for teaching and research purposes. In addition to this, prior to article submission, informed consent was obtained from the patient for the use of photographs for publication.

CRediT authorship contribution statement

Alexander Hedaya: Conceptualization, Visualization, Writing – original draft, Writing – review & editing. **Lawrence Ver Hoef:** Conceptualization, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2024.100649.

References

[1] Hamann S. Mapping discrete and dimensional emotions onto the brain: controversies and consensus. Trends Cogn Sci 2012;16:458–66.
[2] Kragel PA, LaBar KS. Decoding the Nature of Emotion in the Brain. Trends Cogn Sci 2016;20:444–55.
[3] Vytal K, Hamann S. Neuroimaging support for discrete neural correlates of basic emotions: a voxel-based meta-analysis. J Cogn Neurosci 2010;22:2864–85.
[4] Pessoa L. A Network Model of the Emotional Brain. Trends Cogn Sci 2017;21:357–71.
[5] Hermans EJ, van Marle HJ, Ossewaarde L, Henckens MJ, Qin S, van Kesteren MT, et al. Stress-related noradrenergic activity prompts large-scale neural network reconfiguration. Science 2011;334:1151–3.
[6] Rolls ET. Emotion, motivation, decision-making, the orbitofrontal cortex, anterior cingulate cortex, and the amygdala. Brain Struct Funct 2023;228:1201–57.
[7] Roberts EA, Troiano C, Spiegel JH. Standardization of Guidelines for Patient Photograph Deidentification. Ann Plast Surg 2016;76:611–4.
[8] Lindquist KA, Barrett LF. A functional architecture of the human brain: emerging insights from the science of emotion. Trends Cogn Sci 2012;16:533–40.
[9] Tovote P, Fadok JP, Luthi A. Neuronal circuits for fear and anxiety. Nat Rev Neurosci 2015;16:317–31.
[10] Banks SJ, Eddy KT, Angstadt M, Nathan PJ, Phan KL. Amygdala-frontal connectivity during emotion regulation. Soc Cogn Affect Neurosci 2007;2:303–12.
[11] Lee S, Allendorfer JB, Gaston TE, Griffis JC, Hernando KA, Knowlton RC, et al. White matter diffusion abnormalities in patients with psychogenic non-epileptic seizures. Brain Res 2015;1620:169–76.
[12] Fettes P, Schulze L, Downar J. Cortico-Striatal-Thalamic Loop Circuits of the Orbitofrontal Cortex: Promising Therapeutic Targets in Psychiatric Illness. Front Syst Neurosci 2017;11:25.
[13] Zhang L, Li Q, Du Y, Gao Y, Bai T, Ji GJ, et al. Effect of high-definition transcranial direct current stimulation on improving depression and modulating functional activity in emotion-related cortical-subcortical regions in bipolar depression. J Affect Disord 2023;323:570–80.

[14] Kringelbach ML. The human orbitofrontal cortex: linking reward to hedonic experience. Nat Rev Neurosci 2005;6:691–702.
[15] Nogueira R, Abolafia JM, Drugowitsch J, Balaguer-Ballester E, Sanchez-Vives MV, Moreno-Bote R. Lateral orbitofrontal cortex anticipates choices and integrates prior with current information. Nat Commun 2017;8:14823.
[16] Rao VR, Sellers KK, Wallace DL, Lee MB, Bijanzadeh M, Sani OG, et al. Direct Electrical Stimulation of Lateral Orbitofrontal Cortex Acutely Improves Mood in Individuals with Symptoms of Depression. Curr Biol 2018;28(3893–3902):e4.
[17] Blair RJ. The roles of orbital frontal cortex in the modulation of antisocial behavior. Brain Cogn 2004;55:198–208.
[18] Bramham J, Morris RG, Hornak J, Bullock P, Polkey CE. Social and emotional functioning following bilateral and unilateral neurosurgical prefrontal cortex lesions. J Neuropsychol 2009;3:125–43.
[19] Piras IS, Braccagni G, Huentelman MJ, Bortolato M. A preliminary transcriptomic analysis of the orbitofrontal cortex of antisocial individuals. CNS Neurosci Ther 2023;29:3173–82.
[20] Beniczky S, Tatum WO, Blumenfeld H, Stefan H, Mani J, Maillard L, et al. Seizure semiology: ILAE glossary of terms and their significance. Epileptic Disord 2022;24:447–95.
[21] Singh R, Giusiano B, Bonini F, Lagarde S, Brockington A, Trebuchon-Dafonseca A, et al. Characteristics and Neural Correlates of Emotional Behavior during Prefrontal Seizures. Ann Neurol 2022;92:1052–65.
[22] Guillory SA, Bujarski KA. Exploring emotions using invasive methods: review of 60 years of human intracranial electrophysiology. Soc Cogn Affect Neurosci 2014;9:1880–9.
[23] Fox KCR, Yih J, Raccah O, Pendekanti SL, Limbach LE, Maydan DD, Parvizi J. Changes in subjective experience elicited by direct stimulation of the human orbitofrontal cortex. Neurology 2018;91:e1519–27.
[24] Halgren E, Walter RD, Cherlow DG, Crandall PH. Mental phenomena evoked by electrical stimulation of the human hippocampal formation and amygdala. Brain 1978;101:83–117.
[25] Picard F, Bossaerts P, Bartolomei F. Epilepsy and Ecstatic Experiences: The Role of the Insula. Brain Sci. 2021:11.
[26] Bartolomei F, Lagarde S, Scavarda D, Carron R, Benar CG, Picard F. The role of the dorsal anterior insula in ecstatic sensation revealed by direct electrical brain stimulation. Brain Stimul 2019;12:1121–6.
[27] Geschwind M, Picard F. Ecstatic Epileptic Seizures: A Glimpse into the Multiple Roles of the Insula. Front Behav Neurosci 2016;10:21.
[28] Rashid RM, Eder K, Rosenow J, Macken MP, Schuele SU. Ictal kissing: a release phenomenon in non-dominant temporal lobe epilepsy. Epileptic Disord 2010;12:262–9.