Influence of mindfulness meditation on intracranial EEG parameters in epileptic and non-epileptic brain areas

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Author Contributions

Daniel D. Cummins: Conceptualization, data analysis, manuscript preparation and revision.
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Abstract

Objective

Mind-wandering is a pervasive human brain state and, when in excess, may promote negative affect and neuropsychiatric conditions. Mindfulness meditation may promote alternate brain states, improving affect and reducing stress. An understanding of the neural basis between these brain states could thus advance treatment of neuropsychiatric conditions, including those associated with epilepsy.

Methods

To explore the neural basis of mindfulness meditation versus mind-wandering, we enrolled eight patients in a trial of structured mindfulness meditation and open mind-wandering who underwent stereo electroencephalography (sEEG) within the mesial temporal lobe for seizure localization. Electrophysiology was compared between mind-wandering and mindfulness separately for epileptic and non-epileptic MTL. Using fitting-one-over-f modeling, periodic components of electrophysiology were compared in canonical frequency bands of theta (4-8Hz), alpha (8-13Hz), beta (13-30Hz), and gamma (30-55Hz). Aperiodic components of the power spectra were assessed by the model offset, knee, and exponent.

Results

We found a significant reduction in gamma power (30-55Hz) within the mesial temporal lobe (MTL) during mindfulness meditation compared with mind-wandering in non-epileptic ($p=1.20E-4$) but not in epileptic MTL ($p=0.352$).There was also a significant difference between epileptic versus non-epileptic MTL in gamma power between conditions ($p=0.011$). There were no significant changes in power across any frequency band within epileptic mesial temporal MTL between brain states. Conversely, there were significant differences between mind-wandering and mindfulness within epileptic MTL in aperiodic components (offset, knee, and exponent, all $p<0.05$), while no differences in aperiodic components were seen in non-epileptic MTL (all $p>0.70$).

Significance

Intracranial electrophysiologic modulations between brain state (mind-wandering versus mindfulness) may differ between epileptic and non-epileptic MTL. Modulations in gamma activity in non-epileptic MTL may represent functional changes in brain state, while aperiodic changes in epileptic MTL may modulate propensity for seizures.

Keywords: Epilepsy, meditation, mind-wandering, electrophysiology, amygdala, hippocampus

Introduction

Mind-wandering, the spontaneous state of thoughts in absence of external stimuli, is a pervasive human state that occupies up to 50% of waking consciousness,[1] and may at times drive negative emotions such as stress and depression.[2–4] Mindfulness meditation represents a brain state in which thought is focused on a single stimuli, such as the breath. This form of meditation is associated with both reduced stress and reduced negative emotion.[5–7] A body of literature has explored the neural correlates of both mindfulness meditation and mind-wandering, the bulk of which focusing on structural and functional imaging in each respective brain state.[8,9]

Most literature on mind-wandering and meditation comes from functional magnetic resonance imaging (fMRI) and surface electroencephalography (EEG).[10] Functional neuroimaging studies have demonstrated a predominant role of the default mode network in mind-wandering, but regions such as the hippocampus may also play a critical role, including by mediating imagined events of the past or future.[11–13] Similarly, reductions in amygdala activity and functional connectivity have been documented with mindfulness meditation.[14–16] EEG studies, which provide spatiotemporal resolution not provided with functional neuroimaging, have demonstrated state changes in the brain with mind-wandering, including widespread changes in theta, alpha, and gamma activity.[17–19] Evidence from fMRI studies has thus demonstrated that the hippocampus and amygdala play a critical role in human mind-wandering and mindfulness. Simultaneously, scalp EEG has implicated spectral changes between states of mind-wandering and mindfulness meditation but cannot assess mesial temporal structures, deep from the surface of the scalp. Similarly, fMRI lacks high spatiotemporal resolution. Understanding of the neural basis of meditation versus mind-wandering may help treat patients with neuropsychiatric conditions caused by long-term perturbations in such brain states. For instance, excessive mind-wandering has been associated with unhappiness,[1] and certain patterns of mind-wandering may contribute to mood disorders such as depression.[3,4] There remain few reports on a small number of patients on the intracranial effects of meditation on electrophysiology.[20–22] Further, there is little work on how epileptic MTL tissue may be engaged in functional networks involved in changes in brain state. These limited reports have suggested that focused attention (FA) meditation (a component of mindfulness mediation),[23] may be associated with increased interictal activity,[22] and physiological modulations in alpha and gamma power have been seen with both mindfulness and FA meditation.[20,21] Some prior reports have suggested long-term meditation could increase the propensity for seizures,[24] while other work has shown a potential reduction in seizures with meditation and related practices.[25] Here we set out to describe spectral changes from intracranial EEG within the hippocampus and amygdala during mind-wandering versus mindfulness meditation, including the differences between epileptic and non-epileptic mesial temporal electrophysiology.

Methods

Patients

All subjects included were patients with drug resistant epilepsy implanted with intracranial electroencephalography (iEEG) leads for seizure monitoring. Only patients with amygdala and hippocampal leads were included. Contacts were defined as epileptogenic or non-epileptogenic based on the sEEG review by a board-certified epileptologist. Intracranial electroencephalography data was recorded during guided mindfulness meditation and mind-wandering. The meditation task consisted of focused awareness meditation, in which patients were instructed to follow their breath for 10 minutes. This was the first experience with meditation for all subjects. Immediately following the conclusion of meditation, mind wandering was instructed as, "Now let your mind wander for the next 2 minutes." Subjective meditation depth was recorded by the previously described 30-item Meditation Depth Questionnaire (MEDEQ) immediately after each meditation session.[26] Each item had four possible levels including “never” (scored 0), “sometimes” (scored 2), “often” (scored 3), and “very much” (scored 4).

iEEG data analysis

Each trial portion was timestamped to iEEG data using two timestamping methods to record the timing of each meditation session block accurately: a pushbutton-press and manual time notation: (1) Seizure Button Press: At the initiation of each meditation session, researchers executing the session were provided with a dedicated button to press. This button is used to note seizure start times using a clinical recording system, Natus Neuroworks (Natus Medical Inc., Pleasanton, CA), and was used to label task timing. The act of pressing the button served as an event marker for the beginning of each task; the timing of the button press was recorded with millisecond precision. (2) Manual Time Notation: In addition to the pushbutton press timestamping, the start and end times of each task block were manually recorded. The hour, minute, and second of the session's start and end were noted down in patient task notes using a standardized clock reference.

Non-epileptic MTL was defined by non-lesional (normal) MRI on the respective hemisphere, and with no ictal or interictal activity identified on sEEG by the epileptologist. Epileptic MTL was defined by contacts that were in the seizure onset zone and/or had interictal epileptiform discharges. However, to assess functional changes in electrophysiology, periods of time with ictal or interictal activity during meditation or mind-wandering tasks were excluded. Therefore, all data analyzed was free of ictal or interictal epileptic activity. All iEEG data was sampled at 1024Hz from the hippocampus and amygdala in monopolar configuration referenced to a white matter ground. All data was bipolar re-referenced, and bandpass filtered between 2Hz and 250Hz. A notch filter was applied at 60Hz to reduce line artifact. Data was visually inspected and those with notable line artifact were excluded from analysis. Power spectra were calculated using Welch’s method with parameters of 12.4% overlap and a one second Hanning window. The periodic components of each power spectra were calculated using the fitting one-over-f (FOOOF) methodology, previously described.[27] FOOOF analysis was carried out separately from 2Hz – 55Hz (chosen to avoid artifact with the 60Hz notch filter and line noise). Consistent model parameters were chosen with peak widths 0.1Hz – 8.0Hz, maximum number of peaks of six, minimum peak height of 0.1dB, peak threshold of 2.0, and with an aperiodic ‘knee’ model. Electrophysiology preprocessing and analyses were performed using custom MATLAB scripts.

Statistical analyses were carried out separately in the following frequency bands: theta (4-8Hz); alpha (8-13Hz); beta (13-30Hz); and gamma (30-55Hz). Peak power in each frequency band was then determined using only active contacts for each respective frequency band; inactive contacts in each frequency band were excluded for this analysis. We compared the peak power in each frequency band based on the average power across the entire trial interval. Mann-Whitney U tests were used for paired comparisons between conditions (mind-wandering versus mindfulness), given non-normally distributed data via the Shapiro test for normality. Changes in power in mind-wandering versus mindfulness between epileptic versus non-epileptic MTL were then compared using Kruskal-Wallis tests. Aperiodic components (model offset, knee, and exponent) were compared between mind-wandering and mindfulness using Mann-Whitney U tests for paired comparisons. All statistical analyses were performed in R software. Bayes factor analysis was also performed for each statistical comparison using the 'BayesFactor' package in R, using the *generalTestBF* function to determine each respective Bayes Factor. Generalized linear mixed-effects models were further applied to assess the effects of inter-individual variability on results. These analyses were carried out using *glmer* function within the 'lme4' package in R.

Anatomical localization of epileptic and non-epileptic contacts

Contacts within the hippocampus and amygdala were determined by reconstructing 3-Tesla magnetic resonance imaging (MRI) scans obtained preoperatively before iEEG placement with a computed tomography (CT) scan obtained postoperatively. The previously-described Yale-Brain Atlas was used to localize contacts within the hippocampus and amygdala, and position was confirmed by manual inspection.[25] All contacts were non-lesional on MRI. Contacts with ictal activity determined by the clinical epileptologist were labeled as "epileptic," and those that had no ictal or interictal activity over the period of sEEG were labeled as "non-epileptic." Contacts were visualized in Montreal Neurological Institute space on a standardized T1 pre-contrast MRI using MRIcron software.[28]

Results

Eight patients with 65 contacts were included: 45 in non-epileptic MTL and 20 in epileptic contacts MTL; 23 in the amygdala and 42 in the hippocampus. A demonstration of all amygdalohippocampal contacts in amygdala and hippocampal gray matter in Montreal Neurological Institute brain space is shown in **Figure 1.** Each statistical test was designed with two groups of comparison, giving one degree of freedom. We found a significant reduction in gamma power (30-55Hz) within the mesial temporal lobe during mindfulness meditation (peak power = 0.14±0.12dB) compared with mind-wandering in the non-epileptic contacts (0.23±0.12dB, p=1.20E-4, **Figure 2**). There were no significant differences in power between conditions across theta (4-8Hz), alpha (8-13Hz), or beta (13-30Hz) frequencies in non-epileptic contacts. There were no significant differences in power across any frequency band between mindfulness and mind-wandering in epileptic contacts (p>0.100 for all frequency bands). To directly compare the difference between epileptic and non-epileptic contacts on shifts in brain state, the difference in peak power was determined between mind-wandering and mindfulness. Compared to epileptic contacts, non-epileptic contacts had significantly greater reduction in peak gamma power with mindfulness meditation compared to mind-wandering (mind-wandering - mindfulness meditation: Non-epileptic: 0.09±0.09dB; Epileptic: -0.02±0.17dB; p = 0.011, **Figure 2**). Bayes factor analysis was also applied to test the observed statistical findings. The significant reduction in gamma power (30-55Hz) seen during mindfulness meditation was matched with a Bayes factor (BF) of 53.2 ± 0.0. With a BF >30, this finding further indicates very strong evidence of an effect of mind-wandering versus mindfulness meditation on gamma power.[29]

Bayes factor results were inconclusive between conditions in non-epileptic contacts at all other frequency ranges (BF: theta = 0.396 ± 0.010; alpha = 0.352 ± 0.010; beta = 0.817 ± 0.010). Lower

Bayes factors (i.e., <0.3) can be considered equivalent, and intermediate Bayes factors (i.e., 0.3-3.0) inconclusive.[28] In epileptic contacts, Bayes factor analysis again revealed power in each frequency band had inconclusive evidence (BF: theta = 1.818 ± 0.000; alpha = 1.526 ± 0.000; beta = 0.369 ± 0.0; gamma = 0.363 ± 0.000) between conditions.

In converse to findings in periodic oscillations, there were significant differences between mind-wandering and mindfulness within epileptic MTL in aperiodic components (model offset, knee, and exponent, all $p<0.05$), while there were no differences in aperiodic components in non-epileptic MTL (all $p>0.70$), **Figure 3**. These included a significantly higher aperiodic offset with meditation in epileptic contacts (90% of contacts greater in meditation, p=0.0034), knee (75% greater in meditation, p=0.010), and exponent (80.0% greater in meditation, p=0.022). The difference between mindfulness meditation and mind-wandering was significantly greater in epileptic contacts compared with non-epileptic contacts for aperiodic offset ($p<1.00E-5$), knee ($p<2.30E-4$), and exponent (p=8.00E-5), **Figure 3**. Bayes factor analysis again generally reflected results of traditional statistical comparisons. There were significant differences in epileptic contacts in aperiodic offset (BF: 18.3 ± 0.0), and a weaker difference for aperiodic exponent (BF: 2.954 ± 0.010), while aperiodic knee was inconclusive between conditions (BF: 0.983 ± 0.010). In contrast, non-epileptic contacts indicated equivalence for aperiodic parameters between conditions, as seen with traditional statistical comparisons (BF: offset = 0.222 ± 0.020; knee = 0.325 ± 0.020; exponent = 0.221 ± 0.020).

While the effects of inter-individual variability and contact location could affect findings between conditions, we noted results were not driven by a subset of patients or clustered contact pairs. These included 87.0% (40/46) of non-epileptic bipolar contact pairs with higher gamma power during mind-wandering compared to mindfulness, with number of contact pairs relatively evenly distributed from each patient (n=11, n=11, n=10, n=8, n=5). Given the variability in capturing epileptic tissue with stereo EEG, epileptic contacts pairs in each patient were slightly more variable (n=8, n=6, n=4, n=2). However, aperiodic parameters were increased with mindfulness meditation across the majority of epileptic contact pairs for the entire cohort (90% of contacts with increased model offset, 75% for the model knee, and 80% for the model exponent). While there were more contacts in the hippocampus (n=42) compared to amygdala (n=23) available for analysis, no significant effects of contact location were seen on electrophysiologic findings ($p>0.05$ for all periodic and aperiodic parameters, by Kruskal-Wallis testing). **Figure 4** demonstrates representative spectrograms at non-epileptic hippocampus contacts for one subject during mindfulness meditation (**Figure 4A**) and mind-wandering (**Figure 4B**). These spectograms further demonstrate the increased activity seen in gamma (30-55Hz) during mind-wandering compared to mindfulness. Linear mixed-models were further applied to assess the effects of inter-individual variability on the significant results seen. The mixed models demonstrated that accounting for random effects due to inter-subject differences, there was still a significant effect of condition between mindfulness and mind-wandering on gamma power (fixed effect of gamma power: 7.24; 95 % confidence interval: 2.73 – 11.74; residual degrees of freedom: 87). Similarly, within epileptic contacts, there was a significant effect between conditions for aperiodic offset and exponent. The fixed effect of aperiodic offset between conditions: -0.99; 95 % confidence interval: -1.75 – -0.23; residual degrees of freedom: 37). The fixed effect of aperiodic exponent between conditions: -1.13; 95 % confidence interval: -2.18 – -0.08; residual degrees of freedom: 37). The fixed effect of aperiodic knee was not significant between conditions: -0.01; 95 % confidence interval: -0.02 – 0.00; residual degrees of freedom: 37). Overall results between conditions appeared to be maintained, accounting for random variation between subjects.

Meditation depth by the Meditation Depth Questionnaire (MEDEQ)[26] and was available for six of the study subjects.[25] Meditation depth by the MEDEQ scale was 57.7; an average meditation depth of 45.0 across novice meditators has been reported in prior work.[30] Meditation depth varied across subjects, ranging 88, 82, 73, 57, 30, and 16. The sample of patients with meditation depth recorded was insufficient to detect an effect on oscillatory activity (gamma power fixed effect of meditation depth: 0.00; 95% confidence interval 0.00-0.00). Meditation depth was significantly associated with aperiodic offset, knee, and exponent fixed effects. Aperiodic offset: -0.05; 95 % confidence interval: -0.08 – -0.03); aperiodic knee: -2090.9; 95 % confidence interval: -4106.7 – -75.2); aperiodic exponent: -0.03; 95 % confidence interval: -0.05 – -0.01).

Discussion

We demonstrate the intracranial electrophysiology of human mind-wandering versus mindfulness meditation in the mesial temporal lobe in epileptic and non-epileptic MTL in patients with drug resistant epilepsy. Non-epileptic MTL had a decrease in gamma-band activity during first-time mindfulness meditation compared to mind-wandering. The same relationship was not seen in epileptic mesial temporal gray matter during periods free of ictal or interictal activity. In contrast, there were significant differences in aperiodic components only within epileptic MTL, and no differences in aperiodic parameters in "normal," non-epileptic MTL tissue.

Limited work has explored the functional differences of epileptic versus non-epileptic mesial temporal MTL, but has focused primarily on high-frequency oscillations (HFOs, activity >80Hz). Hippocampal HFOs have been found to uniquely decrease in epileptic hippocampus during cognitive tasks compared to periods at rest (which may reflect mind-wandering).[31] In non-epileptic hippocampus, mixed evidence has found either a shift to higher frequency HFOs or no change during cognitive tasks.[32] Contrary to our work, these results suggest that there may be functional changes in epileptic mesial temporal lobe during task-switching. However, low rates of functional connectivity have been found between epileptic and non-epileptic MTL,[33] supporting that epileptic MTL may become functionally dissociated from non-epileptic networks. These findings may further motivate study into the crucial differences in how epileptic versus non-epileptic MTL reacts to shifts in brain state, and how these shifts could relate to both seizure-onset and cognitive performance. A report on three patients with sEEG during mindfulness meditation and mind-wandering by *Bauer et al* found the opposite finding of *decreased* gamma activity with mind-wandering compared to mindfulness in the temporal lobe, but was limited by including only three patients and lacking statistical signficance.[20] This work also focused on high gamma frequencies (50-150Hz),[20] unlike our work. We chose to focus on lower gamma frequency power (30-55Hz) to avoid line noise at 60Hz and parallel ongoing work focused on the responsive neurostimulation device, which due to sampling rate of 250Hz limits analysis of higher frequency ranges.

Neuromodulation of mesial temporal brain, as provided by responsive neurostimulation (RNS), is an effective treatment for drug-resistant epilepsy,[34] and in theory could modulate the contribution of once epileptic tissue to functional neural networks over time with stimulation. Related preliminary work on intracranial electrophysiology within the hippocampus and amygdala in patients with long-term RNS demonstrated functional differences between meditation and control.[35] Interestingly, this work also demonstrated an *increase* in gamma with meditation compared to an active control condition.[35] There are several reasons for this converse result, including the form of meditation studied. This work by *Maher et al* focused on loving-kindness meditation (LKM), which aims to focus attention on thoughts of well-being. In contrast to mindfulness meditation which focuses on stimuli in the present, LKM would likely lead to thoughts invoking memories and emotional salience, thus engaging the hippocampus and amygdala.[16,36] Compared to control, LKM may thus lead to gamma increases in the hippocampus and amygdala,[35] while mindfulness meditation would lead to a decrease in gamma compared to mind-wandering, as found in the current study.

Our finding of decreased mesial temporal gamma-band activity during meditation runs counter to findings from surface EEG, which have generally found widespread increases in gamma activity with meditation.[19,37,38] However, the spatiotemporal resolution afforded by intracranial EEG has been found to better characterize transitions in cognitive brain states.[39] Our finding of decreased gamma activity with mindfulness specific to the mesial temporal lobe may relate to the heavy use of memory during mind-wandering, which would closely implicate the hippocampus.[11–13] Further work is needed to determine the relationship between local intracranial electrophysiology of the mesial temporal lobe and other loci of SEEG contacts in competing or complimentary brain networks, potentially further clarifying surface EEG data in mind-wandering and mindfulness.

Aperiodic activity, modulated uniquely in epileptiform MTL between mindfulness meditation and mind-wandering in this study, may play a role in the mesial temporal epilepsy.[40,41] *Liu et al* demonstrated a decrease in aperiodic exponent and increase in aperiodic offset during periods of seizure within epileptic tissue.[41] *Charlebois et al* conversely found the aperiodic exponent may increase with epileptic activity.[40] Limited work has explored the notion of changes in brain state influencing epileptic potential and induction of seizures, but one interesting case demonstrated an increase in ictal activity with mindfulness meditation compared to baseline.[22] It is therefore possible that modulation of aperiodic activity in epileptic mesial temporal brain between brain states could influence the propensity for seizures. Further work is needed on the potential role of aperiodic parameters on epileptic activity, and the modulation of aperiodic activity and seizure potential between brain states.

Limitations

While statistically significant findings are presented in electrophysiology between states of mind-wandering and mindfulness, the presented work was limited to a relatively small number of eight patients. Line noise limited analysis at higher gamma frequencies (>55Hz) which may be of interest and functionally relevant. Mind-wandering was directly compared to mindfulness meditation without a third control or other forms of meditation, which may have differential effects on electrophysiology. While we did not see any significant impact of anatomical location (amygdala versus hippocampus), this may have been limited by a relatively small number of contacts for comparison. We also did not include objective measures of mind-wandering versus mindfulness that could potentially be captured, such as eye tracking to detect distractedness. A subset of patients had meditation depth recorded, which was associated with aperiodic changes in electrophysiology. However, the sample was insufficient to correlate changes in oscillatory activity (i.e., gamma) with meditation depth. The amount of actual mind-wandering within each meditation session was not recorded. Future work will benefit from both objective measures of mind-wandering and finer subjective reporting of meditative experience in a rigorous, prospective manner. All work was done during the first trial of mindfulness meditation, and therefore the longitudinal impact of meditation on brain function could not be assessed. Future work may explore these factors in a larger number of prospectively recruited patients.

Conclusion

Intracranial electrophysiology is differentially modulated in epileptic versus non-epileptic human mesial temporal MTL between brain states of mind-wandering and mindfulness meditation. Non-epileptic MTL was shown to have a decrease in gamma-band activity during first-time mindfulness meditation compared to mind-wandering. In contrast, there were significant modulations in the aperiodic offset, knee, and exponent in epileptic mesial temporal MTL between mindfulness and mind-wandering. Modulations in gamma activity in non-epileptic MTL may represent functional changes in brain state, while aperiodic changes in epileptic MTL may modulate propensity for seizures.

References

1. Killingsworth MA, Gilbert DT. A wandering mind is an unhappy mind. *Science*. 2010;330(6006):932. doi:10.1126/science.1192439

2. Crosswell AD, Coccia M, Epel E. Mind wandering and stress: When you don't like the present moment. *Emotion*. Published online February 4, 2019:10.1037/emo0000548. doi:10.1037/emo0000548

3. Hoffmann F, Banzhaf C, Kanske P, Bermpohl F, Singer T. Where the depressed mind wanders: Self-generated thought patterns as assessed through experience sampling as a state marker of depression. *J Affect Disord*. 2016;198:127-134. doi:10.1016/j.jad.2016.03.005

4. Marchetti I, Koster EHW, Klinger E, Alloy LB. Spontaneous Thought and Vulnerability to Mood Disorders: The Dark Side of the Wandering Mind. *Clin Psychol Sci*. 2016;4(5):835-857. doi:10.1177/2167702615622383

5. Mrazek MD, Smallwood J, Schooler JW. Mindfulness and mind-wandering: finding convergence through opposing constructs. *Emotion*. 2012;12(3):442-448. doi:10.1037/a0026678

6. Parmentier FBR, García-Toro M, García-Campayo J, Yañez AM, Andrés P, Gili M. Mindfulness and Symptoms of Depression and Anxiety in the General Population: The Mediating Roles of Worry, Rumination, Reappraisal and Suppression. *Front Psychol*. 2019;10:506. doi:10.3389/fpsyg.2019.00506

7. Xu M, Purdon C, Seli P, Smilek D. Mindfulness and mind wandering: The protective effects of brief meditation in anxious individuals. *Consciousness and Cognition*. 2017;51:157-165. doi:10.1016/j.concog.2017.03.009

8. Fox KC, Spreng RN, Ellamil M, Andrews-Hanna JR, Christoff K. The wandering brain: meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes. Neuroimage. 2015 May 1;111:611-21. doi: 10.1016/j.neuroimage.2015.02.039. Epub 2015 Feb 25. Erratum in: Neuroimage. 2016 Aug 15;137:212. doi: 10.1016/j.neuroimage.2016.02.052. PMID: 25725466.

9. Fox KC, Nijeboer S, Dixon ML, Floman JL, Ellamil M, Rumak SP, Sedlmeier P, Christoff K. Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. Neurosci Biobehav Rev. 2014 Jun;43:48-73. doi: 10.1016/j.neubiorev.2014.03.016. Epub 2014 Apr 3. PMID: 24705269.

10. Kam JWY, Rahnuma T, Park YE, Hart CM. Electrophysiological markers of mind wandering: A systematic review. *Neuroimage*. 2022;258:119372. doi:10.1016/j.neuroimage.2022.119372

11. Karapanagiotidis T, Bernhardt BC, Jefferies E, Smallwood J. Tracking thoughts: Exploring the neural architecture of mental time travel during mind-wandering. *Neuroimage*. 2017;147:272-281. doi:10.1016/j.neuroimage.2016.12.031

12. Okuda J, Fujii T, Ohtake H, et al. Thinking of the future and past: the roles of the frontal pole and the medial temporal lobes. *Neuroimage*. 2003;19(4):1369-1380. doi:10.1016/s1053-8119(03)00179-4

13. Schacter DL, Addis DR, Buckner RL. Remembering the past to imagine the future: the prospective brain. *Nat Rev Neurosci*. 2007;8(9):657-661. doi:10.1038/nrn2213

14. Kral TR, Schuyler BS, Mumford JA, Rosenkranz MA, Lutz A, Davidson RJ. Impact of short- and long-term mindfulness meditation training on amygdala reactivity to emotional stimuli. *Neuroimage*. 2018;181:301-313. doi:10.1016/j.neuroimage.2018.07.013

15. Taren AA, Gianaros PJ, Greco CM, et al. Mindfulness meditation training alters stress-related amygdala resting state functional connectivity: a randomized controlled trial. *Social Cognitive and Affective Neuroscience*. 2015;10(12):1758-1768. doi:10.1093/scan/nsv066

16. Desbordes G, Negi L, Pace T, Wallace B, Raison C, Schwartz E. Effects of mindful-attention and compassion meditation training on amygdala response to emotional stimuli in an ordinary, non-meditative state. *Frontiers in Human Neuroscience*. 2012;6. Accessed August 22, 2023. https://www.frontiersin.org/articles/10.3389/fnhum.2012.00292

17. Compton RJ, Gearinger D, Wild H. The wandering mind oscillates: EEG alpha power is enhanced during moments of mind-wandering. *Cogn Affect Behav Neurosci*. 2019;19(5):1184-1191. doi:10.3758/s13415-019-00745-9

18. Rodriguez-Larios J, Alaerts K. EEG alpha-theta dynamics during mind wandering in the context of breath focus meditation: An experience sampling approach with novice meditation practitioners. *Eur J Neurosci*. 2021;53(6):1855-1868. doi:10.1111/ejn.15073

19. Braboszcz C, Cahn BR, Levy J, Fernandez M, Delorme A. Increased Gamma Brainwave Amplitude Compared to Control in Three Different Meditation Traditions. *PLoS One*. 2017;12(1):e0170647. doi:10.1371/journal.pone.0170647

20. Bauer PR, Sabourdy C, Chatard B, et al. Neural dynamics of mindfulness meditation and hypnosis explored with intracranial EEG: A feasibility study. *Neuroscience Letters*. 2022;766:136345. doi:10.1016/j.neulet.2021.136345

21. Colgan DD, Memmott T, Klee D, Ernst L, Han SJ, Oken B. A single case design to examine short-term intracranial EEG patterns during focused meditation. *Neuroscience Letters*. 2019;711:134441. doi:10.1016/j.neulet.2019.134441

22. Delorme A, Grandchamp R, Curot J, et al. Effect of meditation on intracerebral EEG in a patient with temporal lobe epilepsy: A case report. *EXPLORE*. 2021;17(3):197-202. doi:10.1016/j.explore.2020.11.005

23. Cullen B, Eichel K, Lindahl JR, Rahrig H, Kini N, Flahive J, Britton WB. The contributions of focused attention and open monitoring in mindfulness-based cognitive therapy for affective disturbances: A 3-armed randomized dismantling trial. PLoS One. 2021 Jan

12;16(1):e0244838. doi: 10.1371/journal.pone.0244838. PMID: 33434227; PMCID: PMC7802967.

24. St Louis EK, Lansky EP. Meditation and epilepsy: a still hung jury. Med Hypotheses. 2006;67(2):247-50. doi: 10.1016/j.mehy.2006.02.039.

25. Leeman-Markowski BA, Schachter SC. Cognitive and Behavioral Interventions in Epilepsy. Curr Neurol Neurosci Rep. 2017 May;17(5):42. doi: 10.1007/s11910-017-0752-z.

26. Katyal S, Goldin P. Alpha and theta oscillations are inversely related to progressive levels of meditation depth. Neurosci Conscious. 2021 Nov 29;2021(1):niab042. doi: 10.1093/nc/niab042. PMID: 34858638; PMCID: PMC8633885.

27. Donoghue T, Haller M, Peterson EJ, et al. Parameterizing neural power spectra into periodic and aperiodic components. *Nat Neurosci*. 2020;23(12):1655-1665. doi:10.1038/s41593-020-00744-x

28. McGrath H, Zaveri HP, Collins E, et al. High-resolution cortical parcellation based on conserved brain landmarks for localization of multimodal data to the nearest centimeter. *Sci Rep*. 2022;12(1):18778. doi:10.1038/s41598-022-21543-3

29. Stefan AM, Gronau QF, Schönbrodt FD, Wagenmakers EJ. A tutorial on Bayes Factor Design Analysis using an informed prior. Behav Res Methods. 2019 Jun;51(3):1042-1058. doi: 10.3758/s13428-018-01189-8. PMID: 30719688; PMCID: PMC6538819.

30. Piron H. The meditation depth index (MEDI) and the meditation depth questionnaire (MEDEQ). Journal for Meditation and Meditation Research. 2001;1(1):69-92.

31. Pail M, Cimbálník J, Roman R, et al. High frequency oscillations in epileptic and non-epileptic human hippocampus during a cognitive task. *Sci Rep*. 2020;10(1):18147. doi:10.1038/s41598-020-74306-3

32. Cimbalnik J, Pail M, Klimes P, et al. Cognitive Processing Impacts High Frequency Intracranial EEG Activity of Human Hippocampus in Patients With Pharmacoresistant Focal Epilepsy. *Front Neurol*. 2020;11:578571. doi:10.3389/fneur.2020.578571

33. Shamas M, Yeh HJ, Fried I, Engel J, Staba R. Interictal Gamma Event Connectivity Differentiates the Seizure Network and Outcome in Patients after Temporal Lobe Epilepsy Surgery. *eNeuro*. 2022;9(6):ENEURO.0141-22.2022. doi:10.1523/ENEURO.0141-22.2022

34. Nair DR, Laxer KD, Weber PB, et al. Nine-year prospective efficacy and safety of brain-responsive neurostimulation for focal epilepsy. *Neurology*. 2020;95(9):e1244-e1256. doi:10.1212/WNL.0000000000010154

35. Maher C, Tortolero L, Cummins DD, et al. Intracranial substrates of meditation-induced neuromodulation in amygdala and hippocampus. Published online May 10, 2024:2024.05.10.593445. doi:10.1101/2024.05.10.593445

36. Garrison KA, Scheinost D, Constable RT, Brewer JA. BOLD signal and functional connectivity associated with loving kindness meditation. *Brain Behav*. 2014;4(3):337-347. doi:10.1002/brb3.219

37. Lee DJ, Kulubya E, Goldin P, Goodarzi A, Girgis F. Review of the Neural Oscillations Underlying Meditation. *Front Neurosci*. 2018;12. doi:10.3389/fnins.2018.00178

38. Lutz A, Greischar LL, Rawlings NB, Ricard M, Davidson RJ. Long-term meditators self-induce high-amplitude gamma synchrony during mental practice. *Proc Natl Acad Sci USA*. 2004;101(46):16369-16373. doi:10.1073/pnas.0407401101

39. Barborica A, Mindruta I, López-Madrona VJ, et al. Studying memory processes at different levels with simultaneous depth and surface EEG recordings. *Front Hum Neurosci*. 2023;17:1154038. doi:10.3389/fnhum.2023.1154038

40. Charlebois CM, Anderson DN, Smith EH, et al. Circadian changes in aperiodic activity are correlated with seizure reduction in patients with mesial temporal lobe epilepsy treated with responsive neurostimulation. *Epilepsia*. 2024;65(5):1360-1373. doi:10.1111/epi.17938

41. Liu S, Wang J, Li S, Cai L. Epileptic Seizure Detection and Prediction in EEGs Using Power Spectra Density Parameterization. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2023;31:3884-3894. doi:10.1109/TNSRE.2023.3317093

Figures

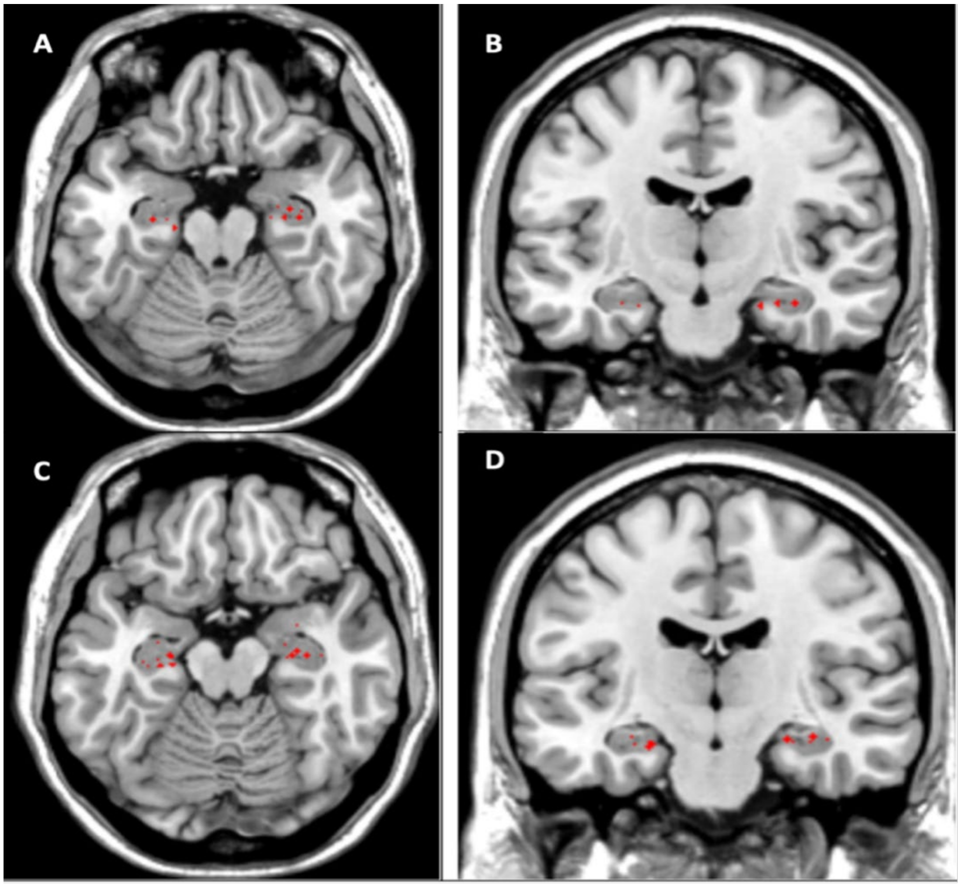

Figure 1: Anatomical confirmation of intracranial contact location in gray matter of the hippocampus and amygdala. Contacts (red) are demonstrated as representations in Montreal Neurological Institute brain space on a standard T1 pre-contrast MRI provided by MRIcron software.[23] All contacts were plotted on one standardized T1 pre-contrast MRI. Epileptic contacts are shown in the axial (**A**) and coronal planes (**B**), as well as for non-epileptic contacts (**C, D**).

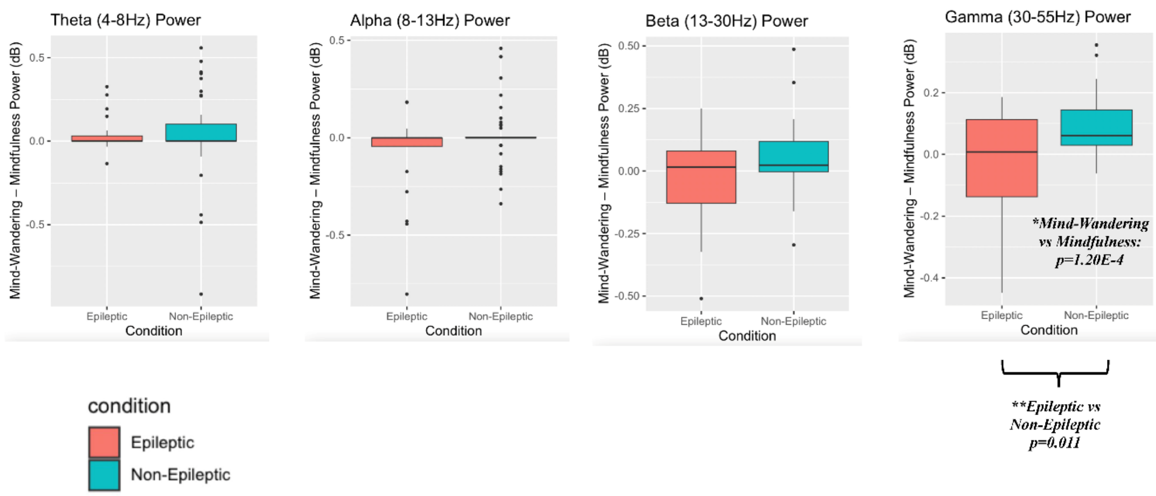

Figure 2 Changes in power between mind-wandering and mindfulness meditation in epileptic and non-epileptic MTL. Plotted are the differences in peak power across canonical frequency bands between mind-wandering and mindfulness meditation. Differences in peak power are plotted for theta (4-8Hz), alpha (8-13Hz), beta (13-30Hz), and gamma (30-55Hz). *Paired comparison by Mann-Whitney U-test for peak power between mind-wandering versus mindfulness in non-epileptiform contacts. **Non-paired comparison by Kruskal-Wallis test for epileptic vs non-epileptic contacts (comparing difference in peak power between mind-wandering and mindfulness in epileptic versus non-epileptic contacts). All other comparisons (mind-wandering versus mindfulness peak power; epileptic versus non-epileptic differences in power) were non-significant (p>0.100).

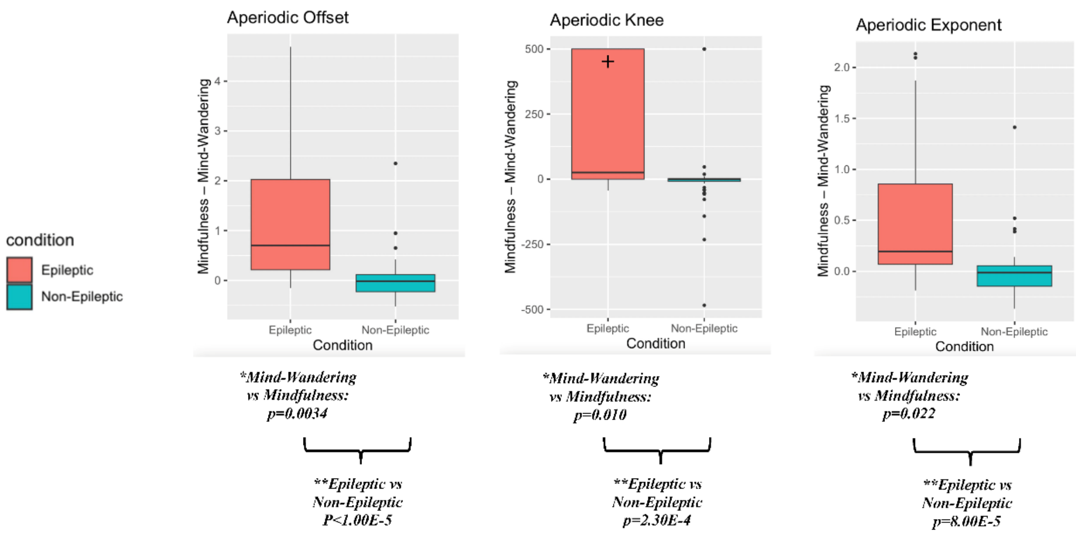

Figure 3: Aperiodic model parameters between mind-wandering and mindfulness in epileptic and non-epileptic MTL. *Paired comparison by Mann-Whitney U-test for value of offset, knee, and exponent between mind-wandering versus mindfulness in epileptiform contacts. **Non-paired comparisons by Kruskal-Wallis test for epileptic versus non-epileptic contacts (comparing difference in offset, knee, and exponent, between mind-wandering and mindfulness in epileptic versus non-epileptic contacts). All other comparisons (mind-wandering versus mindfulness; epileptic versus non-epileptic differences) were non-significant ($p>0.100$).+Knee differences of >500 are plotted at 500 to maintain scale.

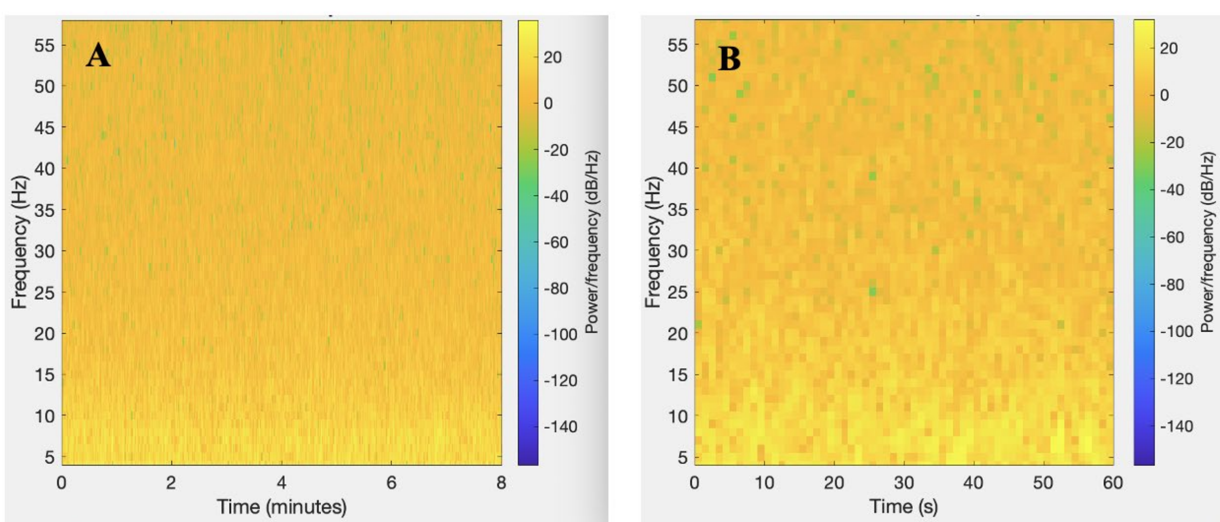

Figure 4: Representative spectrograms during mindfulness meditation and mind-wandering. Representative spectrograms at one pair of non-epileptic hippocampus contacts for one subject during (**A**) mindfulness meditation and (**B**) mind-wandering. These spectograms further demonstrate the increased activity seen in gamma (30-55Hz) during mind-wandering compared to

mindfulness. While minimal activity is seen at higher frequencies during mindfulness meditation (A), periodic increases in gamma activity are seen over the period of mind-wandering (B).