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► **To cite this version:**

A. Delorme, R. Grandchamp, J. Curot, G. Barragan-Jason, M. Denuelle, et al.. Effect of meditation on intracerebral EEG in a patient with temporal lobe epilepsy: A case report. *Explore: The Journal of Science and Healing*, 2021, 17 (3), pp.197-202. 10.1016/j.explore.2020.11.005 . hal-03555558

HAL Id: hal-03555558

<https://ut3-toulouseinp.hal.science/hal-03555558>

Submitted on 24 Apr 2023

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Effect of meditation on intracerebral EEG in a patient with temporal lobe epilepsy: a case report

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Abstract

Meditation has been deemed a miracle cure for a wide range of neurological disorders. However, it is unclear whether meditation practice would be beneficial for patients suffering from epilepsy. Here we report on the comparison of the effects of focused-attention meditation and a control task on electroencephalographic (EEG) activity in a patient undergoing stereoencephalographic (SEEG) investigation for drug-resistant epilepsy. The patient routinely practiced focused-attention meditation and reported that she found it beneficial. During the SEEG investigation, intracerebral EEG data were recorded during meditation as well as during mind-wandering task. The EEG data were analyzed for type of electrical activity (labeled) by two expert epileptologists. We found that the proportion of EEG segments containing activity classified as interictal epileptiform discharges (IEDs; abnormal electrical activity that occurs between seizures) increased significantly during meditation practice. Although the finding was surprising, this increase in IEDs may not correlate with an increase in seizure frequency, and the patient might still benefit from practicing meditation. The finding does, however, warrant further studies on the influence of meditation on epileptic activity.

1. Introduction

In patients with epilepsy, stress has been reported to trigger seizures.¹⁻³ Moreover, patients suffering from epilepsy have to face the intrinsically stressful nature of the pathology, which is often magnified by the unpredictability of their seizures. Among relaxation practices aiming at developing better stress management skills, meditation has gained momentum through increasing interest in the neuroscience, psychological, and medical fields.⁴⁻⁹ The now-famous Mindfulness-Based Stress Reduction Program, formalized and developed by Jon Kabat-Zinn, is one of the most studied psycho-cognitive programs for stress reduction.^{10, 11} However, even if positive outcomes of meditation practice have been widely documented over decades of scientific and clinical studies, there are still some elements suggesting that meditation is not recommended in all cases and might have negative effects.^{12, 13} The effect of meditation on epileptic seizures and patients with epilepsy is currently poorly understood, and this is the topic of this case study.

Meditation involves mental training of brain networks usually not recruited in our daily lives. This type of training has been shown to lead to long-term changes in brain structure¹⁴⁻¹⁶ and connectivity.¹⁷⁻¹⁹ It is thus possible that, during meditation, neural networks in the epileptic region would be retrained away from the epileptic dynamic of brain activity. However, the literature reporting on studies of meditation and epilepsy shows discrepancies. Some authors argue that meditation has no effect on seizures.²⁰ Others claim that meditation increases seizures,²¹⁻²⁵ while yet others claim that meditation reduces seizures.²⁶ One confounding factor might be the fact that these studies have relied on scalp-EEG recordings, which may not be sensitive enough to disambiguate the effect of meditation. Our current study contributes to filling this gap. Specifically, we analyzed whether meditation modified the rate of interictal epileptiform discharges (IEDs; abnormal electrical activity that occurs between seizures [interictally] in

patients with epilepsy) by comparing intracerebral EEG recordings obtained while our patient was meditating to recordings obtained during a control condition.

2. Materials and Methods

2.1. Patient

One patient (female, 42 years old) who suffered from drug-resistant temporal lobe epilepsy and was a candidate for epilepsy surgery participated in this case study. She was left-handed and a music teacher with a permanent position in a music school. She suffered from Leber's hereditary optic neuropathy and was blind. She had her first seizure at the age of 27 years and reported that during this seizure she felt scared and saw a red dot in the left hemifield. She thought she had fainted and started chewing and moaning. Her symptoms remained similar during subsequent seizures. Medical therapy (oxcarbazepine, zonisamide, and levetiracetam) failed to control her seizures. Scalp EEG investigations revealed spike activity recorded primarily by the right temporal electrodes. The findings of a magnetic resonance imaging (MRI) study of the brain were normal except for possible slight left hippocampal atrophy. An interictal brain FDG-PET (positron emission tomography) scan revealed bilateral temporal mesial hypometabolism. Based on these noninvasive assessments, the decision was made to perform a stereoencephalographic (SEEG) evaluation (a type of assessment that involves an invasive procedure, surgical implantation of electrodes within the patient's brain, and subsequent monitoring) in order to determine the localization of the seizure-onset zone. With the patient's informed consent, we conducted a study during this evaluation, analyzing SEEG data obtained during meditation and during a control task in order to evaluate a potential variation of IED occurrence.

Neuropsychological evaluation was limited by the patient's blindness (only verbal tests could be performed). Her score on the verbal IQ portion of the Wechsler Adult Intelligence Scale,

3rd edition (WAIS-III) was 104 (+0.26 standard deviation [SD]). Results of tests of her verbal episodic memory (Free and Cued Selective Reminding test: delayed free recall, 12/16 [-1.04 SD]; delayed free + cued recall: 16/16) and working memory (WAIS III working memory index: 102 [+0.13 SD]) were normal. No language disorder was noted.

Several spontaneous seizures were recorded during the SEEG exploration (detailed below), all starting in the right basal mesial occipito-temporal region, sometimes with quick propagation to the right anterior temporal region or the left temporal region. Based on these observations, epilepsy surgery was proposed and a right amygdalo-hippocampectomy was performed. Histological analysis of removed tissue confirmed the diagnosis of hippocampal sclerosis. As of this writing, after 6 years of follow-up, the patient's seizure frequency is significantly reduced, although rare seizures persist (Class 2 of Engel Classification), and her medical treatment has been reduced to oxcarbazepine monotherapy. No psychiatric complication or worsening of neuropsychological function was noticed. The patient has no cognitive complaints and still works as a piano teacher.

The patient was selected for this study because she had experience in practicing meditation, which she spontaneously started practicing in her room during intracerebral recordings. It was at this point that we asked whether she would agree to participate in a protocol on the effect of meditation. She agreed to participate in the and reported that she had meditated about 200 hours over the course of several years in the context of a Buddhist tradition, counting breaths and focusing on a calm mind for about 15 minutes.

2.2. Recordings and electrode selection

A multi-channel video-SEEG acquisition and monitoring system (Micromed, Treviso, Italy) was used to simultaneously record the intracerebral activity from depth-EEG electrodes at a sampling

rate of 512 Hz. Recordings were performed using intracerebral multiple-contact electrodes (DixiMedical, Besançon, France). The electrodes had between 5 and 18 contacts (length: 2 mm, diameter: 0.8 mm) spaced 1.5 mm apart and were placed according to Talairach's stereotactic method.^{27, 28} A total of 11 electrodes were implanted—6 in the left hemisphere and 5 in the right hemisphere (Figure 1). Their position was approximately orthogonal to the brain midline, exploring both temporal lobes. The anatomical targeting of the electrodes was established according to available data from noninvasive studies and hypotheses about the localization of the seizure-onset zone. Anticonvulsant therapy was progressively reduced during the SEEG exploration in order to facilitate seizure occurrence.

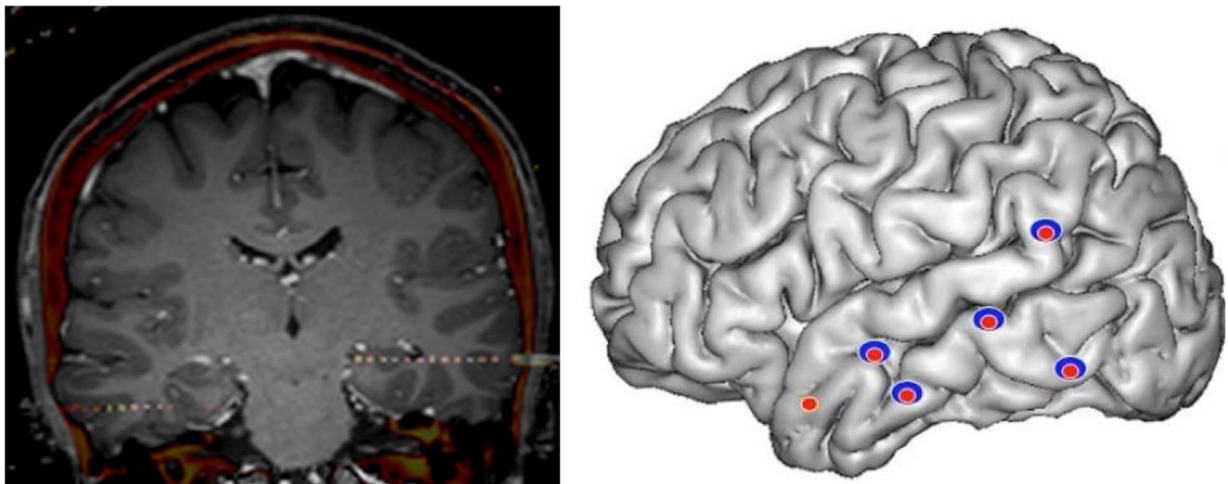


Figure 1. The merged CT/MR image on the left insert shows an example of two electrodes reaching the entorhinal cortex on the right and the hippocampus on the left. Each light dot along the electrode path is a contact. The 3D image on the right shows the location of the different electrodes that were implanted in this patient (blue: right hemisphere; red: left).

In addition, computer-assisted matching between a post-implantation CT scan and a preimplantation 3D MRI data set allowed for visualization of the electrode contacts within the

patient's brain anatomy. This merged file was used to inspect electrode contact locations. Three different channel selections were derived for data analysis in order to distinguish periods of signal containing abnormal EEG activity from periods with no such abnormality (“clean” periods): a first selection composed of 38 channels corresponding to recording sites located in the right hemisphere; a second selection composed of 25 channels corresponding to recording sites located in the left hemisphere; and a third selection composed of 48 bilateral channels excluding channels located in the hippocampus or showing large perturbations. This third selection was chosen to allow inspection with a finer amplitude scale.

A bipolar montage was used for each dataset: for each electrode, we subtracted the values recorded at each considered electrode’s contact from the measures obtained at the next adjacent contact along the electrode when running through the recording sites starting from the tip of the electrode. As a consequence, the last recording site on the electrode is not included in the analysis. Data were high-pass filtered using an elliptic IIR filter with a high-pass cut-off frequency of 0.5 Hz, a 0.17 Hz transition band, a ripple amplitude of 0.01 dB in the pass band, and 30 dB in the stop band.

2.3. Experimental procedure

We asked the patient to perform two different mental tasks: (1) An instructed “mind wandering” control task, during which she was asked to keep her mind active by remembering emotionally neutral elements from the past, such as what she had for breakfast over the past two weeks. (2) A meditation task based on focusing on breath to reach mindfulness. Both tasks were executed with her eyes closed. The two tasks and the protocol were explained to the patient, and the experimenter made sure all instructions were clearly understood.

A recording session was composed of two 15-minute blocks of meditation, intermixed

with three 5-minute blocks of mind wandering, following the sequence represented in Figure 1. Two sessions were recorded on two consecutive days. The experimental sequence is represented in Figure 2.

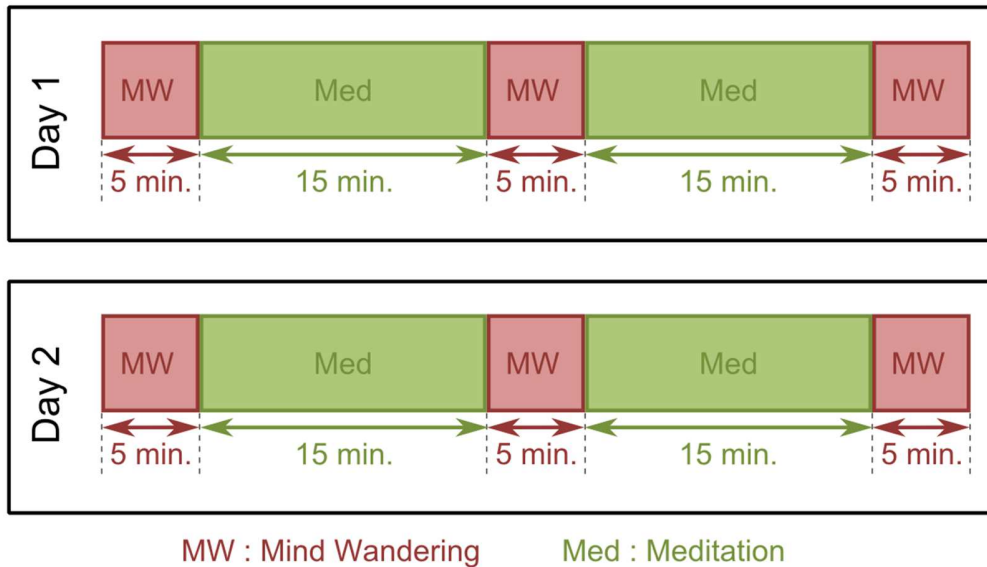


Figure 2. Experimental protocol. Each session is composed of two 15-minute meditation periods (Med) interlaced with three 5-minute instructed mind wandering (MW) periods. Two sessions were recorded on two different days.

The patient filled out a questionnaire after each meditation or mind-wandering period to assess how well she felt she had performed the task. After each period she first rated—on a scale from 1 (not well) to 10 (very well)—how much she felt absorbed in the task. On a second similar scale she rated her thought density (how much thinking she experienced during the period).

2.4. Interictal discharge labeling

This labeling procedure was used to assess IED density, which was chosen as a dependent variable in order to investigate whether meditation practice increases or decreases the density of EEG activity of an epileptic nature.

The 15-minute meditation blocks were separated into three 5-minute blocks, each corresponding to a single data file (i.e., three data files per 15-minute meditation block) and analyzed by two expert epileptologists (authors L.V. and M.D.). All data files had approximately the same length of 5 minutes, and the epileptologists were blind to the type of data block they were processing. We obtained a total of eighteen 5-minute data files to analyze; 12 from the periods of meditation and 6 from the control sections. As explained in the previous section, out of each raw file, three different selections of recording sites were defined. So each expert analyzed a total of 54 recordings of 5 minutes each. For each channel selection scheme, files were inspected in a specific random order. The inspection orders were reversed for the two experts to avoid or at least minimize any potential sequence effect.

The IED density was computed as the proportion of epochs labeled as containing IEDs (including spike and spike-and-wave discharge patterns). This measure was computed on each day of recording separately and on pooled data. SEEG data were labeled using a blind procedure by the two epileptologists, as mentioned above. No assumption or a priori discussion was made regarding the type of interictal spikes that had to be labelled, thus labeling relied on the clinical practice of each of the experts. The labeling consisted of visually inspecting the signal epochs in 1-second intervals and marking these intervals as containing or not containing IED. A specific signal scale of 800 μV was adopted with the advice of the experts and was used during the whole visual inspection procedure.

A chi-squared analysis was conducted on contingency tables obtained using absolute frequencies derived from 1-second epochs labeled as containing IED or not. The analysis was first done on each of the three channel selection sets separately and then considering them all together. Epochs were counted as clean if they were labeled as such by both experts.

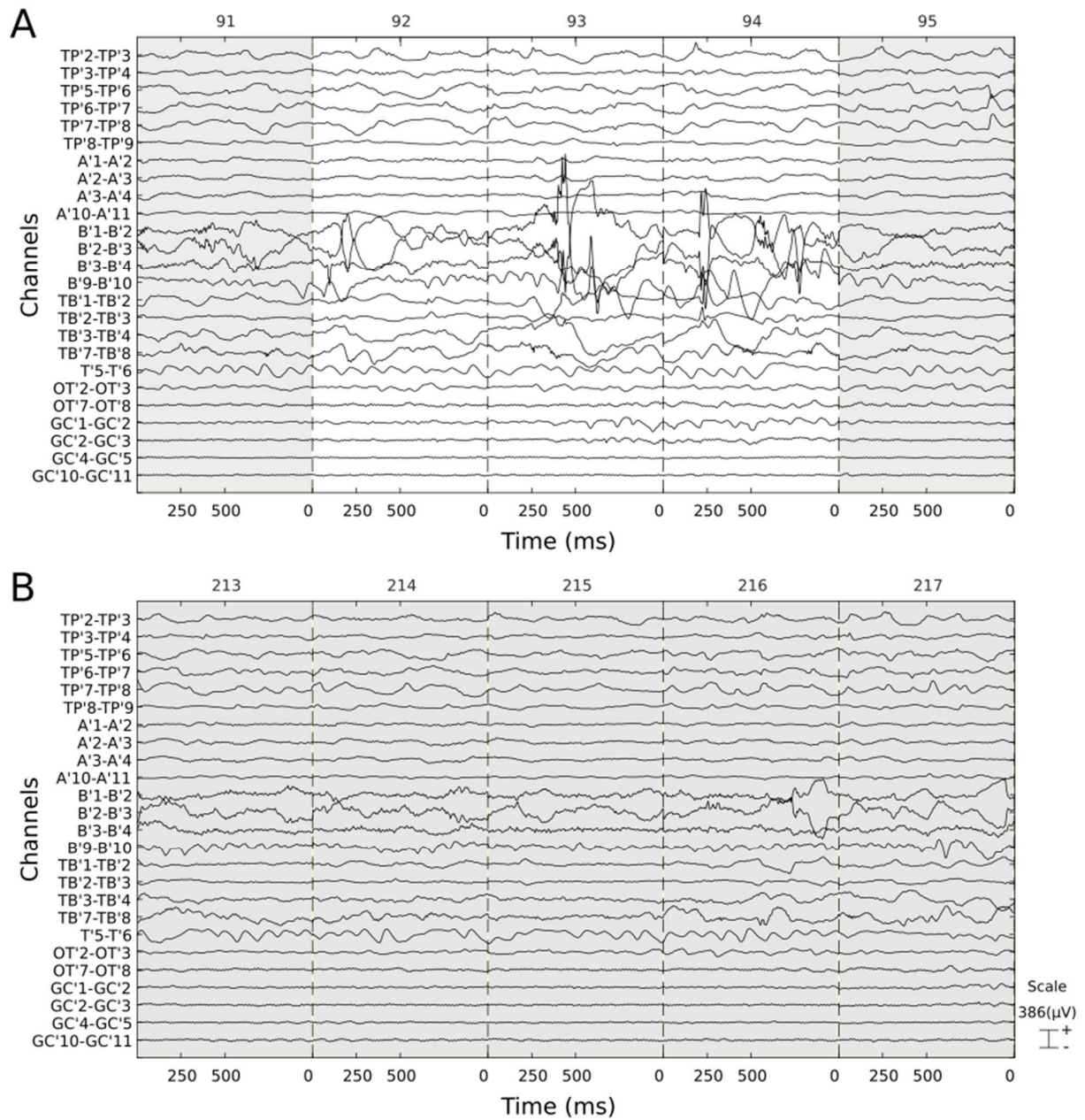


Figure 3. Examples of EEG signals with and without IEDs labeled by one of the experts using a custom software we developed for the purpose of performing blind epoch labeling. Signal is segmented in 1-second non-overlapping epochs demarcated by vertical dashed lines. Epochs labeled as “clean” (i.e., containing no IED) by the expert are displayed on gray background. Epochs labeled as containing IEDs are displayed on white background. Panel A: 5-epoch section

containing 2 epochs contaminated by IEDs. Panel B: 5-epoch section labeled as clean.

3. Results

3.1. Questionnaire analysis

The patient felt absorbed in the task during the instructed mind wandering task (mean rating across the three periods: 8/10 on day 1 and 9/10 on day 2), while she found the meditation task more difficult (mean rating across the two periods: 6.5/10 on days 1 and 2), which could be expected given that she was meditating in a clinical setting with implanted electrodes. She judged her density of thoughts to be higher for the instructed mind wandering task (mean rating across the three periods: 6.7/10 on day 1 and 8.3/10 on day 2) than for the meditation task (mean rating across the two periods: 4/10 on days 1 and 2). The lower density of thoughts during meditation compared to the instructed mind wandering task shows that she performed each task as expected.

3.2. Comparison of the two experts

We first analyzed the overlap of labeling between the two experts in order to quantify the extent to which their judgments were providing similar ratings. For each expert, we considered the epochs labeled as clean, and computed the percentage of these epochs also labeled as clean by the other expert. In addition, an overall percentage of overlap was derived as the percentage of 1-second epochs labeled with the same label by both experts. The proportion of epochs labeled as clean by each expert was computed for each one of the 18 data files on each of the 3 channel selections. The difference between the proportions for expert 1 and expert 2 was calculated for each data file. The overlap between the two experts' labels ranged from 83.7% for the channel selection set 3 to 92.4% for the channel selection set 1 (Table 1). These results highlight the possibility of relatively high variability in epoch labeling across experts even when they are close

colleagues, as was the case here.

	Left hemisphere	
	L.V.	M.D.
Clean epochs	2342	3544
Epochs with IEDs	3500	2298
Proportion of epochs with IEDs	0.6	0.39
Overlap of clean epochs with other expert	99.7%	65.9%
Overall overlap between experts	89.9%	
	Right hemisphere	
	L.V.	M.D.
Clean epochs	4027	4400
Epochs with IEDs	1815	1442
Proportion of epochs with IEDs	0.31	0.25
Overlap of clean epochs with other expert	99.1%	90.7%
Overall overlap between experts	92.4%	
	Selection without hippocampus	
	L.V.	M.D.
Clean epochs	4444	5035
Epochs with IEDs	1398	807
Proportion of epochs with IEDs	0.24	0.14
Overlap of clean epochs with other expert	95.9%	84.6%
Overall overlap between experts	83.7%	

Table 1. Overlap results for each channel selection set. The two expert reviewers are represented by their initials, L.V. and M.D.

3.3. IED density

The patient had a large number of IEDs in both hemispheres, predominating in medial temporal lobe structures (Figure 4).

Labeling Overview

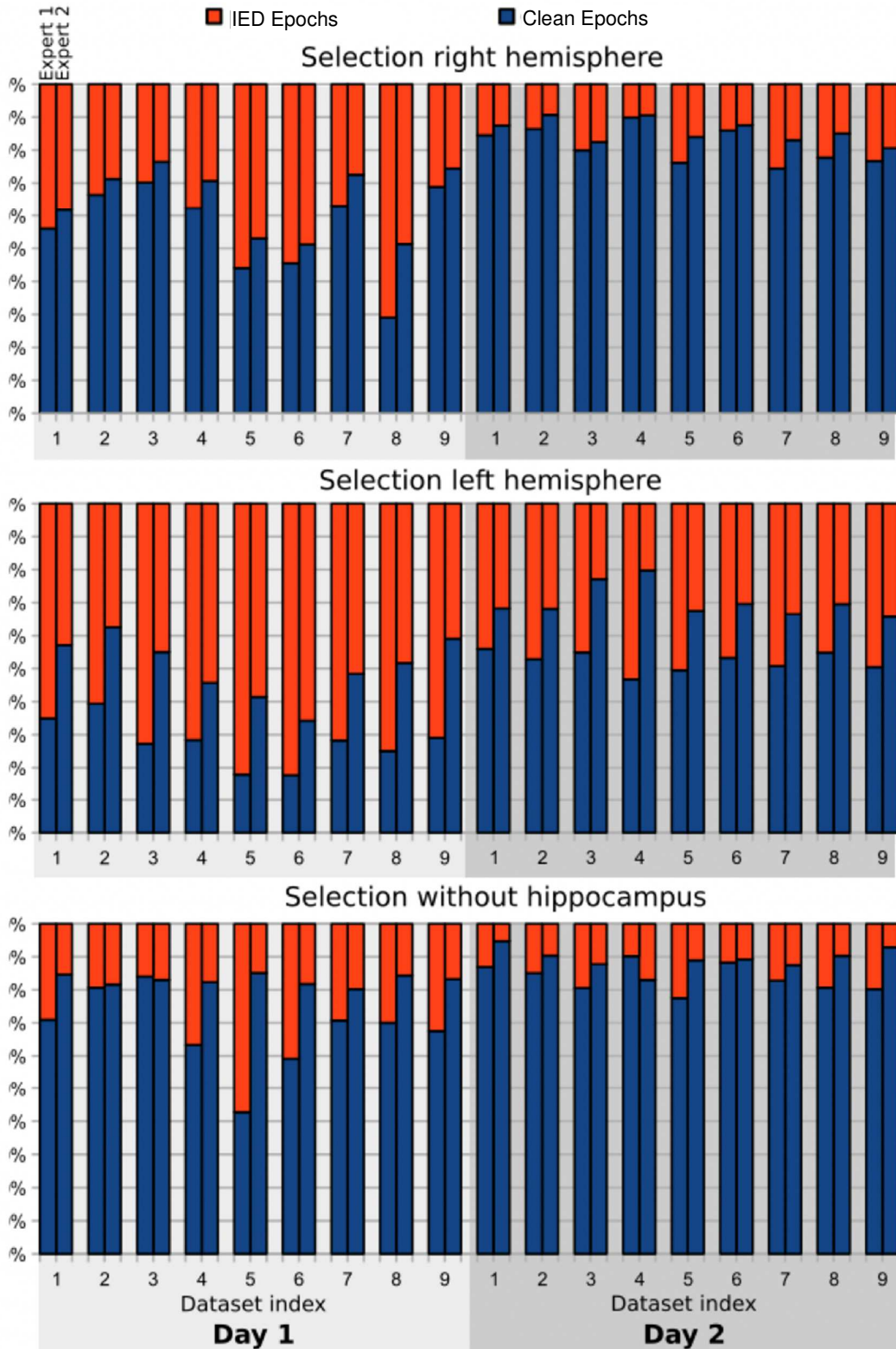


Figure 4. Percentage of epochs labeled as clean (in blue) or containing IEDs (in orange) for each dataset, and for each expert. Dataset file indexes are represented on the x-axis. For each dataset, the first bar corresponds to expert 1 and the second bar to expert 2. The three different channel selections are represented on three different bar charts.

For all 3 channel sets, a chi-squared analysis revealed a significant increase in epochs labeled as containing IEDs during meditation compared to instructed mind wandering (Table 2). When all datasets were pooled together across sessions, there was a significant increase in the proportion of epochs labeled as containing IEDs (increase of 3.45%, $\chi^2 = 7.39$, $p=0.007$). When the two sessions were considered separately in the chi-squared analysis, the difference was still significant (day 1: $\chi^2=18.86$, $p<10^{-4}$; day 2: $\chi^2=3.98$, $p=0.046$). When the three labeling results stemming from the three different channel selection sets used for labeling were considered separately, similar results were obtained (right hemisphere selection: 5.95% increase, $\chi^2=22.15$, $p<10^{-5}$; left hemisphere selection: 4.82% increase, $\chi^2=13.15$, $p<10^{-3}$; selection without hippocampus: 7.14% increase, $\chi^2=35.03$, $p<10^{-8}$). When results for the two days were grouped together, the difference in IED epoch proportion was higher for meditation than for mind wandering, and this was still true for the first day when results for the two days were considered separately. However, when considering the two sessions of recordings separately, the difference was statistically significant for day 1, but only marginally significant for day 2 (see Supplementary Table 1 for details).

One may argue that the meditation state is not reached instantaneously and that meditation depth may vary within the 15-minute blocks. Therefore, we tried to consider only a period of 5-minutes at the middle of the 15-minute blocks. Using only the central 5-minute period of the meditation condition, we observed the same effect on IED proportion, with more IEDs during meditation, and the difference was still statistically significant when data were pooled for the two

recording sessions ($\chi^2=11.3$, $p=0.0007$). However, when considering the two days separately, the difference was only significant for the first day of recording ($\chi^2=31.88$, $p<10^{-7}$), although there was a trend on the second day in the same direction. It would be interesting to pursue further study in other patients to see whether the difference between day 1 and 2 is meaningful.

	Observed absolute frequencies		Statistics	
	MW	Med	χ^2	p
Days 1 and 2 merged				
Clean epochs	736	1142	7.39	0.0066
Epochs with IEDs	1408	2556		
Proportion of epochs with IEDS	0.66	0.69		
Day 1 analyzed separately				
Clean epochs	283	307	18.9	0.000014
Epochs with IEDs	898	1455		
Proportion of epochs with IEDS	0.76	0.83		
Day 2 analyzed separately				
Clean epochs	453	835	3.98	0.046
Epochs with IEDs	510	1101		
Proportion of epochs with IEDS	0.53	0.57		

Table 2. IED proportion analysis results. Fifteen-minute meditation blocks were considered in all cases. Clean epochs were defined as the epochs labeled as clean by both experts. IED epochs were defined as the epochs labeled as having IEDs by both experts. MW, mind wandering; Med, meditation.

4. Discussion

We have shown in a single patient that mindfulness meditation tended to increase IEDs when compared to a control task involving of mind wandering. This is a case report and should be taken as such. We do not necessarily anticipate that results will generalize to other patients.

Our findings simply demonstrate that it is possible for the proportion of EEG segments containing IEDs to increase significantly during meditation practice.

It is unclear what neurophysiological factor can increase IEDs during meditation. A possibility could be that breathing modifications induced by the meditation practice led to hyperoxygenation of the blood, a factor known to be associated with an increase of IEDs.²⁹ Even though meditation is often associated with a decrease of respiration rate and oxygen consumption,^{30, 31} overall brain oxygen consumption during meditation remains relatively stable.³² Future BOLD (blood oxygen level dependent) imaging experiments should aim at determining whether meditation has a tendency to increase blood flow in the seizure-onset zone.

It is also possible that gamma frequency brain synchronization across a wide range of brain areas, which is typically observed in a numerous meditation practices,^{33, 34} modifies the dynamics of the epileptogenic networks and increases the occurrence of IEDs. Denison describes how states of high concentration can lead to instability when experienced meditators relax their attention, leading to seizure-like activity.³⁶

Another point worth considering is the meditation expertise of our patient. Long-term meditators who meditate daily tend to have brain activity that differs from that of novice or even intermediate meditators.³⁵ It is therefore possible that intermediate meditators, such as our patient, still experience some mental strain or effort when practicing meditation and that this is responsible for increased occurrence of IEDs.

There are a number of limitations to consider in this case study. The first one is that our results may apply only to the type of epilepsy our patient had. She had temporal lobe epilepsy with histologically confirmed hippocampal sclerosis. It could be that the effect of meditation varies depending on some of the characteristics of the epilepsy (e.g., localization, etiology, comorbidities). Also, it is possible that the medication our patient was taking could have had an

influence on her intracranial EEG. Even for this single patient, no conclusion should be made about whether meditation is beneficial or detrimental. It is possible, for example, that meditation would increase IEDs in the short term but decrease them in the long term. Moreover, controversy exists with respect to the role of IEDs in seizure occurrence, with some data indicating that they are protective and other data indicating that they play a precipitating role.³⁶

Furthermore, one of the main problems in neuro-cognitive research on meditation is that it still lacks a clear definition and therefore a structured taxonomy of different meditation practices and the different mental states or states of consciousness involved. It is therefore difficult to sort out scientific results in the light of these distinctions. The term *meditation* groups many heterogeneous practices from various more or less distinct traditions. Practice and the mental exercise can differ greatly from one type of meditation to another and can involve different cognitive and neurological processes.³⁴ Even within a given tradition, many different meditation techniques exist, focusing on different aims. While some efforts have been made to study the variety of meditation practices,^{6, 34, 37} the conclusion drawn in this article should not be generalized to other types of meditation.

In summary, meditation had a tendency to increase the occurrence of IEDs throughout the brain in this case study. IEDs may not correlate with seizure frequency,³⁸ however, and the benefits of meditation and mindfulness may be better identified by scores of anxiety and depression.³⁹ In fact, our patient spontaneously meditated because she felt relief during and after her meditation period.

Acknowledgment

We acknowledge the contribution of Anne Stanford, ELS, who provided professional English language editing.

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