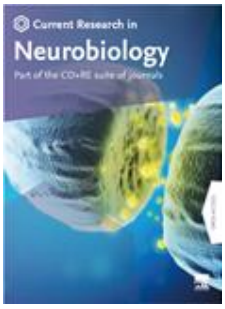
Peer Review Overview



Manuscript Title: Nonlinear EEG signatures of mind wandering during breath focus meditation

Received	Mar 31, 2022
1st Decision	May 04, 2022
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1st Decision letter

Reference: CRNEUR-D-22-00030
Title: Nonlinear EEG signatures of mind wandering during breath focus meditation
Journal: Current Research in Neurobiology

Dear Dr. Lu,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following major revision. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by Jul 03, 2022.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully; outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission will need to be re-reviewed.

Current Research in Neurobiology values your contribution and I look forward to receiving your revised manuscript.

CRNEUR aims to be a unique, community-led journal, as highlighted in the Editorial Introduction. As part of this vision, we will be regularly seeking input from the scientific community and encourage you and your co-authors to take the survey.

Kind regards,

Anna S Mitchell, Ph.D.
Editor in Chief
Current Research in Neurobiology

Comments from Editors and Reviewers:

Reviewer #1:

Overall:
Liu and Rodriguez-Larios analyze EEG recordings from novice meditation practitioners and compare EEG complexity metrics between periods of breath focus and periods of mind wandering, demonstrating overall reduced EEG complexity during mind wandering. This is an interesting study with a clean set of EEG results. However, both the reported neuro-behavioural correlations as well as the unclear neurobiological relevance of the study make the studies relevance hard to judge. Further, there are a number of areas for potential improvement on which I elaborate below.

Major:
- The authors report a link between drowsiness levels and EEG complexity (modulation). Relatedly, there might exist an overall link between experiment duration, drowsiness, and complexity metrics. Given their lack of experience and the nature of the task, participants might have gotten tired with the duration of the experiment. This of course is something that generally takes place during most experiments and by no means unique to meditation studies. Especially since not only behaviour and subjective ratings of drowsiness are affected by such trends of overall arousal but also different markers of EEG activity (e.g., alpha power), controlling results for individual trends of drowsiness appears called for. Since the authors are performing their analyses using the fieldtrip toolbox, my suggestion would be to use the ft_regressconfound function to achieve this or alternatively regress complexity metrics on trial number and continue with residuals.

- Please report sufficient information on signal processing to enable the replication of results. Which and how many components were rejected? How many epochs existed per subject and how many of those were rejected? What are the parameters of used filters?

- Please consider providing an intuition for each used measure of complexity. For example, the authors could, point out that a highly synchronous signal (e.g., a sinusoid or a mix of multiple sinusoids) will result in a low fractal dimension while a more random / complex signal will result in higher fractal dimension estimates. Similar intuitions (maybe with example signals) could be provided for LZC (e.g., extending the notion of binarized sequences to EEG signals by contrasting the number of present sequences between oscillatory and non-oscillatory activity) and SampEn. I realize that this might seem trivial to the authors but I belief that it will not only make their manuscript more accessible to a wider range of readers but also help to emphasize differences in the used metrics and their sensitivity to different signal features (see above). I will of course not insist on this but would imagine that figure that illustrates the application of all three methods to example snippets of (simulated) EEG signals would improve readability even further.

- I suggest to use great care in interpreting the correlations reported in figure 4. Although the authors are using non-parametric correlation estimates, the distribution of drowsiness levels seems problematic. For example, there are only two participants that report a drowsiness level close to 6 or 7 who also seem to be driving the reported correlation to a substantial degree. Given the sparsity of the data and the pseudo-continuous variable "Drowsiness level", I am skeptical regarding the interpretability and usefulness of these correlations altogether. Additionally, as the authors note, these correlations are already non-significant once trial numbers are equated. I would suggest to visualize trial-matched

correlations next to non-matched ones in the manuscript to address the instability of results directly. Also, could the authors please explain once more (maybe I have missed this), why only 16 participants are left after matching trial counts and how this relates to the drowsiness debriefing?

- In introduction and discussion there seems to be relatively little information and on potential neurobiological processes the authors are trying to tackle with their study. For example, one might ask:
o What is the neurobiological basis of altered EEG complexity during mind wandering? In other words, what can we really learn about the brain by analyzing EEG complexity differences during meditation states?
o Is the number of generators the only conceptual link the authors can make out?
o Given the different methods used, might the authors want to elaborate on the potential reasons behind the generally similar but different results across them? Relatedly, while it might be true that no other study has used the exact approach and metrics used here, the authors could use their knowledge of the applied complexity metrics to nevertheless try and compare previous results with the current set of findings. While there might not be a perfect comparison, trying to extract differences and commonalities for the reader based on EEG signal features (LZC effects vs power contrasts from other studies) could improve the discussion section a fair bit.

Minor:
- How many trials did participants perform? How long did the experiment take?
- The authors report a p-value of .05 for the sake of determining significant clusters. Given the absence of a directional hypothesis, shouldn't the appropriate p-value rather be .025 (two-sided test)?
- The authors correlate drowsiness levels with average differences in complexity metrics. For this purpose, they average metrics within significant clusters. While there is nothing wrong with this approach, it might severely hinder the identification of inter-individual differences. The significant cluster expresses maximally reduced inter-individual variance in the difference between MW and BF. Hence, the probability of finding stable inter-individual differences between both states is minimal within this cluster. The authors might instead want to rely on simple electrode-wise correlations or a method that partitions variance in a latent space (e.g., canonical correlation analysis or partial least squares).

Reviewer #2:

This is a well reported study on novice meditators and changes in varies complexity measures during a breath focus meditation compared to mind wandering. There are a few minor revisions that I would recommend before recommending it for publication.

First in the introduction section.
They mention that as far as they know no experience sampling during meditation have been done for mine wondering. This may be true, however it has been used for other meditation studies that deserve mention here. See https://pubmed.ncbi.nlm.nih.gov/29269049/ for example systematic review which includes sampling during meditation.

There is no discussion in the introduction about EEG complexity measures and their rationale for choosing the three complexity measures they use. They do have some information about that in the methods section, but that should really be up in the introduction to set the stage for why the specific measures were chosen in relation to the myriad of other complexity measures that are available.

There is also very little information about the participants meditation experience. They say that they are novices but does that mean that they have never meditated at all or that they have very little meditation experience.

I would also like to see some additional information in the discussion about next steps studies that should be conducted to tease apart the drowsiness, the differences between meditation levels, and perhaps comparison to other complexity measures versus linear measures.

Also, I am curious why they did not include linear measures to compare to the complexity measures. I don't think these necessarily need to be added but some comment as to why they chose not to also include the linear measures would be useful.

1st Author Response Letter

Response to comments from Editors and Reviewers:

Thank you for considering our manuscript for publication in Current Research in Neurobiology. Please see below our responses to the comments from the reviewers. The reviewers' comments are marked in grey and changes in the text are marked in blue. We believe that the reviewers' comments have helped us to improve our manuscript significantly. In the Introduction, we now elaborate on the neurophenomenological underpinning of EEG complexity and our choice of complexity metrics. In the Methods, we now provide a more comprehensive description of the analytical approach, including a new figure depicting the meaning of each of the adopted metrics. In the Results, we now visualize trialmatch and non-trial match correlations together (Supplementary Materials). Lastly, we now discuss the implications of our results from both a basic science and a translational perspective. We would be glad to respond to any further comments that you may have.

Comments from Reviewer 1

Overall:

Liu and Rodriguez-Larios analyze EEG recordings from novice meditation practitioners and compare EEG complexity metrics between periods of breath focus and periods of mind wandering, demonstrating overall reduced EEG complexity during mind wandering. This is an interesting study with a clean set of EEG results. However, both the reported neuro-behavioural correlations as well as the unclear neurobiological relevance of the study make the studies relevance hard to judge. Further, there are a number of areas for potential improvement on which I elaborate below.

Major:

- The authors report a link between drowsiness levels and EEG complexity (modulation). Relatedly, there might exist an overall link between experiment duration, drowsiness, and complexity metrics. Given their lack of experience and the nature of the task, participants might have gotten tired with the duration of the experiment. This of course is something that generally takes place during most experiments and by no means unique to meditation studies. Especially since not only behaviour and subjective ratings of drowsiness are affected by such trends of overall arousal but also different markers of EEG activity (e.g., alpha power), controlling results for individual trends of drowsiness appears called for. Since the authors are performing their analyses using the fieldtrip toolbox, my

suggestion would be to use the ft_regressconfound function to achieve this or alternatively regress complexity metrics on trial number and continue with residuals.

Unfortunately, the level of drowsiness was obtained by debriefings after completion of the whole task. Therefore, we can not assess whether drowsiness and EEG complexity covary within subjects (nor regress out the effects of drowsiness).

Certainly, one could assume that drowsiness increases over time. So we analyzed the correlation between trial complexity and trial serial number per subject. The statistics showed that the complexity value is not affected by the trials over time, across all subjects.

We add this information in the Methods (page 12):

> Assuming that drowsiness increases over time, Spearman's correlation was analyzed between trial complexity and trial serial number per subject, and the *ρ(rho)*-value was obtained for each subject (N = 25). Then a one-sample *t*-test (two-tailed) was performed over the *ρ(rho)*-values. If the H0 hypothesis cannot be rejected (at the 5% significance level), the complexity value is not affected by the trials over time.

And add this information in the Results (page 17):

> Since we lack the drowsiness level per trial, we assume that drowsiness increases over time. But no significant correlation (all $p > 0.5$) was observed between condition-related changes (MW – BF) in EEG complexity (HDF, LZC, and SampEn) and trial numbers (Table S3). This result indicates that the complexity value is not affected by the trials over time.

(Statistical values are in Supplementary Materials Table S3)

Nonetheless, we think that this is a relevant point so we now explicitly mention it in the Discussion (page 19):

In addition to mind wandering, lapses of attention can occur because of drowsiness (Brandmeyer & Delorme, 2018). Crucially, decreases in complexity have also been reported during states of transition from wakefulness to sleep (Broughton and Hasan, 1995; Cantero et al., 2002; Hou et al., 2021). Hence, it is possible that (at least part of) the self-reported mind wandering in our participants is due to drowsiness. We assess this possibility by correlating inter-individual differences in complexity changes (mind wandering – breath focus) and the level of drowsiness. Although we found that subjects with higher drowsiness tended to have a more pronounced reduction in complexity during mind wandering, this latter relationship rendered not significant when controlling for different trial counts between conditions. It is important to note that this latter correlational analysis was performed with a relatively small sample (N = 16, for matched trial counts) because drowsiness scores were not available in all subjects. Moreover, drowsiness was only reported at the end of the task, which did not allow us to assess whether EEG complexity and drowsiness covary within subjects throughout the task. Consequently, these results have to be interpreted with caution and further research is needed to disentangle mind wandering and drowsiness effects on complexity. Specifically, future studies using experience sampling could ask participants for their level of drowsiness (in addition to mind wandering) on a trial-by-trial basis. This would allow to assess the relationship between mind wandering and complexity while controlling for variations in drowsiness.

- Please report sufficient information on signal processing to enable the replication of results. Which and how many components were rejected? How many epochs existed per subject and how many of those were rejected? What are the parameters of used filters?

Thank you for noticing this. We now added this information in the Methods (page 6):

The data was bandpass filtered between 1 Hz and 40 Hz (function pop_eegfiltnew). Abrupt artifacts were corrected using the Artifact Subspace Reconstruction method (function clean_asr with a cut-off value of 20 SD; see Chang et al., 2020). Independent Component Analysis (ICA) was performed to correct for eye movements. Components were rejected based on their spatial topography and their correlation with H/VEOG electrodes. ICA led to an average removal of 1.68 ± SD 0.47 components per subject.

- Please consider providing an intuition for each used measure of complexity. For example, the authors could, point out that a highly synchronous signal (e.g., a sinusoid or a mix of multiple sinusoids) will result in a low fractal dimension while a more random / complex signal will result in higher fractal dimension estimates. Similar intuitions (maybe with example signals) could be provided for LZC (e.g., extending the notion of binarized sequences to EEG signals by contrasting the number of present sequences between oscillatory and non-oscillatory activity) and SampEn. I realize that this might seem trivial to the authors but I belief that it will not only make their manuscript more accessible to a wider range of readers but also help to emphasize differences in the used metrics and their sensitivity to different signal features (see above). I will of course not insist on this but would

imagine that figure that illustrates the application of all three methods to example snippets of (simulated) EEG signals would improve readability even further.

Thank you for the great suggestion, we now add a Figure that depicts each of the metrics in an intuitive way (page 10):

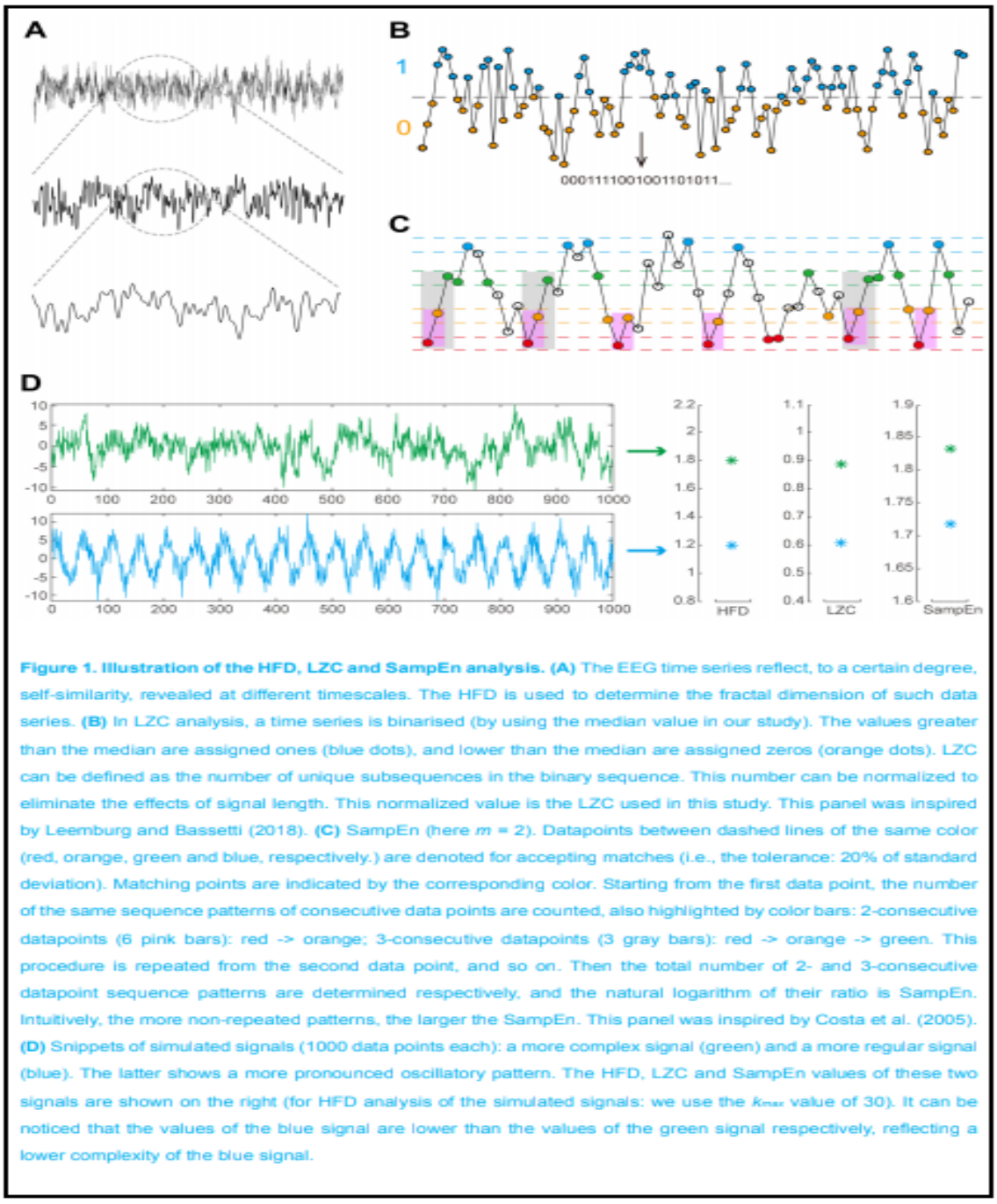

Figure 1. Illustration of the HFD, LZC and SampEn analysis. (A) The EEG time series reflect, to a certain degree, self-similarity, revealed at different timescales. The HFD is used to determine the fractal dimension of such data series. **(B)** In LZC analysis, a time series is binarised (by using the median value in our study). The values greater than the median are assigned ones (blue dots), and lower than the median are assigned zeros (orange dots). LZC can be defined as the number of unique subsequences in the binary sequence. This number can be normalized to eliminate the effects of signal length. This normalized value is the LZC used in this study. This panel was inspired by Leemburg and Bassetti (2018). **(C)** SampEn (here m = 2). Datapoints between dashed lines of the same color (red, orange, green and blue, respectively.) are denoted for accepting matches (i.e., the tolerance: 20% of standard deviation). Matching points are indicated by the corresponding color. Starting from the first data point, the number of the same sequence patterns of consecutive data points are counted, also highlighted by color bars: 2-consecutive datapoints (6 pink bars): red -> orange; 3-consecutive datapoints (3 gray bars): red -> orange -> green. This procedure is repeated from the second data point, and so on. Then the total number of 2- and 3-consecutive datapoint sequence patterns are determined respectively, and the natural logarithm of their ratio is SampEn. Intuitively, the more non-repeated patterns, the larger the SampEn. This panel was inspired by Costa et al. (2005). **(D)** Snippets of simulated signals (1000 data points each): a more complex signal (green) and a more regular signal (blue). The latter shows a more pronounced oscillatory pattern. The HFD, LZC and SampEn values of these two signals are shown on the right (for HFD analysis of the simulated signals: we use the k_{max} value of 30). It can be noticed that the values of the blue signal are lower than the values of the green signal respectively, reflecting a lower complexity of the blue signal.

- I suggest to use great care in interpreting the correlations reported in figure 4. Although the authors are using non-parametric correlation estimates, the distribution of drowsiness levels seems problematic. For example, there are only two participants that report a drowsiness level close to 6 or 7 who also seem to be driving the reported correlation to a substantial degree. Given the sparsity of the data and the pseudo-continuous variable "Drowsiness level", I am skeptical regarding the interpretability and usefulness of these correlations altogether. Additionally, as the authors note, these correlations are already non-significant once trial numbers are equated. I would suggest to visualize trial-matched correlations next to non-matched ones in the manuscript to address the instability of results directly. Also, could the authors please explain once more (maybe I have missed this), why only 16 participants are left after matching trial counts and how this relates to the drowsiness debriefing?

Thank you, we agree that these correlations should be interpreted with great care and they should not be depicted as an essential part of the manuscript. Consequently, we now move Figure 4 to Supplementary Materials (where we visualize trial and non-trial matched correlations; the new figure is Figure S4). In addition, we clarify in the methods (see below) why this analysis is performed with 16 subjects only and we are more explicit in the Discussion about the limitations of these analyses (see text changes in our first answer).

Methods (page 11):

> Six participants were rejected due to insufficient (<10) trial counts in both conditions after MTC. Data from the remaining nineteen participants were used for MTC processed analysis. Note that, due to a technical problem only sixteen of these participants had debriefings for the level of drowsiness at the end of the experiment.

- In introduction and discussion there seems to be relatively little information and on potential neurobiological processes the authors are trying to tackle with their study. For example, one might ask:

o What is the neurobiological basis of altered EEG complexity during mind wandering? In other words, what can we really learn about the brain by analyzing EEG complexity differences during meditation states?

o Is the number of generators the only conceptual link the authors can make out?

Thank you for underlying this. We agree our paper was lacking some elaboration on the neurobiological / functional relevance of EEG complexity in this context. We made substantial changes in the Introduction and Discussion to fix that.

Introduction (page 4):

The neurobiological and phenomenological correlates of EEG complexity are still debated. From a biological standpoint, EEG complexity is thought to be highly influenced by the number of EEG generators and the level of oscillatory synchronization (Ibáñez-Molina & Iglesias-Parro, 2014; Schaworonkow & Nikulin, 2022). In this way, if the EEG signal is dominated by a single rhythm across the cortex, complexity would be minimized. Recent literature also suggests that EEG complexity could be affected by the excitation:inhibition ratio in the brain (as reflected in the EEG power law exponent) (Medel et al., 2020). In this view, greater inhibition would be associated with a more pronounced 1/f slope of the EEG spectrum and lower complexity (Gao et al., 2017; Medel et al., 2020). From a phenomenological perspective, it has been proposed that the level of complexity in brain activity is positively associated with the vividness of subjective experience (Carhart-Harris et al., 2014; Carhart-Harris & Friston, 2019). This theory is based on research with psychedelic drugs, which have indeed shown to transiently increase EEG complexity (Timmermann et al., 2019).

To our knowledge, no previous study has investigated the relationship between EEG complexity and mind wandering in the context of meditation practice with novice meditators. Given previous inconsistencies with linear metrics (Braboszcz and Delorme, 2011; Brandmeyer and Delorme, 2018; van Son et al., 2019; Rodriguez-Larios and Alaerts, 2021; Rodriguez-Larios et al., 2021), studying the non-linear EEG correlates of mind wandering during meditation practice holds high promise from a translational perspective. In this way, EEG complexity could be an alternative to EEG linear metrics to develop EEG-neurofeedback protocols aimed at facilitating meditation practice in novice meditation practitioners (Brandmeyer & Delorme, 2013, 2020).

Discussion (page 17-18):

We here demonstrate that EEG activity is more predictable (i.e. less complex/random/entropic) during lapses of attention in the context of meditation practice. A more predictable EEG signal could be due to at least three different factors: i) reduced number of brain generators (Schaworonkow, & Nikulin, 2022) ii) increase in the power law exponent (Medel et al., 2020) and/or iii) greater presence of oscillatory activity (Timmermann et al., 2019). Concerning the number of generators, we can speculate that during mind wandering a specific network dominates the EEG signal and that is why complexity is reduced. Given its consistent association with mind wandering, a good candidate for this would be the Default Mode Network (DMN) (Brewer et al., 2011; Ellamil et al., 2016). On the other hand, if reduced EEG complexity is due to increases in the power law exponent and/or the presence of oscillatory activity (Medel et al., 2020), it is likely that this is reflecting increased cortical inhibition (Gao et al., 2017; Klimesch et al., 2007). In this line, lapses of attention have been previously associated with both low-frequency power increases and decreased excitability of the cortex (Braboszcz & Delorme, 2011; Smallwood et al.,2008). In this regard, it is important to note that our previous analysis of this data set

indeed revealed a relative increase in low-frequency power during mind wandering relative to breath focus (which could be reflective of increased oscillatory activity and/or a more pronounced slope of the power law exponent) (Rodriguez-Larios & Alaerts, 2021). Our analysis has revealed that this increase is negatively correlated with reduced EEG complexity (Figure S5).

The 'entropic brain' theory posits that there is a correspondence between the 'richness' of brain activity and subjective experience (Carhart-Harris et al., 2014; Carhart-Harris & Friston, 2019). According to this theory, when brain activity is more diverse (higher entropy/complexity) subjective experience is more vivid. In support of this idea, it has been shown that after psychedelics intake both the EEG signal and subjective experience become more complex and disorganized (Timmermann et al., 2019). Given the similarities between meditative and psychedelic states (Millière et al., 2018), the entropic brain theory predicts that meditation should also increase complexity in brain activity (Carhart-Harris & Friston, 2019). In this line, we here show that moments of focused meditation in novice meditators have a relatively higher EEG complexity than moments of distraction. However, this is not fully consistent with previous literature with experienced meditators. Although some studies have indeed associated meditative states with higher EEG complexity (Kakumanu et al., 2018; Vivot et al., 2020), other studies have reported the opposite effect (Aftanas and Golocheikine, 2002; Young et al., 2021) [···]

o Given the different methods used, might the authors want to elaborate on the potential reasons behind the generally similar but different results across them? Relatedly, while it might be true that no other study has used the exact approach and metrics used here, the authors could use their knowledge of the applied complexity metrics to nevertheless try and compare previous results with the current set of findings. While there might not be a perfect comparison, trying to extract differences and commonalities for the reader based on EEG signal features (LZC effects vs power contrasts from other studies) could improve the discussion section a fair bit.

Since all complexity metrics lead to similar results in our main analysis, we believe that the priority should be to discuss i) how complexity and power differences might relate and ii) why the relation between EEG complexity and meditation is not fully consistent. We made changes in the discussion to underline these two points more explicitly:

Discussion (page 18):

[···] if reduced EEG complexity is due to increases in the power law exponent and/or the presence of oscillatory activity (Medel et al., 2020), it is likely that this is reflecting increased cortical inhibition (Gao et al., 2017; Klimesch et al., 2007). In this line, lapses of attention

have been previously associated with both low-frequency power increases and decreased excitability of the cortex (Braboszcz & Delorme, 2011; Smallwood et al.,2008). In this regard, it is important to note that our previous analysis of this data set indeed revealed a relative increase in low-frequency power during mind wandering relative to breath focus (which could be reflective of increased oscillatory activity and/or a more pronounced slope of the power law exponent) (Rodriguez-Larios & Alaerts, 2021). Our analysis has revealed that this increase is negatively correlated with reduced EEG complexity (Figure S5).

Discussion (page 18-19):

[…] It is possible that inconsistencies regarding the relationship between EEG complexity and meditative states are due to differences in the meditation tradition, the level of expertise and the adopted complexity metric (Aftanas and Golocheikine, 2002; Huang and Lo, 2009; Kakumanu et al., 2018; Kumar et al., 2020; Martinez Vivot et al., 2020; Young et al., 2021). Given the great number of possible EEG metrics/traditions/levels of expertise that can be assessed, the only way of achieving a consensus in this field would be to make raw EEG data from different studies publicly available thereby allowing to assess these factors systematically.

Minor:

- How many trials did participants perform? How long did the experiment take?

We add this information in the Methods (page 6):

Each participant performed a total of 40 trials (the experiment lasted for approximately 40 minutes).

- The authors report a p-value of .05 for the sake of determining significant clusters. Given the absence of a directional hypothesis, shouldn't the appropriate p-value rather be .025 (two-sided test)?

In fact, the threshold of 0.05 in a two-sided test corresponding to: cfg.alpha = 0.025, and cfg.tail = 0;

The official explanation can be seen:
https://www.fieldtriptoolbox.org/tutorial/cluster_permutation_freq/ and
https://www.fieldtriptoolbox.org/workshop/madrid2019/tutorial_stats/

That is what we did, as shown in our code: https://github.com/y-q-l/MW-BF-NL/blob/main/Code/Stat_and_Topoplot.m

We add this information in the Methods to clarify it (page 11):

In FieldTrip, the cluster-level statistic at the threshold of 0.05 (two-sided test) is by setting the parameters cfg.alpha = 0.025 and cfg.tail = 0.

- The authors correlate drowsiness levels with average differences in complexity metrics. For this purpose, they average metrics within significant clusters. While there is nothing wrong with this approach, it might severely hinder the identification of inter-individual differences. The significant cluster expresses maximally reduced inter-individual variance in the difference between MW and BF. Hence, the probability of finding stable inter-individual differences between both states is minimal within this cluster. The authors might instead want to rely on simple electrode-wise correlations or a method that partitions variance in a latent space (e.g., canonical correlation analysis or partial least squares).

Thank you for your suggestion. We performed a new analysis and add information in the Methods (page 12):

In order to uncover the information hidden by significant clusters, we also assessed the correlations between differences in complexity measures and drowsiness levels, per electrode (the complexity value of each electrode) and for all electrodes (the mean value across all electrodes) across subjects.

And add new information in the Results (page 16-17):

[···] The previous results were derived from the significant clusters. Additionally, we found at the single-electrode level that C3, P3 and P4 showed a negative correlation (all $p < 0.01$) between the difference in HFD and the drowsiness (Table S1) after FDR correction. The correlation between complexity and drowsiness did not reach statistical significance for other single-electrode, nor the mean complexity values across all electrodes.

[···] Similarly, for the MTC approach, the correlation analysis was also performed at the single-electrode level and the all-electrode level, and no significant result was found (Table S2).

(Statistical values are in Supplementary Materials Table S1 and S2)

Comments from Reviewer 2

This is a well reported study on novice meditators and changes in varies complexity measures during a breath focus meditation compared to mind wandering. There are a few minor revisions that I would recommend before recommending it for publication.

First in the introduction section.

They mention that as far as they know no experience sampling during meditation have been done for mine wondering. This may be true, however it has been used for other meditation studies that deserve mention here. See https://pubmed.ncbi.nlm.nih.gov/29269049/ for example systematic review which includes sampling during meditation.

Thank you for your suggestion, we now added the reference in our paper (page 3):

For experience sampling during meditation, also see a recent systematic review by Wahbeh et al. (2018).

There is no discussion in the introduction about EEG complexity measures and their rationale for choosing the three complexity measures they use. They do have some information about that in the methods section, but that should really be up in the introduction to set the stage for why the specific measures were chosen in relation to the myriad of other complexity measures that are available.

Thank you for noting this. We now added some sentences in the Introduction summarizing the rationale behind our choices (page 5):

Our choice of complexity metrics is due to several factors. First, these three metrics are widely used in the EEG literature and therefore, it would facilitate comparing our results with previous findings. Second, these metrics can be applied to relatively short time series, which is normally the case in EEG studies that adopt experience sampling paradigms. Lastly, HFD, LCZ and SamEn have a relatively low computational cost, which could eventually facilitate their application in real-time EEG neurofeedback protocols.

There is also very little information about the participants meditation experience. They say that they are novices but does that mean that they have never meditated at all or that they have very little meditation experience.

Participants had not meditation experience at all. This information is now added in the Methods section (page 5).

All participants had no previous meditation experience.

I would also like to see some additional information in the discussion about next steps studies that should be conducted to tease apart the drowsiness, the differences between meditation levels, and perhaps comparison to other complexity measures versus linear measures.

We agree that these issues should be mentioned more explicitly in the Discussion. We made changes for that purpose:

Discussion (page 18):

[…] On the other hand, if reduced EEG complexity is due to increases in the power law exponent and/or the presence of oscillatory activity (Medel et al., 2020), it is likely that this is reflecting increased cortical inhibition (Gao et al., 2017; Klimesch et al., 2007). In this line, lapses of attention have been previously associated with both low-frequency power increases and decreased excitability of the cortex (Braboszcz & Delorme, 2011; Smallwood et al.,2008). In this regard, it is important to note that our previous analysis of this data set indeed revealed a relative increase in low-frequency power during mind wandering relative to breath focus (which could be reflective of increased oscillatory activity and/or a more pronounced slope of the power law exponent) (Rodriguez-Larios & Alaerts, 2021). Our analysis has revealed that this increase is negatively correlated with reduced EEG complexity (Figure S5).

Discussion (page 19):

In addition to mind wandering, lapses of attention can occur because of drowsiness (Brandmeyer & Delorme, 2018). Crucially, decreases in complexity have also been reported during states of transition from wakefulness to sleep (Broughton and Hasan, 1995; Cantero et al., 2002; Hou et al., 2021). Hence, it is possible that (at least part of) the self-reported mind wandering in our participants is due to drowsiness. We assess this possibility by correlating inter-individual differences in complexity changes (mind wandering – breath focus) and the level of drowsiness. Although we found that subjects with higher drowsiness tended to have a more pronounced reduction in complexity during mind wandering, this latter relationship rendered not significant when controlling for different trial counts between conditions. It is important to note that this latter correlational analysis was performed with a relatively small sample (N = 16, for matched trial counts) because drowsiness scores were not available in all subjects. Moreover, drowsiness was only reported at the end of the task, which did not allow us to assess whether EEG complexity and drowsiness covary within subjects throughout the task. Consequently, these results have to be interpreted with caution and further research is needed to disentangle mind wandering and drowsiness effects on complexity. Specifically, future studies using experience sampling could ask participants for their level of drowsiness (in addition to mind wandering) on a trial-by-trial basis. This would allow to assess the relationship between mind wandering and complexity while controlling for variations in drowsiness.

Also, I am curious why they did not include linear measures to compare to the complexity measures. I don't think these necessarily need to be added but some comment as to why they chose not to also include the linear measures would be useful.

Thank you for your suggestion, we now add a new analysis for the correlation between complexity and linear measures:

In Methods (page 12):

To investigate whether condition effects in complexity measures were associated with the differences in the low-frequency (4-12 Hz) range, we also calculated the averaged difference (MW minus BF) in amplitude (both absolute amplitude and relative amplitude) in theta (4–7 Hz) and alpha (8–12 Hz) frequency range in identified significant clusters for each subject (N = 25, data from Rodriguez-Larios and Alaerts, 2021). Pearson's correlations were then performed between the averaged difference of complexity measures and amplitudes across subjects.

In Discussion (page 18):

[···] it is important to note that our previous analysis of this data set indeed revealed a relative increase in low-frequency power during mind wandering relative to breath focus (which could be reflective of increased oscillatory activity and/or a more pronounced slope of the power law exponent) (Rodriguez-Larios & Alaerts, 2021). Our analysis has revealed that this increase is negatively correlated with reduced EEG complexity (Figure S5).

And in Supplementray Materials (Figure S5):

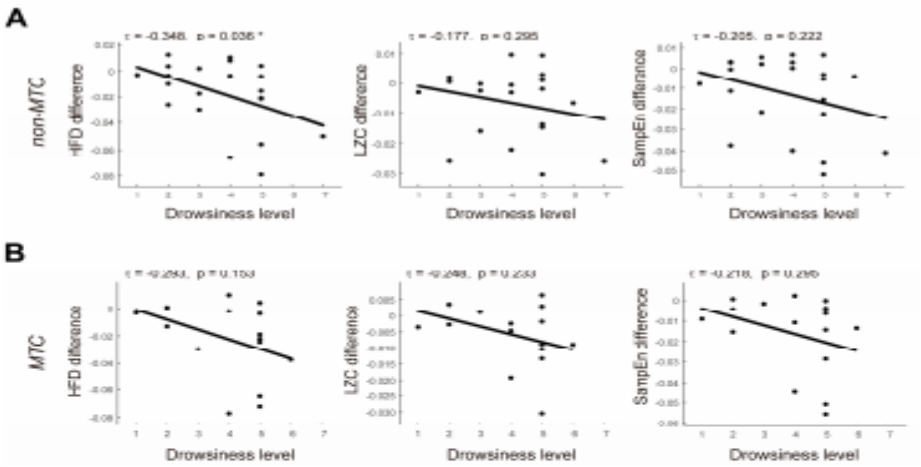

Figure S5. Correlations between condition-related changes in EEG complexity and amplitude modulations in the theta-alpha frequency range. Theta: 4–7 Hz; alpha: 8–12 Hz. In each panel, the difference (MW – BF) in complexity for each metric (HDF, LZC, and SampEn) is plotted as a function of the difference (MW – BF) in amplitude (absolute amplitude: columns 1 and 2; relative amplitude: columns 3 and 4). Each dot represents one subject (mean values across electrodes showing significant condition effects). The amplitude values are from our previous study (Rodriguez-Larios and Alaerts, 2021). Pearson's correlation coefficients and *p*-values (the original *p*-values, uncorrected by FDR) are shown at the top of their corresponding panels. Asterisks indicate the presence of significance after FDR correction (threshold: 0.05). A negative correlation was observed between complexity and amplitude modulations in the theta range, i.e., a decrease in complexity during MW was associated with an increase in theta power (columns 1 and 3). On the contrary, a positive correlation was observed between complexity and amplitude modulations in the alpha range, i.e., a decrease in complexity during MW was associated with a decrease in alpha power (columns 2 and 4). Note: a positive correlation was observed between LZC and alpha power (both for absolute amplitude and relative amplitude), but they did not reach statistical significance.

2nd Decision letter

Reference: CRNEUR-D-22-00030
Title: Nonlinear EEG signatures of mind wandering during breath focus meditation
Journal: Current Research in Neurobiology

Dear Dr. Lu,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following minor revision and modification. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by Sep 15, 2022.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully; outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission will need to be re-reviewed.

Current Research in Neurobiology values your contribution and I look forward to receiving your revised manuscript.

CRNEUR aims to be a unique, community-led journal, as highlighted in the Editorial Introduction. As part of this vision, we will be regularly seeking input from the scientific community and encourage you and your co-authors to take the survey.

Kind regards,

Anna S Mitchell, Ph.D.
Editor in Chief
Current Research in Neurobiology

Comments from Editors and Reviewers:

Reviewer #1:

The authors did a good job revising the manuscript.
I only have some very minor comments:

- Please report the order of the filter used.
- Please be more precise (e.g., in the caption of the new methods figure): which median is the basis for LZC binarization? The individual channel median of voltage across the whole experiment?

2nd Author Response Letter

Response to comments from Editors and Reviewers:

Comments from Reviewer 1

The authors did a good job revising the manuscript.

I only have some very minor comments:

- Please report the order of the filter used.

Thank you for noting this. The filter order is estimated automatically through a heuristic in the EEGLAB function 'pop_eegfiltnew.m'. In our analysis, the resulting filter order was 1690 for the high pass filter and 170 for the low pass filter. We now add this information in the Methods (*EEG acquisition and pre-processing, page 6*).

- Please be more precise (e.g., in the caption of the new methods figure): which median is the basis for LZC binarization? The individual channel median of voltage across the whole experiment?

We thank the reviewer for the suggestion. We now clarify the LZC binarization in the caption of Figure 1 (page 10):

(B) In LZC analysis, a time series is binarised (by using the median value of each channel of each epoch ~~in our study~~).

We also clarify this information in the Methods (Lempel-Ziv complexity (LZC), page 8):

[···] Here we used the median value (of each channel of each epoch): *md*.

==========

Corrigendum:

1) There was an error in the description of Table S3 in the Supplementary Materials: "No significant correlation was observed between condition-related changes (MW – BF) in EEG complexity (HDF, LZC, and SampEn) and trial numbers" should instead be: "No significant correlation was observed between EEG complexity (HDF, LZC, and SampEn) and trial numbers". Accordingly, the descriptions of Table S3 in the Results and the Supplementary Materials have been corrected. The analysis and the results were not affected. We now update our response to the comment from Reviewer 1 for the 1st revision (new changes are marked in blue):

-The previous comment from **Reviewer 1:**

The authors report a link between drowsiness levels and EEG complexity (modulation). Relatedly, there might exist an overall link between experiment duration, drowsiness, and complexity metrics. Given their lack of experience and the nature of the task, participants might have gotten tired with the duration of the experiment. This of course is something that generally takes place during most experiments and by no means unique to meditation studies. Especially since not only behaviour and subjective ratings of drowsiness are affected by such trends of overall arousal but also different markers of EEG activity (e.g., alpha power), controlling results for individual trends of drowsiness appears called for. Since the authors are performing their analyses using the fieldtrip toolbox, my suggestion would be to use the ft_regressconfound function to achieve this or alternatively regress complexity metrics on trial number and continue with residuals.

-Our response:

Unfortunately, the level of drowsiness was obtained by debriefings after completion of the whole task. Therefore, we can not assess whether drowsiness and EEG complexity covary within subjects (nor regress out the effects of drowsiness).

Certainly, one could assume that drowsiness increases over time. So we analyzed the correlation between trial complexity and trial serial number per subject. The statistics showed that the complexity value is not affected by the trials over time, across all subjects.

We add this information in the Methods (page 12):

> Assuming that drowsiness increases over time, Spearman's correlation was analyzed between trial complexity and trial serial number per subject, and the *ρ(rho)*-value was obtained for each subject (N = 25). Then a one-sample *t*-test (two-tailed) was performed over the *ρ(rho)*-values. If the H0 hypothesis cannot be rejected (at the 5% significance level), the complexity value is not affected by the trials over time.

And add this information in the Results (page 17) (*here we update this paragraph to improve the description of the results – in purple*):

> ~~Since we lack the drowsiness level per trial, we assume that drowsiness increases over time. But~~ If changes in complexity metrics reflect changes in drowsiness and/or fatigue, we could assume that complexity would decrease over time within subjects (as drowsiness would be expected to increase). However, we found no significant correlation (all $\rho > 0.5$) was observed between ~~condition-related changes (MW – BF) in~~ EEG complexity (HDF, LZC, and SampEn) and trial numbers (Table S3). This result indicates that changes in complexity cannot be fully explained by drowsiness or fatigue.~~the complexity value is not affected by the trials over time~~.

(Statistical values are in Supplementary Materials Table S3)

Nonetheless, we think that this is a relevant point so we now explicitly mention it in the Discussion (page 19):

In addition to mind wandering, lapses of attention can occur because of drowsiness (Brandmeyer & Delorme, 2018). Crucially, decreases in complexity have also been reported during states of transition from wakefulness to sleep (Broughton and Hasan, 1995; Cantero et al., 2002; Hou et al., 2021). Hence, it is possible that (at least part of) the self-reported mind wandering in our participants is due to drowsiness. We assess this possibility by correlating inter-individual differences in complexity changes (mind wandering – breath focus) and the level of drowsiness. Although we found that subjects with higher drowsiness tended to have a more pronounced reduction in complexity during mind wandering, this latter relationship rendered not significant when controlling for different trial counts between conditions. It is important to note that this latter correlational analysis was performed with a relatively small sample (N = 16, for matched trial counts) because drowsiness scores were not available in all subjects. Moreover, drowsiness was only reported at the end of the task, which did not allow us to assess whether EEG complexity and drowsiness covary within subjects throughout the task. Consequently, these results have to be interpreted with caution and further research is needed to disentangle mind wandering and drowsiness effects on complexity. Specifically, future studies using experience sampling could ask participants for their level of drowsiness (in addition to mind wandering) on a trial-by-trial basis. This would allow to assess the relationship between mind wandering and complexity while controlling for variations in drowsiness.

2) In our 1st response letter, Figure S4 was erroneously pasted in the response to the last comment. In fact, the figure that should be pasted correctly in the response is Figure S5. All texts (including the figure legend) are unaffected. The corresponding texts and figures in the Supplementary Materials are unaffected. This error does not affect the results and conclusions. We now correct our response to the comment from Reviewer 2 for the 1st revision (new changes are marked in blue):

-The previous comment from **Reviewer 2:**

Also, I am curious why they did not include linear measures to compare to the complexity measures. I don't think these necessarily need to be added but some comment as to why they chose not to also include the linear measures would be useful.

-Our response: Thank you for your suggestion, we now add a new analysis for the correlation between complexity and linear measures:

In Methods (page 12):

To investigate whether condition effects in complexity measures were associated with the

differences in the low-frequency (4-12 Hz) range, we also calculated the averaged difference (MW minus BF) in amplitude (both absolute amplitude and relative amplitude) in theta (4–7 Hz) and alpha (8–12 Hz) frequency range in identified significant clusters for each subject (N = 25, data from Rodriguez-Larios and Alaerts, 2021). Pearson's correlations were then performed between the averaged difference of complexity measures and amplitudes across subjects.

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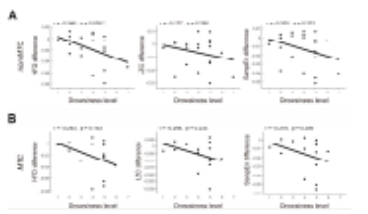
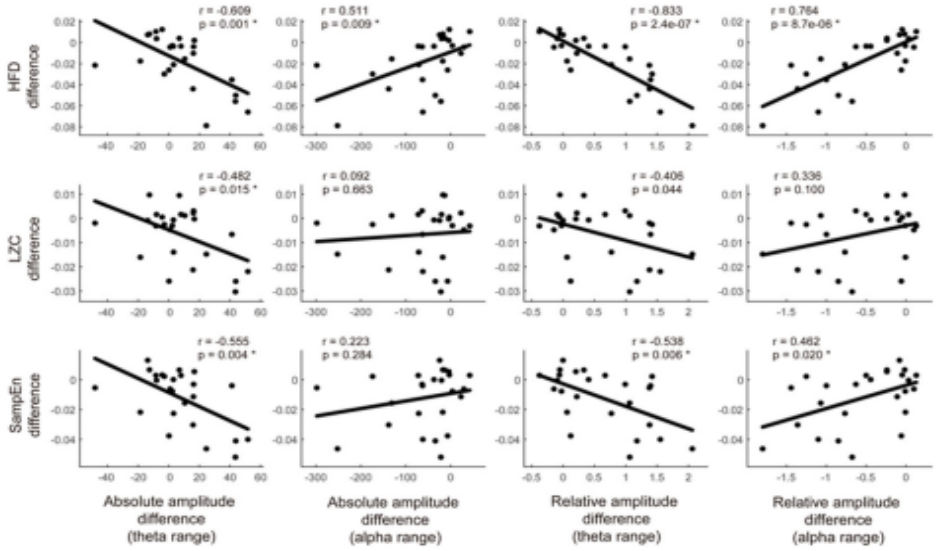
And in Supplementary Materials (Figure S5):



[← This Figure was erroneously pasted in the previous response letter.]

[↓ The following figure is correct.]



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Accept Letter

Dear Dr. Lu,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I am pleased to inform you that your manuscript has been accepted for publication. Congratulations.

Your accepted manuscript will now be transferred to our production department. We will create a proof which you will be asked to check, and you will also be asked to complete a number of online forms required for publication. If we need additional information from you during the production process, we will contact you directly.

We appreciate and value your contribution to Current Research in Neurobiology. We regularly invite authors of recently published manuscript to participate in the peer review process. If you were not already part of the journal's reviewer pool, you have now been added to it. We look forward to your continued participation in our journal, and we hope you will consider us again for future submissions.

CRNEUR aims to be a unique, community-led journal, as highlighted in the Editorial Introduction. As part of this vision, we will be regularly seeking input from the scientific community and encourage you and your co-authors to take the survey.

We would also like to invite you to take part in our CRNEUR Author Question & Answer (Q&A), which could get published alongside your article and help to promote it. We suspect you might have an interesting story of perseverance or team work that was required for the research study to complete, or a diversity of perspectives that you might share, as a way of inspiring others about neuroscience.

Kind regards,
Anna S Mitchell, Ph.D.
Editor in Chief
Current Research in Neurobiology

-------- End of Review Comments --------