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COMPLEXITY-BASED EVALUATION OF THE CORRELATION BETWEEN HEART AND BRAIN RESPONSES TO MUSIC

TISARA KUMARASINGHE,[*] ONDREJ KREJCAR,[†,‡] ALI SELAMAT,[†,‡,§]
NORAZRYANA MAT DAWI,[¶,‡‡,¶¶] ENRIQUE HERRERA-VIEDMA,[‖,**]
ROBERT FRISCHER[††] and HAMIDREZA NAMAZI[*,†,§§,¶¶]

[*]*School of Engineering, Monash University*
Subang Jaya, Malaysia

[†]*Faculty of Informatics and Management*
Center for Basic and Applied Research
University of Hradec Kralove, Hradec Kralove, Czechia

[‡]*Malaysia Japan International Institute of Technology (MJIIT)*
Universiti Teknologi Malaysia, Kuala Lumpur, Malaysia

[§]*Media and Games Center of Excellence (MagicX)*
Universiti Teknologi Malaysia
Johor Bahru, Malaysia

[¶]*Sunway University Business School, Sunway University*
Subang Jaya, Malaysia

[‖]*Andalusian Research Institute in Data Science and*
Computational Intelligence
University of Granada, Granada, Spain

[**]*Department of Electrical and Computer Engineering*
Faculty of Engineering, King Abdulaziz University
Jeddah, Saudi Arabia

[¶¶]Corresponding authors.

[††]Institute of Technology and Business in České Budějovice
České Budějovice, Czechia
[‡‡]norazryanad@sunway.edu.my
[§§]hamidreza.namazi@monash.edu

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Abstract

The evaluation of the correlation between the activations of various organs has great importance. This work investigated the synchronization of the brain and heart responses to different auditory stimuli using complexity-based analysis. We selected three pieces of music based on the difference in the complexity of embedded noise (including white noise, brown noise, and pink noise) in them. We played these pieces of music for 11 subjects (7 M and 4 F) and computed the fractal dimension and sample entropy of EEG signals and R–R time series [as heart rate variability (HRV)]. We found strong correlations ($r = 0.9999$ in the case of fractal dimension and $r = 0.7862$ in the case of sample entropy) among the complexities of EEG signals and HRV. This finding demonstrates the synchronization of the brain and heart responses and auditory stimuli from the complexity perspective.

Keywords: Heart; Heart Rate Variability (HRV); Brain; EEG Signals; Complexity; Fractal Dimension; Sample Entropy; Music.

1. INTRODUCTION

Physiological systems are very complex under neural regulatory mechanisms.[1] Although the nature of the underlying control mechanisms is not fully understood, however, it is very important to quantify the coupling between the changes in different organs versus the alterations in brain activity. Since the chemical and structural entities in the brain which control the heart rate are known, it is of interest whether this relationship can also be seen in the synchronization of the brain and heart activity. Some researchers evaluated the coupling among the alterations of heart rate variability (HRV) and EEG signals employing the same method (e.g. Fast Fourier Transform,[2] multiscale entropy,[3] information theory[4]). On the other hand, some researchers investigated the alterations of EEG signals and HRV using different techniques.[5–8] Besides, some studies examined the variations in heart activity versus brain activity recorded using other methods such as fMRI.[9] However, there has not been any work that analyzed the synchronization of HRV, EEG signals, and stimuli employing the same technique. EEG signals and R–R time series (HRV) have complex structures.[10,11] On the other hand, sounds (as auditory stimuli) also have complex structures. Therefore, the fractal theory can investigate the coupling of EEG and ECG signals versus the alterations of the sound (as auditory stimuli).

In general, fractals have repeating patterns that are distributed on various scales inside them. The fractal dimension quantifies the complexity of fractals.[12] Many works applied fractal theory to quantify the complexity of various biomedical and bio-signals (e.g. EMG signals,[13] GSR signals,[14] random genome walks,[15,16] speech signals[17]) and images (e.g. X-ray images[18]).

Specifically, some researchers investigated the complex structure of EEG signals using fractal theory. The works that quantified the alterations in EEG signals' complexity in external stimulation,[19] walking,[20] aging,[21] and brain diseases[22] are worthy of being mentioned. We can also call some studies that applied fractal theory to investigate the variations of the complex structure of HRV. The studies that evaluated the changes in HRV in normal subjects of different ages,[23] for the prediction of cardiac death,[24] to investigate the effect of pharmacological adrenergic and vagal modulation,[25] during non-REM sleep,[26] in patients with the peripheral arterial disease,[27] diabetes,[28] and Chronic Obstructive Pulmonary Disease (COPD)[29] can be mentioned.

Similarly, other nonlinear analysis methods can be utilized to study the complexity of EEG signals, HRV, and sound. In this research, we chose sample entropy for our analysis. The reason for choosing sample entropy is because it is independent of the length of data and works well in the case of data with short lengths.[30] Since the extracted R–R time series for different subjects were short and had different lengths, calculating the sample entropy helps us verify the fractal analysis results. Sample entropy has been applied widely for the analysis of various biomedical and biological time series (e.g. EMG signals,[31] speech signals,[32] random genome walks,[33] PCG signals[34]). We can also call several studies that employed sample entropy to evaluate EEG signals[35–37] and HRV.[38–40]

Since no study has investigated the correlation among the complexity of HRV, EEG signals, and external stimuli, we apply fractal theory and sample entropy to investigate this synchronization from the complexity point of view.

In the following section, we explain our method of analysis based on fractal theory and sample entropy. Then, we present the data collection and analysis steps. After that, we will bring the results which will be followed by the conclusion and discussion.

2. METHOD

In this study, we want to evaluate the synchronization of heart and brain activities. To examine this correlation in different conditions, we stimulate subjects using various music as auditory stimuli. We benefit from the complexity concept as our method of analysis to investigate the correlation between the variations of heart rate and brain signals and also the complexity of auditory stimuli. Since R–R time series, EEG signals, and audio signals have complex structures, we utilize fractal theory to investigate how their complexities are related. We calculate the fractal dimension of EEG signals and HRV, and in this way, we relate their complexities. It is known that bigger values of fractal exponent indicate greater complexities.[41]

There have been similar developed techniques for the calculation of the fractal dimension.[42] In this research, we employ the box-counting method for our analysis. In this technique, an object is covered with boxes in different steps, where all boxes have the same size (ε) in each step.[43] The calculation algorithm counts the number of used boxes (N) for coverage of the object in each step, and in the last step, it calculates the fractal dimension using the following equation[44]:

$$\mathrm{FD} = \lim_{\varepsilon \to 0} \frac{\log N(\varepsilon)}{\log 1/\varepsilon}. \tag{1}$$

The general form of fractal dimension of order c is formulated as follows:

$$\mathrm{FD}_c = \lim_{\varepsilon \to 0} \frac{1}{c-1} \frac{\log \sum_{j=1}^{N} r_j^c}{\log \varepsilon}, \tag{2}$$

where r_j indicates the probability of occurrence:

$$r_j = \lim_{T \to \infty} \frac{t_j}{T}, \tag{3}$$

where t_j and T, respectively, indicate the time in the jth bin and whole signals.

In this research, we also employ sample entropy to verify the fractal analysis results. Sample entropy can be used to quantify the complexity of signals. Its main characteristic is its independence from the data length.[45] Since the recorded ECG signals from different subjects lead to R–R time series with different lengths, sample entropy can overcome this bias (which can affect the calculation). For a signal, $\{y(1), y(2), y(3), \ldots, y(n)\}$, a template vector of length z can be defined as $Y_z(i) = \{y, y_{i+1}, y_{i+2}, \ldots, y_{i+z-1}\}$. The sample entropy (SamEn) is formulated as follows:

$$\mathrm{SamEn} = -\log \frac{B}{C}. \tag{4}$$

Considering the distance function, $d[Y_z(i), Y_z(j)]$ $(i \neq j)$ as Chebyshev distance and ε as the tolerance ($0.2 \times$standard deviation of data), B and C indicate the number of template vector pairs with conditions in (5) and (6), respectively.

$$d[Y_{z+1}(i), Y_{z+1}(j)] < \varepsilon, \tag{5}$$

$$d[Y_z(i), Y_z(j)] < \varepsilon. \tag{6}$$

As previously mentioned, we also would like to bring the complexity of music (as auditory stimuli) to our analysis. Therefore, we chose three pieces of music with different complexities. These music files were obtained from Ref. 46. Hunt *et al.*[46] embedded different noises with different levels of complexity to the Fur Elise song to change its complexity and create three new pieces of music with various complexities. The noises include white noise, pink noise, and brown noise with the fractal exponent

Table 1 Fractal Dimension and Sample Entropy of Noises.[46]

Noise	Fractal Exponent	Sample Entropy
White noise	1.5	2.2
Pink noise	1	1.75
Brown noise	0.5	0.25

and sample entropy listed in Table 1. As this table shows, the fractal dimension and sample entropy of noises decrease from white to brown noise, which indicates the reduction in their complexities. For further information about the generation of noises and taken procedures for embedding the noises to the base music, refer Ref. 46.

We play the music files for subjects and then investigate the correlation of the complexities of HRV and EEG signals.

3. DATA COLLECTION AND ANALYSIS

Monash University's ethics committee approved the experiment (No. 17454). Eleven students (7 M and 4 F, 18–22 years old) have attended the experiment. They did not drink alcohol/caffeine before the experiment. Subjects signed the informed consent form and agreed to participate. The experiment has been done in an isolated room from external disturbances.

After obtaining the consent form, we initiated the data collection while participants sat comfortably on a chair. We collected EEG and ECG signals using Muse EEG and Shimmer ECG devices at 256 and 128 Hz. The EEG electrodes placement (based on the 10–20 system) is shown in Fig. 1. Besides, one reference (V) and four recording (LA, RA, LL, RL) electrodes of the ECG device were connected to the subject's chest under his/her shirt. Figure 2 shows the placement of ECG electrodes.

Initially, we recorded the signals during rest for 3 min. Then, we played the first, second, and third music. Each music was played for 3 min with considering 1-min rest among different music. We re-ran the data collection in another session.

Out of 88 sets of recorded data from 11 subjects in four conditions (rest and different stimuli), some recorded data have been removed from processing due to disconnection (or low connection) of recording devices in some periods. First, our developed code in MATLAB (MathWorks, USA)

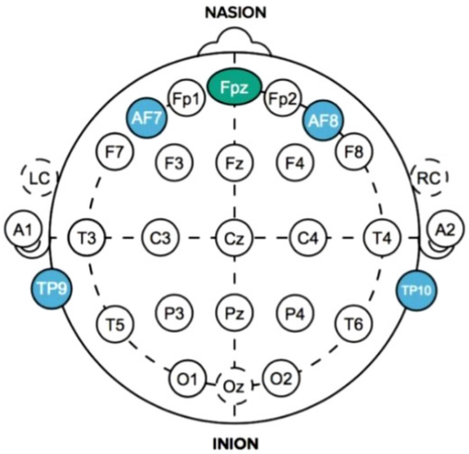


Fig. 1 The placement of EEG electrodes.

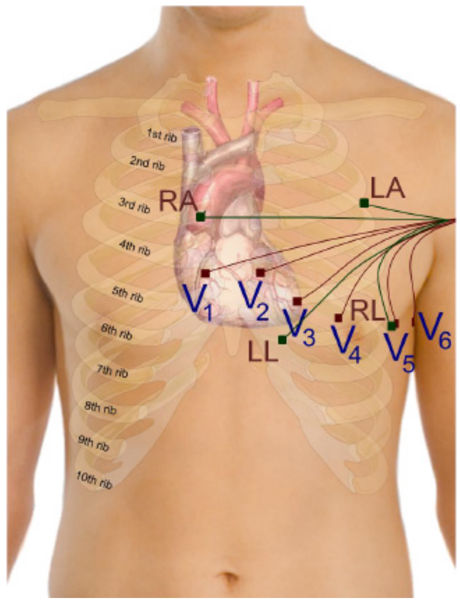
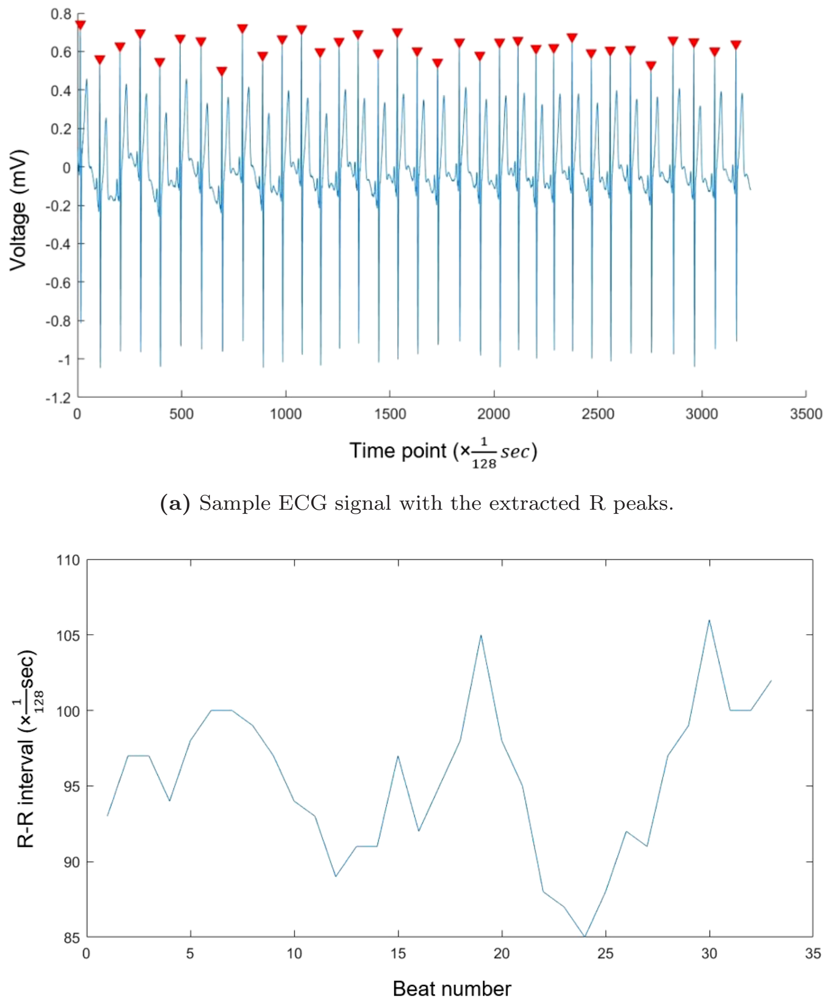


Fig. 2 The placement of ECG electrodes.

selected R peaks of ECG signals. Then, it generated the R–R interval time series from extracted R peaks. We checked the extracted R peaks visually for better accuracy. A sample raw ECG signal with extracted R peaks and its R–R time series are shown in Figs. 3a and 3b, respectively.

Since auditory stimuli play a major role in changing the brain's activity, in this research, we only analyzed the brain's reaction to these stimuli by analysis of the recorded EEG signals from TP9 and TP10 electrodes. This selection is due to the positions of these electrodes that are closest to the auditory cortex.

After removing the DC offset, we filtered the recorded EEG signals employing a fourth-order



(a) Sample ECG signal with the extracted R peaks.

(b) Sample generated R–R time series from the ECG signal **(a)**.

Fig. 3 Sample raw ECG signal **(a)** and R–R time series **(b)**.

Butterworth band-pass filter (1–40 Hz). A sample filtered EEG signal (1 min) and its frequency information [using a periodogram power spectral density (PSD) estimate] during rest is shown in Fig. 4.

We computed the fractal dimension and sample entropy of EEG signals and R–R time series. The box-counting algorithm was ran using box sizes $1/2, 1/4, 1/8, 1/16, \ldots$. All the analyses were conducted in MATLAB.

We checked the normality of the fractal dimension and sample entropy of the R–R time series and filtered EEG signals by running the Anderson–Darling test in MATLAB. In the case of different groups of data, the test's result indicates a failure to reject the null hypothesis. In other words, the data had normal distributions.

We checked the significance of variations of the complexity of signals by running the ANOVA test ($\alpha = 0.05$). We also conducted pairwise comparisons by running the post-hoc Tukey test and effect size analysis ($\alpha = 0.05$). We should note that we computed Cohen's d as the effect size. We quantified the correlation between the variations of complexities of EEG signals, HRV, and music using the Pearson correlation coefficient.

4. RESULT

Figure 5 shows the mean fractal dimension of EEG signals (a) and added noises to the music files (b).

As shown in Fig. 5a, EEG signals obtained the smallest fractal dimension while subjects rest. The EEG signals' fractal dimension increases in response to the first music, which is because of the sudden reaction of the resting brain to the music. However, it decreases by playing the second and third

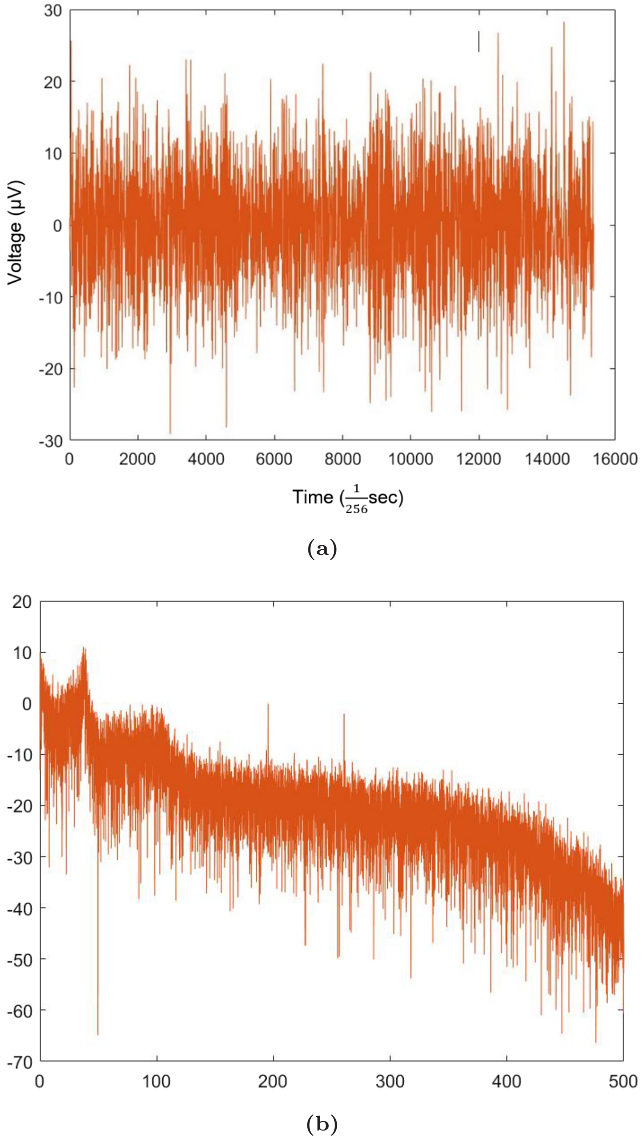


Fig. 4 The filtered EMG signal (1 min) **(a)** and its periodogram PSD estimate **(b)** for a subject during rest.

music. In other words, the complexity of EEG signals increases and then decreases in response to the music. Comparing Fig. 5a with Fig. 5b indicates similar trends of variations for the fractal dimension of EEG signals and music. Based on these figures, playing a music file with lower complexity caused a lower complexity in EEG signals. The correlation coefficient ($r = 0.9925$) among the variations of complexities of EEG signals and music demonstrates a strong positive correlation among them.

$p = 0.0382$ and $F(3, 79) = 2.9399$ demonstrate that the variations of the EEG signals' complexity were significant. Furthermore, the values of Cohen's d and p-values from the post-hoc test in Table 2

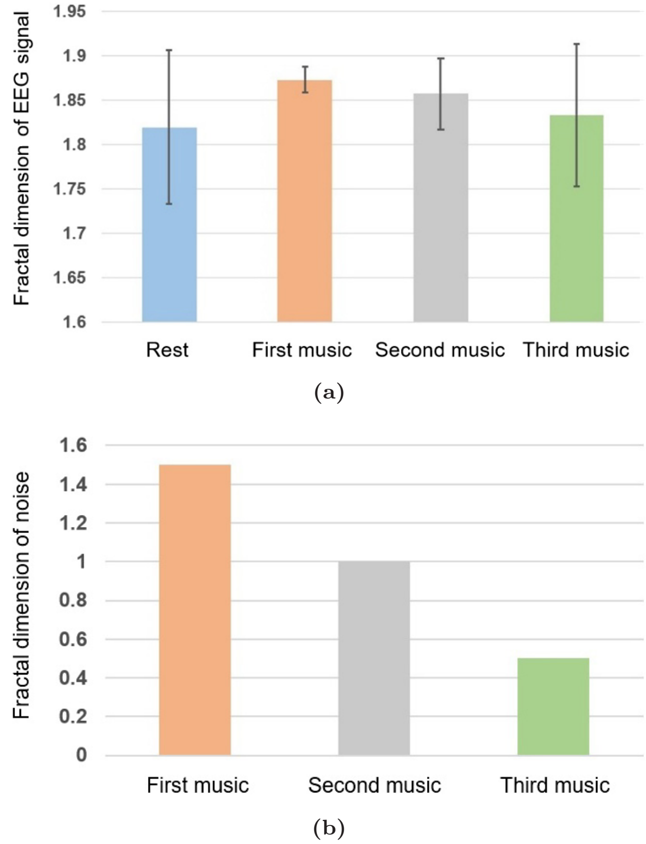


Fig. 5 The fractal exponent of EEG signals **(a)** and added noises to the music **(b)** Error bars indicate standard deviation.

Table 2 Comparisons of EEG Signal's Fractal Dimension.

Comparison	p (Post-Hoc Test)	Cohen's d
Rest condition versus 1st music	0.0403	−0.8586
Rest condition versus 2nd music	0.2306	−0.5581
Rest condition versus 3rd music	0.8989	−0.1617
1st music versus 2nd music	0.8642	0.5197
1st music versus 3rd music	0.1961	0.6915
2nd music versus 3rd music	0.6197	0.3814

demonstrate that a more significant variation of the music's complexity causes a more significant variation in the EEG signals' complexity.

Figure 6 illustrates the R–R time series' fractal dimension during rest and auditory stimulation.

As shown, the HRV has the biggest fractal dimension during rest. The fractal exponent of the HRV decreases in response to the first music. Playing the second and third music led to reducing the fractal dimension of HRV. Therefore, the complexity of HRV decreases in response to the first to the third

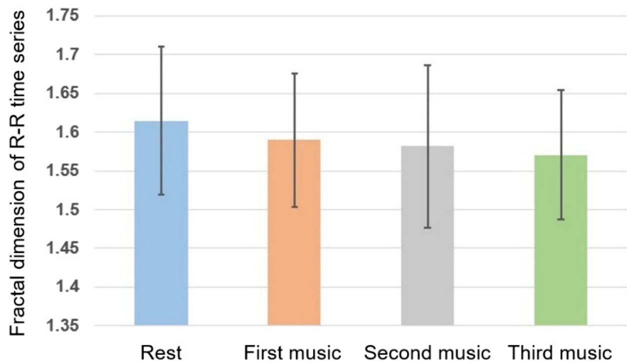


Fig. 6 R–R time series' fractal dimension. Error bars indicate standard deviation.

Table 3 Comparisons of R–R Time Series' Fractal Dimension.

Comparison	p (Post-Hoc Test)	Cohen's d
Rest condition versus 1st music	0.8276	0.2698
Rest condition versus 2nd music	0.6678	0.3251
Rest condition versus 3rd music	0.4102	0.4907
1st music versus 2nd music	0.9927	0.0842
1st music versus 3rd music	0.9072	0.2299
2nd music versus 3rd music	0.9791	0.1204

music. Since the heart has less reaction to the music compared to the brain, therefore, we cannot see any increment in the complexity of HRV after playing the first music for subjects. Comparing Fig. 6 with Fig. 5b indicates similar trends of variations for the fractal dimension of HRV and the fractal dimension of noises in the music. Based on these figures, playing a music file with lower complexity caused a lower complexity in HRV. The correlation coefficient ($r = 0.9951$) between the changes of the complexity for HRV and music demonstrates a strong correlation among them.

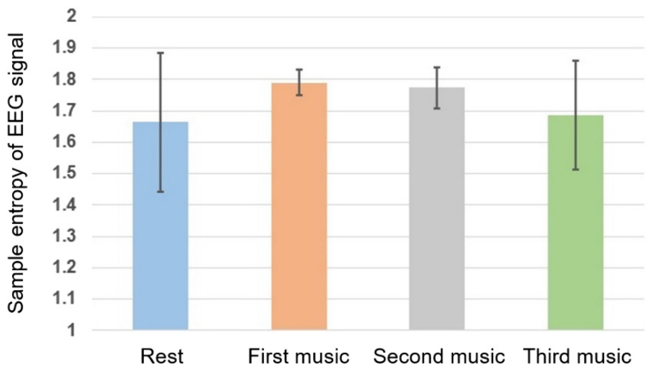
Furthermore, comparing the complexities of HRV (Fig. 6) and EEG signals (Fig. 5a) demonstrates similar trends in the case of stimulations. In other words, the changes in brain and heart responses to music are correlated; playing music with higher complexity causes higher complexity in EEG signals and HRV. In addition, the correlation coefficient ($r = 0.9999$) states a strong correlation among the complexities of EEG signals and R–R time series. This finding demonstrates the synchronization among heart and brain responses.

$p = 0.4597$ and $F(3, 79) = 0.8712$ indicate that the alterations in the complexity of HRV were insignificant. This result was expected since, in general, the heart has less reaction to the music compared to the brain, which is the main processing unit of the body (and showed a significant response to the music). The effect sizes in Table 3 state that a more significant change in the music's complexity causes a more significant alteration in the HRV's complexity. Furthermore, the post-hoc test findings in this table demonstrate no significant difference in the complexity of the R–R time series between different conditions. As can be seen, making a larger alteration in music's complexity causes a more significant alteration in R–R time series' complexity. In this research, we look for the coupling among the changes in the complexity of EEG signals and HRV, not the significance of variations in response to different music. The difference in the complexity of HRV between different groups could become significant if we change the tempo and specifically the volume of different music. However, to make the experiment pleasant for the participants, we kept the volume low.

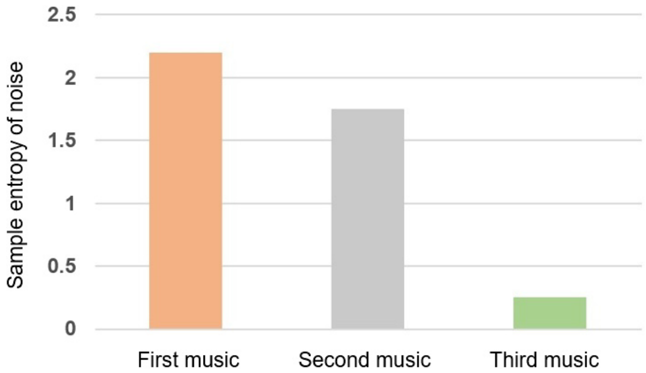
As was mentioned previously, since the HRV of subjects had various lengths, to verify the fractal analysis results, we also computed the sample entropy of EEG signals and R–R time series in various conditions. Figure 7 illustrates the EEG signals' sample entropy (a) and the sample entropy of added noises to music files (b).

As can be seen in Fig. 7a, during rest, EEG signals had the smallest sample entropy. By playing the first music, the EEG signals' entropy increases. By playing second and third music for participants, the EEG signals' entropy decreases. Therefore, EEG signals' complexity increases in response to the first music. As was indicated, this result is due to the sudden reaction of the resting brain to the music. After that, by playing other music files to subjects, the complexity of their EEG signals decreases. Comparing Fig. 7a with Fig. 7b indicates similar trends of variations. The correlation coefficient ($r = 0.9968$) indicates a strong correlation between the complexities of EEG signals and music. Therefore, like the fractal analysis results, the alterations in the complexities of EEG signals and music are synchronized.

$p = 0.0143$ and $F(3, 79) = 3.7434$ state the significant variations in the EEG signals' entropy. The effect sizes and p-values from the post-hoc test in Table 4 demonstrate that a more significant variation in the music's complexity causes a more significant change in the EEG signals' complexity.



(a)



(b)

Fig. 7 The sample entropy of EEG signals **(a)** and added noises to the music **(b)** Error bars indicate standard deviation.

Table 4 Comparisons of the EEG Signals' Sample Entropy.

Comparison	p (Post-Hoc Test)	Cohen's d
Rest condition versus 1st music	0.0347	−0.8006
Rest condition versus 2nd music	0.0812	−0.6830
Rest condition versus 3rd music	0.9523	−0.1201
1st music versus 2nd music	0.9866	0.2879
1st music versus 3rd music	0.1261	0.8145
2nd music versus 3rd music	0.2447	0.6626

Figure 8 illustrates the sample entropy of the R–R time series during rest and auditory stimulation.

According to the result, the R–R time series had the biggest sample entropy during the rest. As can be seen, the entropy of HRV decreased in response to the first music. Similarly, the sample entropy of HRV decreased when we played second and third music for subjects, which means reductions in the complexity of HRV. As was stated previously, since the heart has less reaction to the music compared to the brain, therefore, we cannot see any increment in the complexity of HRV after playing the first music for subjects. Comparing Fig. 8 with Figs. 7a and 7b in the case of stimulations indicates similar trends of variations for the entropy (complexity) of HRV, EEG signals, and the music. The correlation coefficient ($r = 0.8324$) indicates a strong correlation among the complexities of HRV and music. Furthermore, the correlation coefficient ($r = 0.7862$) indicates a strong synchronization between the sample entropies of EEG signals and HRV.

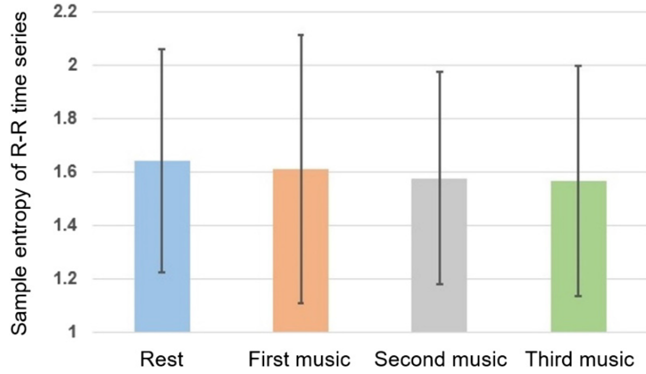


Fig. 8 The sample entropy of the R–R time series. Error bars indicate standard deviation.

Table 5 Comparisons of the Sample Entropy of R–R Time Series.

Comparison	p (Post-Hoc Test)	Cohen's d
Rest condition versus 1st music	0.9958	0.0665
Rest condition versus 2nd music	0.9636	0.1586
Rest condition versus 3rd music	0.9414	0.1788
1st music versus 2nd music	0.9947	0.0752
1st music versus 3rd music	0.9875	0.0966
2nd music versus 3rd music	0.9991	0.0267

$p = 0.9410$ and $F(3, 79) = 0.1317$ indicate that the changes of the complexity of HRV were insignificant. The effect sizes in Table 5 state that a more significant alteration in the music's complexity causes a more significant alteration in the complexity of the R–R time series. Furthermore, the p-values in this table indicate no significant difference in the complexity of the HRV among various conditions. As can be seen, making a larger alteration in the music's complexity causes a more significant alteration in the R–R time series' complexity. As previously mentioned, we look for the coupling among the changes in the complexity of EEG signals and HRV, not the significance of their variations in response to different music.

Therefore, the results of the sample entropy of EEG signals and HRV verified the results of the fractal analysis. Overall, our findings show that the heart and brain responses to auditory stimuli are synchronized.

5. DISCUSSION

We evaluated the coupling among brain and heart activities by assessing the complexity of their physiological signals. For this purpose, three pieces of music with different levels of complexity were played for the participants. We quantified the complexity of EEG signals and R–R time series using fractal theory. Besides, we analyzed the sample entropy of these signals to verify the fractal analysis results.

According to the findings, when we stimulate subjects, EEG signals' complexity increased. This increase is related to the sudden reaction of the brain to music.[47] Besides, making a bigger decrease in the music's complexity caused a bigger decrease in the EEG signals' complexity. Analysis of the complexity of the R–R time series showed that it decreased in response to the music. This result is potentially due to the lower reaction of the heart than the brain to external stimuli.[48] Applying a bigger decrease in the music's complexity caused a bigger decrease in the complexity of HRV. Statistical analyses also supported these results. Furthermore, a strong positive correlation was obtained among the changes of the EEG signals and HRV in response to stimulations.

In this study, we observed that the complexity of EEG signals increased due to listening to the first music, whereas the complexity of HRV decreased. We mentioned that this behavior is potentially due to the reaction of the resting brain to a stimulus that causes a bigger change in the complexity of EEG signals. On the other hand, since the heart has less reaction to the music compared to the brain, therefore, we cannot see any increment in the complexity of HRV after playing the first music for subjects. In fact, the increment in the EEG signals' complexity or decrement in the complexity of HRV due to the first music is dependent on the tempo, type, and volume of the music. We can find studies that found increases in the EEG signals' complexity in response to music (auditory stimuli).[49] In contrast, some works stated that the EEG signals' complexity decreases in response to the auditory stimulation using music.[50] It should be noted that this behavior is not limited to EEG signals. We can find some works that investigated the fractal dimension of HRV in response to auditory stimuli. For instance, the reported results on decrement[51] and increment[52] of the fractal dimension of HRV signals in response to auditory stimulation compared to the rest condition are worthy of being mentioned. Therefore, this behavior of variations of complexity compared to the rest does not indicate the weakness of the fractal dimension and sample entropy in quantifying the complexity of signals.

Besides, the changes in the complexity of EEG signals can be verified by comparing them to other studies. As an example, in Ref. 53, it was shown that presenting a visual stimulus increases the complexity of EEG signals, and by increasing the complexity of visual stimuli, the complexity of EEG signals increases. A similar trend was observed in another research[54] for the application of olfactory stimuli with increasing complexities.

Therefore, the alterations in the responses of the heart and brain and applied auditory stimuli are correlated. Our methodology (simultaneous application of fractal theory and sample entropy) is one step forward compared to the works[55–57] that only focused on employing techniques that are dependent on the length of data, without considering that the HRVs of subjects may have different lengths even for the same duration of data recording, and it can affect the results.

When we listen to a piece of music, ERPs capture electrical responses in the cortex due to the stimulus. Then, ANS will communicate with the cardiac system. When the heart's intrinsic nervous system processed the information, signals are transferred to the heart's sinoatrial node and other tissues in the heart. Although the exact descending pathway responsible for the autonomic and cardiovascular effects of auditory stimulation with musical auditory stimulation remain to be determined, however, the neural connection between the hypothalamic tuberomammillary nucleus (TMN) and the suprachiasmatic nucleus (SCN) could be a part of the neural pathway. The details of the mechanism are not certain, and further study will be needed.

In Ref. 58, we have shown that the Hurst exponents of EEG signals and auditory stimuli vary together. Due to the direct relationship[59] between the Hurst exponent (H) and fractal dimension of time series, $F = 2 - H$, the fractal dimension of EEG signals and auditory stimuli vary together. Since the heart activity is controlled by the brain, the trend of the changes of the complexities of EEG signals and auditory stimuli is reflected in the variations of the complexity of HRV and auditory stimuli.

In this study, we considered three music with the same base. However, in further studies, we can investigate the coupling between heart and brain activities in the case of other types of music without a similar base. We can further evaluate this coupling in the case of other stimuli. As an example, we can present different olfactory stimuli with various complexities to subjects and then investigate how the complexities of EEG signals, R–R time series, and stimuli are correlated. We can also evaluate the coupling among other organs (e.g. skin) and the brain due to stimulation. Since the human body is controlled by the brain, we expect to see similar synchronizations.

We can conduct similar investigations on patients with heart [e.g. coronary artery disease (CAD)[60]] and brain (e.g. Epilepsy[61]) disorders. Therefore, we can discover the heart–brain synchronization when these organs have disorders that affected their activities. Modeling the relationship between HRV and EEG signals versus stimuli is another potential future work that can help for the prediction of HRV based on the influence of stimuli on brain activity. To do this, we can potentially benefit from mathematical modeling (e.g. fractional diffusion equations[62–66]) and computational analysis.[67–69]

This study analyzed the interaction between the brain and heart. Besides correlation with the brain, different organs also interact.[70] Therefore, we can potentially extend our investigation and analyze the complex structures of different biosignals (e.g. EMG, ECG signals). Overall, all these studies can help researchers decode the relationship among different organs' activities versus brain activities, which significantly impact health sciences.

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