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CHANGES IN CARDIOVASCULAR, RESPIRATORY, AND NEURAL ACTIVITY BY MUSIC: EFFECTS OF BREATHING PATHWAY ON FEELING EMOTIONS

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CHANGES IN CARDIOVASCULAR, RESPIRATORY, AND NEURAL ACTIVITY BY MUSIC: EFFECTS OF BREATHING PATHWAY ON FEELING EMOTIONS

DISSERTATION

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Engineering at the University of Kentucky

By
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ABSTRACT OF DISSERTATION

CHANGES IN CARDIOVASCULAR, RESPIRATORY, AND NEURAL ACTIVITY BY MUSIC: EFFECTS OF BREATHING PATHWAY ON FEELING EMOTIONS

Listening to music can induce emotional and physiological changes. Increasing recognition of the palliative effects of music has led to its use as an adjuvant therapeutic tool in the treatment of various diseases. It is also well known that autonomic nervous activities and some cardiorespiratory rhythms change in correspondence with music. However, less is known about how these effects triggered by music come about. Listening to music affects synchronization between electroencephalograms (EEGs) and cardiac rhythmic activity. This interaction between cardiac and electrical responses led us to investigate whether EEG segments synchronized to different portions of the cardiac cycle can better reveal the effects produced while listening to music. In this dissertation, we investigated the effects of music from two different perspectives. Effects of the tempo of music, which has a relatively stronger effect on physiological variables compared to the other structural features, and effects of cognition of music were considered to compare the effects of a strong acoustical feature of music with effects of a feature not related to the structure of music to determine whether these effects were better revealed within certain portion of the cardiac cycle. We use effects of cognition to mean as those not directly resulting from structural features of music. 14 subjects participated in this study.

In a second study, we investigated how the breathing pathway can affect the processing of emotion induced by music. There is evidence of the presence of respiratory entrainment of local field potential activity in human limbic brain networks and the importance of nasal airflow in shaping this entrainment, but the effects of breathing pathway (nasal vs. oral) on the processing of various emotions, which happens in the limbic region, are not yet well-understood, we compared the degree of various emotions triggered by different pieces of music during purely oral breathing (OB) and purely nasal breathing (NB). Also, changes in some physiological parameters during OB and NB were compared, and the correlation of different structural musical features with different emotions was investigated. 12 subjects participated in this study.

Results showed, as indicated by eigenvalue decomposition, an increase in complexity of brain response by an increase in the tempo of the music, specifically in the parietal lobe, and triggering the smallest changes by slow tempo song, possibly explaining the calming effects of slow music. A stronger effect of cognition of music was observed in frequencies >38 Hz, particularly in the temporal lobe, and a stronger response to slower tempo music was observed in frequencies<38 Hz. The larger sensitivity of EEGs to portions of the cardiac cycle was in frequency bands <38 Hz. Alpha and Beta bands were the most sensitive bands to auditory stimuli and cardiac phases, respectively, and in both of them, effects of tempo were larger than cognition of music. Overall, we observed that the EEG portion which contained data points that were temporally farthest from R-waves of ECG showed the effects of music in a much more pronounced way than the other two portions. This observation was consistently supported by all of the used features and statistical indices which were based on eigenvalue decomposition, the effect size of changes, and p values.

In the study related to investigating the effects of breathing pathway on processing emotion, our results revealed that during NB, subjects found songs happier and more relaxing, and they felt more arousal states from songs when compared to the same songs during OB. On the other hand, during OB, subjects' average rate of more negative emotions was higher when compared to NB. We observed that the consonance degree of songs had significantly high positive correlations with positive emotions and significantly high negative correlations with negative emotions, while the higher complexity rate of songs had a positive correlation with negative emotions. Also, our results demonstrated slightly higher synchronization of respiration with various EEGs and with heartrate variations during NB in both control and listening to music.

KEYWORDS: music; emotion; cognition; nasal breathing pathway; oral; tempo

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03/01/2021

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DEDICATION

I dedicate my dissertation work to my loving parents who have supported me throughout the process of completing my PhD. This achievement was not possible without their endless love, encouragement, and support.

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I would like to express my sincere thanks to my advisor Dr. Abhijit Patwardhan for his continuous guidance, support, and patience during my PhD program. He has been a true mentor and always has some helpful advice about my research while always trying to grow independent thinking in me.

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CHAPTER 1. INTRODUCTION AND BACKGROUND

1.1 Physiological changes by music

Listening to music can induce emotional and physiological changes. Increasing recognition of the palliative effects of music [1-3] has led to its use as an adjuvant therapeutic tool in the treatment of various diseases [4, 5]. Previous studies have shown that the rhythmic components of music do affect and entrain cardiovascular autonomic regulation [6, 7], including regulation of blood pressure (BP) [8, 9]. An increase in parasympathetic nervous activity is observed during listening to sedative music or slow tempo songs [10] while an increase in sympathetic nervous activity is observed during listening to pleasurable music [11, 12] or songs with a higher tempo [7]. A review of the effects of music on the autonomic nervous system is provided by Ellis *et.al* [13]. Neuronal coherence, which is hypothesized to serve as a neural communication mechanism, can be dynamically modulated by cognitive demands [14]. Because of this dynamic modulation of neural coherence and changes in the autonomic nervous system induced by music, in [15] coherence was used to investigate how neural electrical oscillations and autonomic mediated rhythms in respiratory and cardiovascular regulation changed by tempo and cognition of music. Additional studies have demonstrated the entrainment of respiratory rate to musical tempo, trials using simple rhythmical patterns showed the adaptation of respiratory frequency to the tempo of the metronome in an unconscious manner [16].

Several studies have reported that the tempo of the music is a major determinant of physiological changes induced by music compared to other acoustic features [17, 18]. The effects of music are a result of complex combinations that are not limited to the structural features of the auditory stimuli, i.e. the sensory input, but also include cognitional contribution resulting from memory association and recall. In one of our previous studies [15], we attempted to separate the effects induced by acoustical aspect of music, i.e. the purely sensory component, from that resulting from the cognitional component. In [15] and in chapter 2, we use the word "cognition" to refer to that component of the effect of music not directly resulting from the structural acoustical features of the song, i.e. sensory stimulation, but that component of the effect that comes about because of the memory recall and its associated effects triggered by the music. In [15], subjects listened to slow and fast tempo songs, an unknown song (which was the fast tempo song) and a subject-chosen song which "moved" them and was their favorite song. To provide less subjective results for cognitive performance, the locally phase randomized (LPR) version of subjects' favorite song and the unknown song were also played. The expectation was that the use of LPR would change the sensory components of stimuli in a subtle way while preserving the overall acoustical features.

The main observation of our study was an overall increase in coherence, which indicates the degree of synchronization, among cerebral, cardiovascular and respiratory rhythms while listening to music. Further, we observed that listening to music decreased respiratory frequency bandwidth, showing that the respiratory pattern becomes less variable and more uniform than silence. Systolic and diastolic blood pressures were not significantly changed during listening to music but significant changes in their synchronization with other rhythms were observed. The randomization of local phase of songs blunted the respiratory periodicity and rate compared to their original versions. It is possible that decrease in variance in and between rhythms (i.e. increased uniformity) is one of the reasons for the known pleasurable and adjuvant therapeutic effects of music, however, this link is speculative at this time and needs further investigation.

1.2 Music and Emotion

Often it is being suggested that the major reason why people involve in musical activities is the emotional effects of it [19-21]. The power of music in inducing various emotions is the main reason that music is being used in different areas such as music therapy, sports, film and gaming industry, and marketing. There is a large number of studies have been conducted to investigate why and how music is able to induce such a strong grip on humans [22-27]. However, the science behind how music produces these effects is far behind being complete.

The potential of music to enhance physical work performance has been known for about 2,800 years. In Ancient Greece, music was played during the Olympic Games to enhance sporting performances, and it has been shown that this improvement in athletic performances by music is about 15% [3].

1.3 Music Therapy

Music therapy is increasingly being used in various disciplines, from neurological diseases to palliative care and intensive care. Relaxing music has been studied in the pre-operative, intra-operative, and postoperative settings [28]. One study compared music with diazepam in the pre-operative state showing that music was as effective as diazepam [29]. Another study showed that relaxing music decreased anxiety more effectively than midazolam before surgery [30, 31]. The difference between relaxing music and midazolam is clear. Music has no side effects. Moreover, it does not lead to any post-operative hangover after an operation. However, some types of music like techno or heavy metal are not only ineffective but also can even cause severe adverse effects, particularly in patients under intensive care medicine [32]. The types of music with the most benefits on health, especially for patients in intensive care units, are observed in classical music (Mozart, Bach, or Italian composers), and meditation music [3].

1.4 Processing of emotion by human

Scientists have shown that many different regions of the brain are involved in the processing of emotion by using MRI cameras, and these brain regions work together to process emotions and only one place is not responsible to do so. The network of brain areas that process emotions is called the emotion-processing network and includes the prefrontal cortex, the amygdala, the cingulate cortex, the hippocampus, and the basal ganglia [33]. Also, some studies by using Positron Emission Tomography (PET) scanning and functional MRI (fMRI) imaging showed that some emotions are more possible to be linked to different parts of the limbic system compared to other types of emotions. Diseases in some parts of the brain can cause changes in the processing of emotions, and they can trigger changes in emotional status which can cause in person's personality. Some studies have shown that positive emotions can have undoing effects and reduce adverse effects caused by negative emotions. They suggest that positive emotions can be useful in preventing and treating health problems caused by negative emotions [34-36].

1.5 Dissertation organization

This dissertation has four chapters. Chapter 1 provides some background information about music and emotion and their effects on human body which is relevant to the perspectives in other chapters. Chapter 2 describes the study where EEG segments synchronized to different portions of cardiac cycles and two aspects of music, tempo and cognition of songs, were used to investigate changes triggered by the external auditory stimuli and to determine which portion better showed the changes. Chapter 3 describes the study that investigated the effects of breathing pathway on processing of music-induced emotions and how they are correlated with the structural features of pieces of music which triggered the emotions. Chapter 4 contains discussion of the significant results from chapters 2 and 3, and includes study limitations and future work.

The study described in chapter 2 is based on a published paper: Mohammad Javad Mollakazemi, D. Biswal, S. Sunderam, and A. Patwardhan. "EEG segments synchronized to be temporally farthest from the R-waves in ECG are more informative during listening to music". *Biomedical Signal Processing and Control* – https://doi.org/10.1016/j.bspc.2021.102660, (2021).

The study described in chapter 3 is based on a manuscript that is ready for submission: Mohammad Javad Mollakazemi, D. Biswal, B. Place, and A. Patwardhan. "Effects of breathing pathway on processing of emotions: correlation of musical features and emotions" Ready for submission.

CHAPTER 2. CARDIAC-SYNCHRONIZED EEGS: *INVESTIGATING EFFECTS OF COGNITION AND TEMPO OF MUSIC*

2.1 Introduction

It is well known that autonomic nervous activities change in correspondence with music [37]. The two-way interaction between the brain and the cardiovascular system, i.e. one affecting the function of the other and vice versa has also been recognized for over a century and a half [38, 39].

The effect of the electrical field of the heart on surface potentials on the scalp is called heartbeat-evoked potential (HEP) which is an electrophysiological response synced with R peaks of electrocardiogram (ECG) [40, 41]. Heart cycle-related EEG averaging showed the effects of cardiac electrical field on EEG which was most prominent during QRS complex and was explained by propagation of heart electrical field throughout the body [42]. In other studies [43, 44], the presence of heartbeat-evoked responses in EEG was explained as an indicator of the cortical representation of cardiac information, and their largeness associated with interoceptive and empathy abilities [45, 46]. In another study [47], they showed an increased HEP was followed by weaker somatosensory detection and timing of stimulation relative to cardiac cycles affected the perception and showed that stimuli detection rate and sensitivity were higher when stimuli were presented during diastole. In [48], they showed the sensory sensorimotor reactions were faster during systole. In our previous study [15], we observed a significant increase in synchronization of cardiorespiratory variables (heart rate, systolic and diastolic blood pressures, and respiration) with cerebral electrical oscillations (EEG), during listening to music, regardless of its type and structure. This increased synchronization may also be an indicator of change in cardiac information in cortical activity represented in cortical electrical oscillations.

Because of the extensive heart-brain interactions by afferent and efferent pathways, neuronal oscillations are affected by these neurocardiologic pathways. Cerebral autoregulation (CA), metabolic activity, and vascular tone are coupled [49, 50] which supports the possible interaction of neuronal oscillations with heart cycles which could be different while doing a task or in the existence of an external stimulus such as music [7, 51, 52].

In this study, we used an internal body trigger (heartbeat) to investigate changes in EEGs while listening to music. The internal stimulus-locked (heartbeat) i.e. cardiac synchronous measures of EEG includes heartbeat-evoked potential (HEP) as well. The fact that music can trigger changes in cardiac function via autonomic nervous system (ANS) response by changing the sympathetic and parasympathetic nervous activity [53] suggests that heartbeat would be a good candidate as an internal trigger to find the effects of music.

In this study, we used tempo and cognition of songs as two aspects of music and used EEG portions synchronized to three different portions of cardiac cycles (pre-R-peak, post-R-peak, and mid-R-peak) to investigate changes triggered by the external auditory stimuli and to see which portion shows the changes in a better way. The reason for focusing on tempo was because among the rhythmic aspect of music, tempo, compared to other aspects of music such as pitch level, pitch range, melodic direction, harmonic complexity, being consonant, and so forth, is considered the major determinant of physiological responses due to music [18]. We used cardiac synchronized EEGs previously [54, 55], where eigenvalue decomposition of only pre-R-peak EEG portions and analysis of four largest eigenvalues showed that slow song reduced the number of eigenvalues needed to reconstruct 80% of the variance of data in all EEGs [54], and cognition of song had a large impact on Gamma bands of EEGs from right hemisphere [55]. These observations lead us to the present study which covers the entire cardiac cycles and to compare EEG responses synchronized to different portions of cardiac cycles. Briefly, in this study, we sought to answer these questions: 1. What are the effects of phases of cardiac cycles on brain electrical oscillations? 2. Which frequency bands of EEGs are affected the most by phases of cardiac cycles? 3.Which cardiac synchronized EEG portions reflect the changes of auditory stimuli in the most pronounced way? 4. What are the effects of cognition and tempo of music on the complexity of brain response while comparing strength and localization of their effects? 5. Which frequency bands are targeted by specifically tempo and cognition of music? Answers to these questions has the potential to further our understanding of how the well documented effects of music come about and also, reveal the cardiac synchronized time intervals of EEGs when stronger impact of auditory stimuli can be observed.

2.2 Methods

Data were recorded from 14 healthy subjects (7 men and 7 women) between 18 to 37 years old with a mean age of 27.43. All study procedures were approved by the Institutional Review Board at the University of Kentucky. Subjects gave written informed consent before participation in the study. All subjects had normal hearing as assessed by a short audio acuity test [16] that was administered to rule out overt hearing loss. Subjects were asked to inform us about the song of their choice that moves them the most and is their favorite to be used during the experiment. Data used in the present study were collected as a part of a previously conducted study, details of the study and results that address aspects different than the present study have been reported previously [15, 54-57].

Subjects listened to the music through a pair of circumaural headphones while sitting in a comfortable chair and were asked to set the volume level of their choosing. During the study, participants listened to the songs while keeping their eyes closed. Data used in this study were six channels of EEG, bi-laterally two of each from frontal (F3 F4), temporal (T3 T4), and parietal (P3 P4) lobes, and a single channel of ECG (lead II). The EEG electrodes were located according to the international 10–20 system. First, data was recorded for 10 minutes for control when there was no song played (silence), no headphones over ears, and eyes closed. To evaluate the effects of tempo, slow and fast tempo songs were played for subjects. To evaluate the effects of cognition of music, an unknown song and a well-known (favorite) song for the subjects were played. A phase randomized version of known and unknown songs were also played to change the degree of cognition of music by using local phase randomization (LPR). To reduce the duration of the experiment, the fast song was chosen in a way that was unknown to all subjects, so it played the role of both the unknown song and the fast song. To make sure the fast song was unknown to all subjects, we picked it from the Italian language as we knew none of our subjects were likely to be Italian, and also we asked them whether they listened to that specific song before or not. After playing LPR songs, subjects were asked whether they recognized the original version of the LPR song or not. These five songs were played in random order. There was about a two-minute pause between songs. The duration of the study, including instrumentation, was about two hours. A schematic of study trials and a flow chart of analysis of the collected data are shown in Figure 2.1.

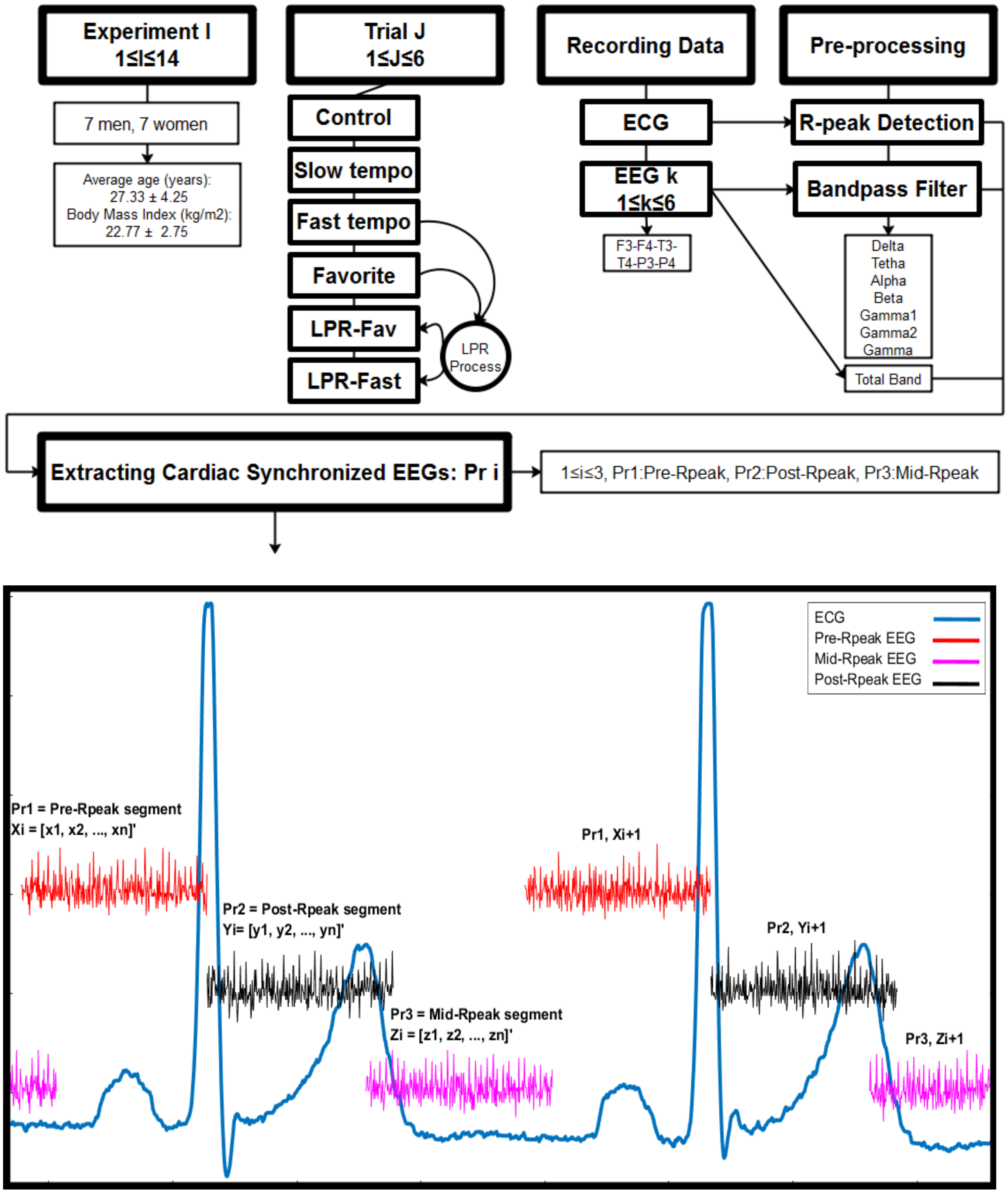
The signals, ECG (Spacelabs) and EEG (Biopack) were digitized online at a rate of 1000 samples/second using a commercial system (Windaq). A synchronization analog pulse was recorded concurrently with these signals to align the music with these physiological variables.

Bandpass Butterworth IIR filter (order 4) was used to filter EEG recordings into frequency bands: Delta (0.5-3 Hz), Theta (3-8 Hz), Alpha (8-12 Hz), Beta (12-38 Hz), Gamma1 (38-42 Hz), Gamma2 (42-100 Hz), and Gamma (38-100 Hz). The R-peaks of ECG were detected. Three segments of EEGs synchronized to three portions of cardiac cycles were extracted. Portion 1 (Pr1) was the segment ending at R-peak of ECG, portion 2 (Pr2) was the segment starting at R-peak, and portion 3 (Pr3) was the segment midway between two consecutive R-peaks. The length of each segment was 300 milliseconds (ms). The average heart rate of the subjects over all the trials was 74 beats per minute. The average heartrate and our objective of investigating the effects seen in EEG segments synchronized to three portions of the cardiac cycle gave an average duration of 0.27 seconds to each portion. Therefore, the segment length was rounded up to 0.3 (300 ms) as the segments covered all or most of the instances of RR intervals in subjects with lower heartrate while had relatively less overlap in subjects with higher heartrate and yet provided adequate segment length. Each segment of EEG was put in a column of matrix A and the mean of each column of A was subtracted from that column. Therefore, for each trial three A matrices were extracted, one for each of three cardiac portions, and the duration of data equal to 300 heartbeats was used which gave a square A matrix. In few trials for two subjects because of their lower heartrate there were few heartbeats (<10) which were repeated from the beginning of the data to complete 300 cardiac cycles. Then, normalized covariance matrices B were computed from matrices A using Eq. 1.1, where N is the number of segments, and eigenvalue decomposition of covariance matrix B was performed (Eq. 1.2). Extracted eigenvalues of each trial were normalized by the largest eigenvalue in the control trial of the same subject to remove any variation in amplitudes of EEGs recorded from different subjects because of subtle differences in electrode placement and contact while preserving inter-subject comparisons. Eigenvalues of covariance matrix show the variance of data in direction of corresponding eigenvector (principal components), and usually, principal components of EEGs can be represented by the first few largest eigenvalues which cover a significant portion of the variance of input data. Here the averages of the four largest eigenvalues (FLE) of the covariance matrix (Eq. 1.3) are considered as a measure of how data varied during listening to auditory stimuli. Also, the mean and median of absolute values and energy of each segment were extracted as features to investigate the differences of EEGs synchronized to different phases of cardiac cycles. This process was repeated for each of the EEG frequency bands. The portions and a schematic of this process are shown in Figure 2.1.

$$B = \frac{A^t A}{N - 1} \qquad \text{Eq. 1.1}$$

$$B = U \Lambda U^{-1} \qquad \text{Eq. 1.2}$$

$$FLE = \frac{1}{4} \sum_{i=1}^{4} \Lambda_i \qquad \text{Eq. 1.3}$$


Experiment I
1≤I≤14
7 men, 7 women
Average age (years):
27.33 ± 4.25
Body Mass Index (kg/m2):
22.77 ± 2.75
Trial J
1≤J≤6
Control
Slow tempo
Fast tempo
Favorite
LPR-Fav
LPR-Fast
LPR Process
Recording Data
ECG
EEG k
1≤k≤6
F3-F4-T3-T4-P3-P4
Pre-processing
R-peak Detection
Bandpass Filter
Delta
Tetha
Alpha
Beta
Gamma1
Gamma2
Gamma
Total Band
Extracting Cardiac Synchronized EEGs: Pr i
1≤i≤3, Pr1:Pre-Rpeak, Pr2:Post-Rpeak, Pr3:Mid-Rpeak
ECG
Pre-Rpeak EEG
Mid-Rpeak EEG
Post-Rpeak EEG
Pr1 = Pre-Rpeak segment
Xi = [x1, x2, ..., xn]'
Pr2 = Post-Rpeak segment
Yi= [y1, y2, ..., yn]'
Pr3 = Mid-Rpeak segment
Zi = [z1, z2, ..., zn]'
Pr1, Xi+1
Pr2, Yi+1
Pr3, Zi+1

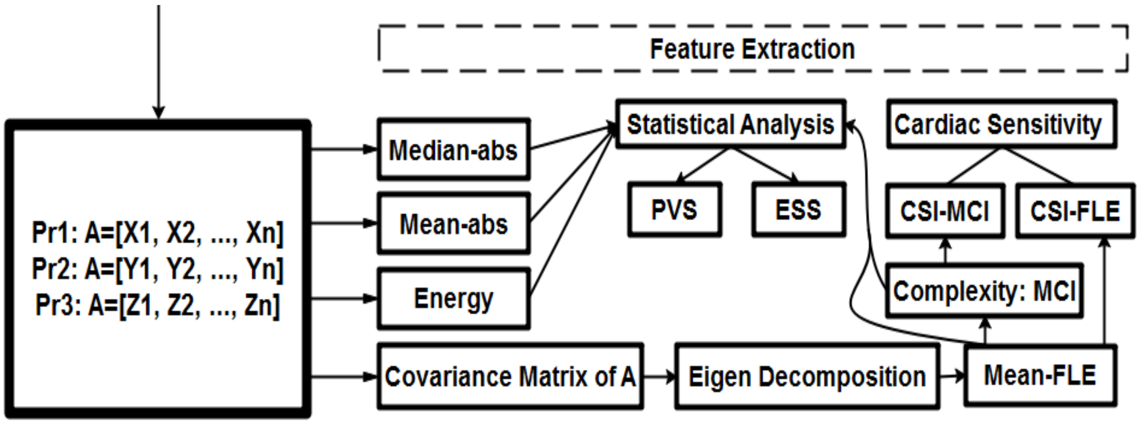


Figure 2.1 A schematic overview of the study including experiments: trials and data recorded in each experiment; analyzing data: pre-processing, extracting cardiac synchronized EEG segments, Eigen value decomposition and extracting the indices needed. The cardiac synchronized EEG signal shown is for one EEG channel and is plotted into three different heights only for demonstration purpose.

2.2.1 Mean Complexity Index

To measure the complexity of electrical response of the brain to cognition and tempo of music an index based on the distribution of variance on different eigenvectors was used. We defined the complexity index (CI) as the number of needed eigenvectors to reconstruct a certain amount of variance of the data, which in this study was 80% of the total variance. Equations 1.4 and 1.5 show the formulas used to compute CI, where S is the maximum number of eigenvalues in each dataset (=300). The mean complexity index (MCI) is the average of CIs over all subjects. If the number of eigenvectors needed to reconstruct a certain amount of variance is increased, i.e. if the variance is distributed over more eigenvectors, then this would indicate that the complexity of response is increased.

$$\sum_{i=1}^{I} \Lambda_i \geq 0.8 \sum_{i=1}^{S} \Lambda_i \,, \quad \mathrm{I} < \mathrm{S} \qquad \text{Eq. 1.4}$$

$$CI = \min(I) \qquad \text{Eq. 1.5}$$

2.2.2 Statistical Analysis

To compare the effects of cognition of music with tempo and their size of effect and significance of the changes in different locations of the brain and within different frequency bands, two scores were calculated: P-value score and effect size score.

Pvalue score (PVS): To test the statistical significance of the results, a paired t-test was used, and a difference was considered significant for p<0.05. To compare the significance of effects of songs on different frequency bands of the three cardiac synchronized portions, a score was assigned to all the frequency bands and cardiac portions. The assigned score for each comparison was according to the different ranges of the significance level of the comparison, and it was assigned through a *Pscore* function defined by Eq. 1.6. The sum of PVS of different frequency bands and cardiac portions over songs and EEGs were computed by Eq. 1.7, where K is the number of EEGs (6) and L is the number of played songs (5).

$$Pscore(p) = \begin{cases} 3, & p < 0.001 \\ 2, & 0.001 \leq p < 0.01 \\ 1, & 0.01 \leq p < 0.05 \\ 0.5, & 0.05 \leq p < 0.1 \\ 0, & p \geq 0.1 \end{cases} \qquad \text{Eq. 1.6}$$

$$PVS(frequency\ band\ i) = \sum_{z=1}^{K}\sum_{s=1}^{L} Pscore(p_{z,s}) \qquad \text{Eq. 1.7}$$

Effect size score (ESS): To measure the size of effects triggered by songs, Cohen's d effect size was computed. This measure quantifies the size of the difference between trial and control without conflating with sample size, rather than statistical significance level which can get affected by sample size. The mean of ESS for different frequency bands and cardiac portions over songs and EEGs were computed by Eq. 1.8 and were computed only for each song by Eq. 1.9.

$$ESS(frequency\ band\ i) = \frac{1}{KL}\sum_{z=1}^{K}\sum_{s=1}^{L}\frac{|M_t(z,s) - M_c(z)|}{SD_{pooled}} \qquad \text{Eq. 1.8}$$

$$ESS(frequency\ band\ i, song\ s) = \frac{1}{K}\sum_{z=1}^{K}\frac{|M_t(z) - M_c(z)|}{SD_{pooled}} \qquad \text{Eq. 1.9}$$

$$SD_{pooled} = \sqrt{\frac{SD_t^2 + SD_c^2}{2}} \qquad \text{Eq. 1.10}$$

Where M_t and SD_t are mean and standard deviation of trials and M_c and SD_c are mean and standard deviation of control, K is the number of EEGs (6) and L is the number of played songs (5).

2.2.3 Local Phase Randomization

Details of the local phase randomization (LPR) process are provided in [15], briefly: digitized songs (mono, sampled at 22050 samples/second) were transformed to the frequency domain by Fast Fourier Transform (FFT) using 3 second long segments with 50% overlapping tapered windows. In frequency domain, the phase component of each segment was randomized while the magnitude component was untouched and symmetry of all components in the frequency domain was maintained. Then, they were transformed back to the time domain. The segments were patched together to generate the LPR version of the songs.

2.2.4 Cardiac Sensitivity Index

To understand how cardiovascular activity affects brain electrical response, cardiac sensitivity index (CSI) was computed for both MCI (CSI-MCI) and FLE (CSI-FLE) parameters which were computed by Eqs. 1.11 and 1.12. These indices show how these parameters are different for segments synchronized to different portions of cardiac cycles.

$$\text{CSI\_MCI} = \frac{100}{Np} \sum_{i=1}^{Np} \sum_{j=i+1}^{Np} \frac{\left| \sum_{n=1}^{N} CI(n,i) - \sum_{n=1}^{N} CI(n,j) \right|}{\sum_{n=1}^{N} CI(n,i)} \qquad \text{Eq. 1.11}$$

$$\text{CSI\_FLE} = \frac{100}{Np} \sum_{i=1}^{Np} \sum_{j=i+1}^{Np} \frac{\left| \sum_{n=1}^{N} FLE(n,i) - \sum_{n=1}^{N} FLE(n,j) \right|}{\sum_{n=1}^{N} FLE(n,i)} \qquad \text{Eq. 1.12}$$

Where Np is the number of portions (3) and N is the number of subjects (14).

2.3 Results

In this section, the results of the complexity of brain response to tempo and cognition of music and sensitivity of this complexity to cardiac portions in different frequency bands are presented. Additionally, the power of effect of tempo and cognition of music on brain response in different frequency bands, and its sensitivity to cardiac portions are presented, and it is shown that how significant the changes were in EEG segments synchronized to three portions of cardiac cycles in different frequency bands. To avoid having a long list of results, non-significant (NS) changes are not mentioned and changes with PVS of one and larger are reported which means at least one cardiac synchronized EEG portion is significantly changed in that trial or had at least two changes with PVS of 0.5. Most of these results are also reported in our paper [58].

2.3.1 Complexity of brain electrical response

To measure complexity of brain electrical response, MCI was used. The MCIs for all trials of the total band of EEGs for the three portions of cardiac cycles for all EEGs and from frontal, temporal, and parietal lobes and from the right (RH) and left hemispheres (LH) are shown in Figure 2.2.

MCI over all EEGs for each trial and cardiac portion (Figure 2.2.A): The favorite song caused the largest MCI in each of three portions over all EEGs (average over portions=6.58, PVS=1), while MCI during Pr3 was the largest (6.9, $p<0.05$). The smallest MCI in each of three portions was induced by slow tempo song (averaged over portions=5.73, PVS=5, $p<0.023$), which were even smaller than during control (average over portions=6.23). The LPR process caused a reduction of MCI in all portions for both fast and favorite songs, while this reduction was larger for favorite song. Also, the MCI over all EEGs and trials was the largest in Pr3.

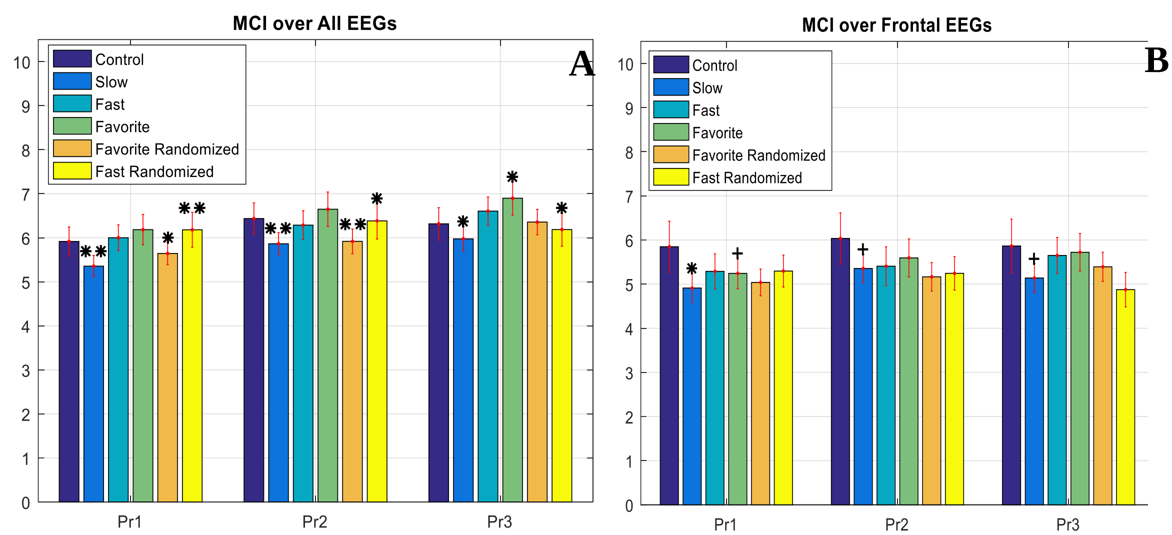
MCI over frontal, temporal, and parietal lobes for each trial and cardiac portion (Figure 2.2.B, C, D): All of the songs reduced MCIs of the frontal lobe, and except for the slow song, all of the reductions in all portions were statistically not significant (NS). Considering all three portions and all trials (silence and with music), the frontal lobe had the lowest MCI (5.40) and the temporal lobe had the largest MCI (7.60). In temporal EEGs, in all three portions, the favorite song caused the largest MCI (8.26, PVS=1) and the slow song caused the smallest MCI (6.87, PVS=2.5) which was even smaller than during control (7.46). In parietal EEGs, the fast song caused the largest MCI (5.96, PVS=1.5) and the slow song caused the smallest (5.19, NS). Temporal EEGs were the most sensitive ones to cardiac portions and Pr3 had the largest MCI during control and listening to music compared to other portions, and its difference with Pr1 and Pr2 was 14.04% and 4.15%, respectively, and the difference between Pr1 and Pr2 was 11.7%. In parietal EEGs also Pr3 had the largest MCI, but it was less sensitive to cardiac portions (changes <3.96%) than temporal EEGs. Sensitivity of frontal lobe to cardiac portions was the least (changes<3.7%). These sensitivities are represented by CSI-MCI and are shown in Table 2.2 which indicates how sensitive temporal EEGs are compared to EEGs from other lobes.

MCI over Left and right hemispheres for each trial and cardiac portion (Figure 2.2. E, F): The changes of MCI induced by songs were stronger over the right hemisphere:

- The amount of increase of MCI for favorite songs: RH (PVS=1) > LH (PVS=0)

- The amount of drop in MCI for favorite songs after LPR process: RH (PVS=1) > LH (PVS=0.5)
- The amount of drop in MCI for slow song: RH (PVS=5) > LH (PVS=0.5)

The first two observations indicate the effect of cognition and the third observation indicates the effect of the tempo of song, both were larger in RH than LH. In all trials, including during control, the MCI of RH was larger than LH, and in both hemispheres, the MCI of Pr3>Pr2>Pr1.



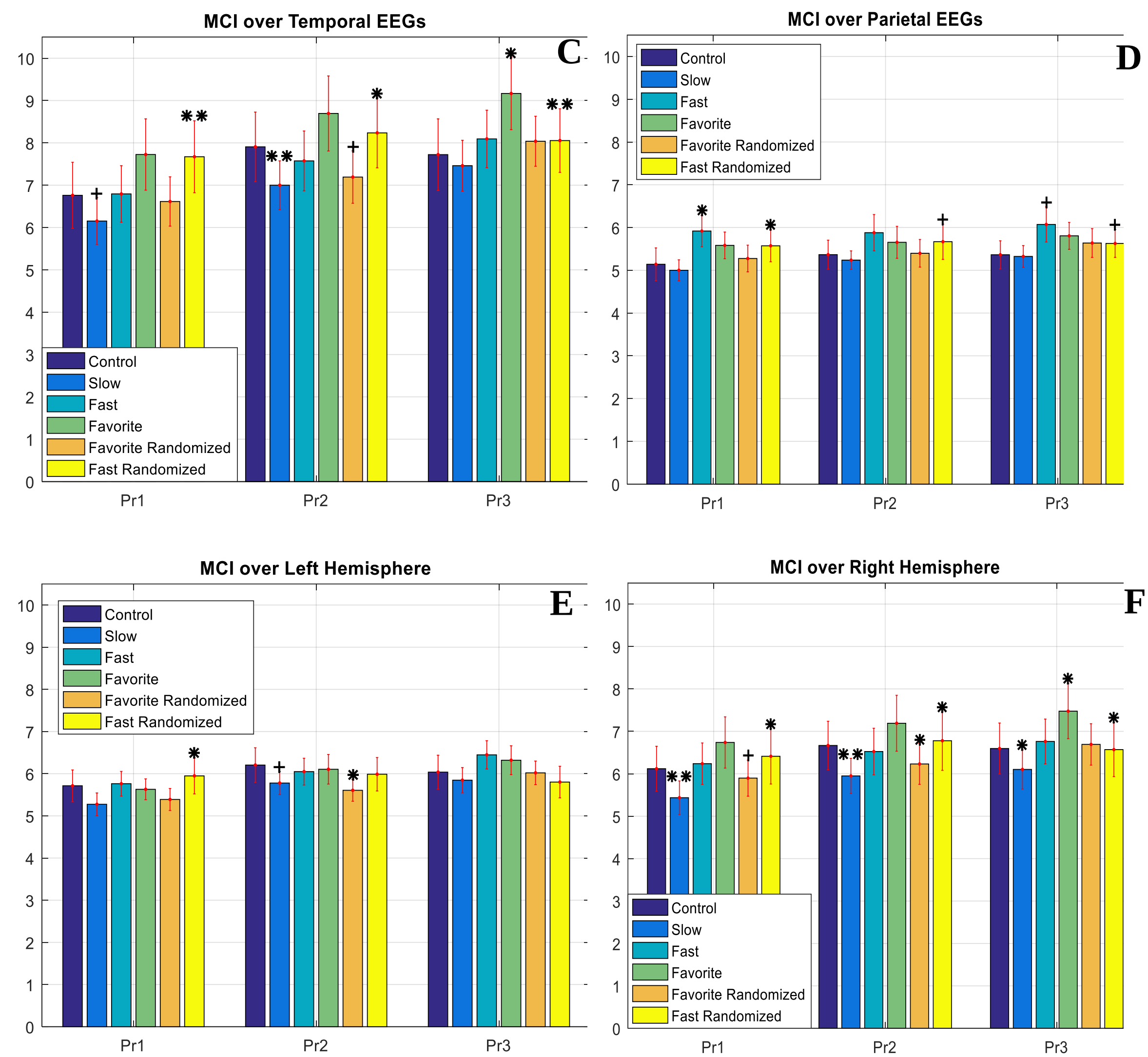


Figure 2.2 Mean complexity indices for each trial and cardiac portion over all EEGs (A), frontal EEGs (B), temporal EEGs (C), parietal EEGs (D), LH (E), and RH (F) for total frequency band of EEGs. +0.05<p<0.1, *0.01<p<0.05, **p<0.01 (relative to control)

2.3.2 Complexity of brain response in different frequency bands

Delta band: The MCI for all EEGs and portions and in all trials was one.

Theta and Alpha bands: The variation of MCI among different songs and cardiac portions was small, while parietal EEGs had the largest MCI values in all the trials, including control.

Beta band: The slow song caused a decrease in MCI over this frequency band, in all portions and EEGs, most of which were also statistically significant (Table 2.1). The fast song triggered a larger MCI than the slow song, and some of them were statistically significant (Table 2.1). Favorite song caused NS changes in MCIs in this band. Variation of MCI over cardiac portions was large both during control and listening to music in all EEGs: MCI of Pr3>Pr2>Pr1. This variation is presented by CSI-MCI shown in Table 2.2 which shows higher sensitivity of MCI of Beta band to cardiac phases than other frequency bands.

Gamma band: All the MCIs of this band, in all EEGs and during listening to all songs and during control, were much larger than the corresponding values in all other bands, including the total band. Out of 90 MCIs (6 EEGs for 5 songs and 3 portions), 83 of them reduced compared to control and 28 of these reductions were statistically significant ($p<0.05$) or close to significance level ($0.05<p<0.1$); while the 7 increases were small and NS. The fast song caused a larger reduction in MCI of all EEGs than the slow song, except in P4. The average reduction of MCI during listening to music was larger in Pr3 (7.7%) than in Pr1 (6%) and Pr2 (6.3%). Also, the average reduction in MCI of P4 over three portions was larger than other EEGs which was 14.35%, while this average in other EEGs was<7.5% (min:2.1%, mean:5.1%, max: 7.5%).

2.3.3 Cardiac sensitivity index of MCI

As shown in Table 2.2, in frequencies<38 Hz, the cardiac sensitivity indices were relatively large, and the temporal lobe had the largest sensitivity, specifically in the Beta band which had had the largest CSI-MCI in all the lobes and both RH and LH. The total band of EEG had the second-largest sensitivity index. Gamma bands had the smallest sensitivity to cardiac portions. As in the Delta band, all MCIs were one, CSI-MCI for this band was zero, so this index was not sensitive to cardiac phases in the Delta band.

Table 2.1 MCI over Beta and Gamma bands for each EEG portion and trial

EEG	Portion 1						Portion 2						Portion 3						AVG: all songs and Prs
	Control	Slow	Fast	Fav	LPR		Control	Slow	Fast	Fav	LPR		Control	Slow	Fast	Fav	LPR		
					Fav	Fast					Fav	Fast					Fav	Fast	
Beta band																			
F3	7.5	7.3	7.6	7.5	7.5	7.8	7.9	7.7	8.2	8.3	8	7.9	8.2	7.7	8.4	8.2	8	8.1	**7.9**
F4	7.5	7	7.5	7.4	7.4	7.5	8	7.7	8.1	8.1	7.8	7.9	8.5	8	8.2	8.4	8.2	8.3	**7.9**
T3	7.4	6.7	7.1	7.4	6.8	7.4	8.3	7.8	8.1	8.3	8.1	8.4	9.1	8.6	8.6	9	8.8	9.1	**8.1**
T4	7.9	7.2	7.5	7.9	7.5	8	8.5	8.3	8.6	8.8	8.5	8.9	9.2	9	9.1	9	8.7	9.5	**8.4**
P3	7	6.9	7.2	7.2	7.1	7.2	7.5	7.3	7.6	7.5	7.4	7.4	7.6	7.5	7.6	7.7	7.6	7.5	**7.4**
P4	7.6	6.8	7.2	7.4	6.9	7.1	7.7	7.3	7.6	7.6	7.5	7.5	8	7.5	7.6	7.9	7.7	7.6	**7.5**
AVG	**7.5**	**7**	**7.4**	**7.5**	**7.2**	**7.5**	**8**	**7.7**	**8**	**8.1**	**7.9**	**8**	**8.4**	**8**	**8.3**	**8.4**	**8.1**	**8.3**	**7.8**
Gamma band																			
F3	13	12.6	12.1	12.6	11.6	12.1	13.2	12.8	12	12.7	11.6	12.3	13.2	12.4	11.5	12.5	11.7	11.5	**12.3**
F4	14.9	15.2	14.3	14.6	14.2	14.9	15.4	15.1	14.6	14.9	14.1	15.2	15.4	15.2	13.9	14.4	14.2	14.5	**14.7**
T3	13.5	13.8	12.8	12.9	13.4	12.9	13.4	14.1	13.2	13.2	12.8	13.3	13.6	14.1	12.8	13.1	13.1	13	**13.3**
T4	14.4	13.8	13.2	13.1	12.7	15.5	14.5	13.8	13.4	13.2	12.6	15.5	14.5	14.1	13	13.3	12.8	15.1	**13.8**
P3	13.3	12.5	12.2	12.6	12.2	12.8	13.2	12.3	12.2	12.5	12.2	12.5	13.2	12.5	11.8	12.5	12.1	12.5	**12.5**
P4	14.4	11.2	11.9	12.6	12.3	13.6	14.2	10.6	11.9	12.7	12.1	13.8	14.2	10.7	11.6	12.6	12.2	13.4	**12.6**
AVG	**13.9**	**13.2**	**12.7**	**13.1**	**12.7**	**13.6**	**14**	**13.1**	**12.9**	**13.2**	**12.6**	**13.8**	**14**	**13.2**	**12.4**	**13.1**	**12.7**	**13.3**	**13.2**

p<0.05 | 0.05<p<0.1

Table 2.2 CSI-MCI for all EEGs, EEGs from different lobes, and two hemispheres in all EEG bands

EEG Bands Name	All EEGs	Frontal Lobe	Temporal Lobe	Parietal Lobe	Left Hemisphere	Right Hemisphere
Total Band	5.32	2.48	10.74	2.75	5.13	5.51
Theta	4.17	2.52	8.62	1.36	4.53	3.81
Alpha	3.67	2.57	6.13	2.3	3.72	3.62
Beta	8.37	6.29	14.03	4.8	8.36	8.39
Gamma1	1.29	0.77	2.25	0.85	1.5	1.08
Gamma2	0.83	1.15	0.54	0.8	0.88	0.78
Gamma	0.91	1.49	0.28	0.94	0.95	0.86

2.3.4 Power of effects

2.3.4.1 PVS

In total band, the PVS of Pr3 was larger than Pr2 and Pr1 in all four features (Table 2.3). In all four features, the changes in PVS among cardiac cycles were observed only in temporal and parietal lobes and not in the frontal lobe. Also, the band which was the most sensitive to auditory stimuli was the Alpha band as its PVS for all four features were much larger than other bands. In the higher frequency range (>38 Hz), the Mean-FLE had a much larger PVS than other features. In total, Delta, Theta, and Alpha bands, in all the four features, all the changes were NS in the frontal lobe. The significant changes by auditory stimuli in the frontal lobe started from the Beta band. In the Alpha band, the most of PVS, for all features, were from parietal EEGs which were significantly affected by almost all songs. The higher PVS of Mean-FLE of favorite song was in higher frequency bands (>38

Hz) and in lower frequency bands (<38 Hz) changes by favorite song were NS, except Alpha band of parietal EEGs, which were significantly changed by all other songs as well.

2.3.4.2 ESS

As was the case with PVS, in the total band of all four features, Pr3 had the highest ESS (Table 2.4). In all frequency bands, Mean-FLE had a higher score than the other three features, suggesting that this feature can reflect the effects of music on EEGs in a better way. Therefore, the ESS of Mean-FLE for different songs is shown in Table 2.5. In high-frequency bands of EEGs (>38 Hz), there were less variations in scores of different portions of cardiac cycles. According to p-value scores and ESS of the Mean-FLE feature, among low-frequency bands (<38 Hz), the Beta band had the largest variations of scores in different cardiac portions.

Table 2.3 Sum of PVSs over all songs and EEGs for each frequency band and cardiac portion

	P-Value Scores															
	Mean-FLE				Median-abs				Mean-abs				Energy			
EEG Band	**Pr 1**	**Pr 2**	**Pr 3**	**Sum**	**Pr 1**	**Pr 2**	**Pr 3**	**Sum**	**Pr 1**	**Pr 2**	**Pr 3**	**Sum**	**Pr 1**	**Pr 2**	**Pr 3**	**Sum**
Total Band	3.5	3	14	**20.5**	11.5	7	18.5	**37**	9.5	6.5	18.5	**34.5**	5	5.5	10.5	**21**
Delta	2	2.5	3.5	**8**	0	0	2.5	**2.5**	0	0	2.5	**2.5**	0	0	0.5	**0.5**
Theta	2	1.5	3	**6.5**	7	5.5	7.5	**20**	6.5	5	8	**19.5**	5.5	4.5	7	**17**
Alpha	21	17.5	15.5	**54**	24	24	18	**66**	21	23.5	16.5	**61**	16	16	11.5	**43.5**
Beta	3.5	5.5	6.5	**15.5**	3.5	4	3	**10.5**	1.5	4	3.5	**9**	0.5	3.5	2.5	**6.5**
Gamma1	9	7	10.5	**26.5**	4.5	4	5	**13.5**	4	4	4	**12**	2	2.5	3.5	**8**
Gamma2	17	14.5	19	**50.5**	3.5	3.5	3.5	**10.5**	3.5	3.5	3.5	**10.5**	3.5	2	2.5	**8**
Gamma	16.5	14.5	17	**48**	3.5	3.5	3.5	**10.5**	3.5	3.5	3.5	**10.5**	3	2	2	**7**

Sum	**74.5**	**66**	**89**	**229.5**	**57.5**	**51.5**	**61.5**	**170.5**	**49.5**	**50**	**60**	**159.5**	**35.5**	**36**	**40**	**111.5**

According to Table 2.5, the smallest average score was for slow tempo song and the highest score was for fast tempo song, and in all the bands, fast tempo song had a larger score than slow song. Both slow and fast tempo songs had larger ESS in the Alpha band than other songs. The favorite song caused the largest changes in Gamma bands while it caused small changes in lower frequency bands. Table 2.6 shows the CSI for each EEG band. According to Table 2.6, the total, Delta, and Beta bands had large CSIs, and the Alpha band had the smallest CSI. The high-frequency bands (>38 Hz) had smaller CSIs than in lower frequency bands and their CSIs in the frontal lobe were significantly higher than temporal and parietal lobes.

Table 2.4 Average of ESSs over all songs and EEGs for each frequency band and cardiac portion

	Effect Size Scores Mean-FLE			**Average**	**Effect Size Scores Median-abs**			**Average**	**Effect Size Scores Mean-abs**			**Average**	**Effect Size Scores Energy**			**Average**
EEG Band	**Pr 1**	**Pr 2**	**Pr 3**		**Pr 1**	**Pr 2**	**Pr 3**		**Pr 1**	**Pr 2**	**Pr 3**		**Pr 1**	**Pr 2**	**Pr 3**	
Total Band	0.18	0.15	0.23	**0.19**	0.1	0.09	0.15	**0.11**	0.1	0.09	0.14	**0.11**	0.1	0.12	0.18	**0.13**
Delta	0.28	0.3	0.26	**0.28**	0.05	0.08	0.16	**0.1**	0.05	0.08	0.15	**0.09**	0.12	0.13	0.28	**0.18**
Theta	0.2	0.17	0.17	**0.18**	0.14	0.11	0.14	**0.13**	0.14	0.11	0.15	**0.13**	0.18	0.14	0.19	**0.17**
Alpha	0.61	0.59	0.5	**0.56**	0.09	0.1	0.09	**0.09**	0.09	0.09	0.09	**0.09**	0.07	0.07	0.06	**0.07**
Beta	0.22	0.28	0.21	**0.24**	0.16	0.17	0.15	**0.16**	0.15	0.17	0.15	**0.16**	0.12	0.17	0.13	**0.14**
Gamma1	0.49	0.49	0.5	**0.49**	0.24	0.24	0.23	**0.24**	0.24	0.23	0.23	**0.23**	0.19	0.22	0.2	**0.2**
Gamma2	0.62	0.61	0.61	**0.61**	0.18	0.18	0.18	**0.18**	0.17	0.17	0.17	**0.17**	0.23	0.22	0.22	**0.22**
Gamma	0.62	0.6	0.6	**0.61**	0.18	0.18	0.18	**0.18**	0.17	0.17	0.17	**0.17**	0.22	0.22	0.22	**0.22**
Average	**0.4**	**0.4**	**0.39**	**0.4**	**0.14**	**0.14**	**0.16**	**0.15**	**0.14**	**0.14**	**0.16**	**0.14**	**0.15**	**0.16**	**0.19**	**0.17**

Table 2.5 ESSs of Mean-FLE for each song and EEG band

	Portion 1					Portion 2					Portion 3				
EEG Band	Slow	Fast	Fav	LPR		Slow	Fast	Fav	LPR		Slow	Fast	Fav	LPR	
				Fav	Fast				Fav	Fast				Fav	Fast
Total Band	0.13	0.21	0.15	0.19	0.19	0.13	0.16	0.14	0.18	0.16	0.29	0.28	0.19	0.19	0.22
Delta	0.16	0.34	0.25	0.35	0.32	0.11	0.44	0.33	0.38	0.23	0.47	0.24	0.21	0.19	0.2
Theta	0.16	0.35	0.14	0.1	0.26	0.1	0.24	0.15	0.16	0.2	0.17	0.31	0.12	0.09	0.15
Alpha	0.7	0.85	0.42	0.57	0.5	0.74	0.79	0.45	0.51	0.44	0.61	0.7	0.36	0.44	0.39
Beta	0.16	0.41	0.15	0.16	0.21	0.34	0.4	0.22	0.23	0.22	0.26	0.31	0.17	0.16	0.17
Gamma1	0.3	0.43	0.73	0.36	0.61	0.34	0.43	0.69	0.38	0.59	0.38	0.45	0.73	0.36	0.58
Gamma2	0.41	0.72	0.72	0.57	0.69	0.38	0.68	0.72	0.58	0.68	0.33	0.77	0.76	0.54	0.66
Gamma	0.43	0.7	0.74	0.55	0.68	0.39	0.64	0.74	0.56	0.67	0.34	0.74	0.78	0.51	0.65
Average	**0.31**	**0.5**	**0.41**	**0.36**	**0.43**	**0.32**	**0.47**	**0.43**	**0.37**	**0.4**	**0.35**	**0.48**	**0.42**	**0.31**	**0.38**

The possible effect of tempo and cognition

None of the auditory stimuli triggered consistent significant changes in Mean-FLE of Delta, Theta, and Beta bands. According to Table 2.8, the Alpha band of parietal EEGs changed significantly by almost all the songs. The fast and slow tempo songs triggered the largest changes in this band. Also, Table 2.6 shows that the Alpha band has the smallest CSI while Tables 2.3 to 2.5 show this band was the most sensitive band to auditory stimuli compared to the other bands.

Table 2.6 CSI for each EEG band of all EEGs, different lobes and left and right hemispheres

EEG Bands Name	All EEGs	Frontal Lobe	Temporal Lobe	Parietal Lobe	Left Hemisphere	Right Hemisphere
Total Band	72.47	55.27	81.2	80.94	47.14	97.8
Delta	48.97	47.24	24.93	74.74	47.03	50.91
Theta	29.82	12.01	64.41	13.03	14.24	45.39

Alpha	9.46	13.79	10.81	3.79	7.24	11.68
Beta	45.18	35.24	73.61	26.7	49.05	41.31
Gamma1	16.62	28.34	8.47	13.06	16.13	17.12
Gamma2	17.97	34.68	13.87	5.37	12.62	23.33
Gamma	18.9	38.32	12.12	6.27	13.78	24.03

According to Table 2.8, Pr3 of the total band had the largest average changes for all songs which were the same when other features were used as well. A comparison of average of changes and statistical scores in different features during listening to music in three cardiac portions are shown in Table 2.7. All the features showed that Pr3 had the largest average change and statistical scores. Additionally, Table 2.5 shows this sensitivity was more from the parietal and temporal lobes and less from the frontal lobe. Also, CSI for the total band for RH was much larger than LH. The same results were observed when instead of total band, band-passed filtered EEGs (both 0.5-100 Hz, or 0.5-125 Hz) were used.

In the total band, the average of changes in P3 was the largest and most of them were also statistically significant. The largest average changes for each of the songs happed in Pr3. The favorite songs did not cause any significant changes in frequencies <38 Hz and in the total band while the significant changes by the favorite songs were in frequencies >38 Hz except the Alpha band of the parietal lobe, which was affected by all other songs as well.

In frequencies >12 Hz, the average changes in the temporal lobe were larger than the frontal lobe and the average changes in parietal lobes were the smallest. According to Table 2.9, in frequencies >38 Hz (Gamma bands), the smallest changes were induced by slow tempo song, and by the increase in the tempo of song, the average changes increased significantly in Gamma bands. Also, in the same frequency ranges, the average changes from RH in temporal and parietal (T4 and P4) lobe were larger than LH (T3 and P3), and each of the individual songs triggered larger changes in RH than LH, except LPR-fast in the temporal lobe.

Table 2.7 Comparison of percent change and statistical scores of total band of EEGs in cardiac portions using four different features

Total Band	Portion 1			Portion 2			Portion 3		
	%Change	PVS	ESS	%Change	PVS	ESS	%Change	PVS	ESS
Mean-FLE	5.31	3.5	0.18	5.37	3	0.15	**8.37**	**14**	**0.23**
Mean-abs	3.51	9.5	0.1	2.91	6.5	0.09	**4.53**	**18.5**	**0.14**
Median-abs	3.7	11..5	0.1	2.96	7	0.09	**4.78**	**18.5**	**0.15**
Energy	5.8	5	0.1	5.17	5.5	0.12	**8.01**	**10.5**	**0.18**

Table 2.8 Percent change of Mean-FLE for each song and EEG synchronized to three cardiac portions for total band and Alpha band

EEG Band	EEG	Portion 1					Portion 2					Portion 3					AVG: all songs and Prs
		Slow	Fast	Fav	LPR		Slow	Fast	Fav	LPR		Slow	Fast	Fav	LPR		
					Fav	Fast				Fav	Fast				Fav	Fast	
		AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	
Total Band	**F3**	0.3	-3.1	0.1	2.6	-4.3	2.2	4.4	8.1	7.8	0.5	-2.6	-6.9	-4.4	-1	2.3	**3.4**
	F4	1.6	-2.8	9.7	4.8	4.7	0.6	3.7	10	5.6	-0.3	-2	-2.1	1.8	1.3	3.4	**3.6**
	T3	-5.2	-5.7	-5.3	4.9	-0.9	-0.7	2.7	3.9	16.4	8.1	-12.1	-5.2	-8.1	4	4.1	**5.8**
	T4	-2.9	-6.1	-1.8	-0.8	8.1	-3	-2	6.2	4.6	14.3	-17.2	-14.9	-14.4	-12	4.9	**7.6**

	P3	-4.1	-13.9	-7.7	-8.9	-9.6	-11.3	-8.7	-2.7	-4.9	-9.4	-14.1	-13.5	-10.9	-12.9	-7.5	**9.3**
	P4	-2.3	-16.1	-5.6	-9.5	-6.1	-2.7	-11.5	0.3	-4	0.5	-9.1	-17.6	-13.5	-14.2	-13.1	**8.4**
	AVG	**2.7**	**8**	**5**	**5.2**	**5.6**	**3.4**	**5.5**	**5.2**	**7.2**	**5.5**	**9.5**	**10**	**8.8**	**7.6**	**5.9**	**6.4**
Alpha	F3	-7.2	-9.7	1.1	-5	-6.1	-9.5	-10.8	0.4	-5.4	-5.1	-6.6	-11.4	1	-5.6	-3.9	**5.9**
	F4	-2.6	-7.1	4.6	1.2	-1	-4.4	-7.4	1.4	-1.1	-0.9	-2.6	-6.1	1.3	1	-0.4	**2.9**
	T3	-13.6	-15.8	-6.7	-9.9	-7.2	-14.4	-14	-7.8	-5.2	-2.6	-15.2	-11.9	-7.8	-7.8	-5.1	**9.7**
	T4	-9.7	-13.2	-5.2	-9.4	1.1	-11.1	-11.9	-7.9	-10.5	2.5	-10.1	-9.9	-6.5	-9.1	2.5	**8**
	P3	-17.7	-17.2	-14.8	-18.2	-14.9	-19.8	-15.4	-15.9	-14.7	-12.5	-17.9	-16.5	-15.8	-16.2	-12.7	**16**
	P4	-14.1	-17.8	-12.2	-16	-10.8	-13.3	-16.9	-13.6	-15.6	-12.3	-14.6	-15.2	-11.8	-13.7	-12	**14**
	AVG	**10.8**	**13.5**	**7.4**	**10**	**6.9**	**12.1**	**12.7**	**7.9**	**8.7**	**6**	**11.2**	**11.8**	**7.4**	**8.9**	**6.1**	**9.4**

0.05<p<0.1 | 0.01<p<0.0.05 | 0.001<P<0.01 | P<0.001

*AVG=average (all the averages are from absolute values of percent changes)

Table 2.9 Percent change of Mean-FLE for each song and EEG synchronized to three cardiac portions for frequencies>38 Hz

	EEG	Slow	Fast	Fav	LPR		Pr 1	Slow	Fast	Fav	LPR		Pr 2	Slow	Fast	Fav	LPR		Pr 3	
					Fav	Fast					Fav	Fast					Fav	Fast		
		AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	AVG	
Gamma1	F3	3.2	46.4	59.1	82.2	23.1	42.8	1.3	49	69.7	81.7	29.5	46.2	11.4	88.6	70.4	89	27.3	57.3	**48.8**
	F4	-19.5	11.8	48.1	10.6	22.6	22.5	-21.4	20.3	53.9	38.4	41.4	35.1	-23	17	46	24.3	41.4	30.3	**29.3**
	T3	13.4	61.3	77.8	218	79.6	90.2	9.8	56	180	162	84.2	98.5	6.2	56.6	186	196	80.1	105	**97.9**
	T4	8	73.5	159	71	146	91.7	-1.5	68.5	161	110	156	99.9	0.4	94.5	143	120	143	100	**97.3**
	P3	-5.3	23.1	40.4	50.5	4.6	24.8	-5.7	29.3	55.4	51	11.7	30.6	-9.6	26.6	52.9	55.5	6.5	30.2	**28.5**
	P4	-10.3	21	50.8	34.6	25.9	28.5	-13.7	21.4	64.5	34.7	27.3	32.3	-13.5	20.8	62.5	42.6	25.9	33.1	**31.3**
	AVG	**10**	**39.5**	**72.6**	**78**	**50.4**	**50.1**	**8.9**	**40.7**	**97.6**	**79.8**	**58.5**	**57.1**	**10.7**	**50.7**	**93.5**	**87.9**	**54.1**	**59.4**	**55.5**
Gamma2	F3	52.3	132	79.4	143	72	95.9	48.2	149	98	137	80.7	102	58.9	195	95.9	126	111	117	**105**
	F4	-18.2	39.6	45.7	18.8	125	49.6	-5.3	64.1	107	96	127	80.1	-12.4	103	106	59.9	182	92.7	**74.2**
	T3	7.2	72.1	43.4	78.7	166	73.5	7	66.2	47.7	85.9	139	69.3	4.1	89.2	60.8	71.6	191	83.3	**75.4**
	T4	15.2	108	296	177	117	142	17.7	137	328	267	121	174	9.6	164	313	219	145	170	**162**
	P3	30.6	76.9	53.3	61.4	32	50.8	37.8	67.9	54.4	63.1	32	51.1	20.6	80.7	46.5	44.6	23.9	43.3	**48.4**
	P4	71.6	243	107	82.9	74.5	116	85.1	220	110	97.8	62.5	115	69.1	253	111	73.8	67.7	115	**115**
	AVG	**32.5**	**112**	**104**	**93.8**	**97.9**	**88.1**	**33.5**	**117**	**124**	**124**	**94.1**	**98.8**	**29.1**	**147**	**122**	**99.2**	**120**	**104**	**96.9**
Gamma	F3	51.5	130	84.5	150	68.2	96.9	45.7	150	100	142	79	103	63.2	206	105	131	117	124	**108**
	F4	-20	30.4	45.9	13.4	119	45.8	-11.5	59	108	96.7	124	79.9	-17.6	89.5	102	53.3	174	87.3	**71**
	T3	6.6	68.2	46.8	86	161	73.9	3.8	62	61.4	90.4	134	70.4	1.2	84.3	68.6	74.8	184	82.6	**75.6**
	T4	17.4	105	287	158	121	138	16.5	123	314	248	124	165	10.2	151	300	196	151	162	**155**

	P3	29.8	69.9	54.3	62.7	31.2	49.6	34.7	64.7	58.3	69.9	33	52.1	19.5	75.2	50.6	47.7	23.3	43.3	**48.3**
	P4	64	227	99.5	77.5	73.3	108	74.4	209	102	98.2	59.2	108	59.1	238	103	71.2	64.6	107	**108**
	AVG	**31.6**	**105**	**103**	**91.3**	**96**	**85.5**	**31.1**	**111**	**124**	**124**	**92.3**	**96.7**	**28.5**	**141**	**121**	**95.8**	**119**	**101**	**94.4**

0.05<p<0.1 | 0.01<p<0.0.05 | 0.001<P<0.01 | P<0.001

*AVG=average (all the averages are from absolute values of percent changes)

2.4 Discussion

Our results show that Pr3 of cardiac-synchronized EEGs has the highest potential to capture the changes in EEGs triggered by auditory stimuli. Further, results suggest an increase in complexity of EEG response during increased tempo of the music (specifically in the parietal lobe) and during increased cognition of music (specifically in the temporal lobe). The slow tempo song caused the lowest complexity in EEG response, even less than that during control, and triggered the smallest effect size in EEGs as well, suggesting a possible reason for why slow songs are perceived to have calming effects. Two different cardiac sensitivity indices consistently showed that in the total band and in frequency bands <38 Hz (especially in the Beta band), EEG responses were much more sensitive to the three phases of cardiac cycles than frequency ranges of >38 Hz. Based on our results, the cognition of music was observed to have stronger changes in frequencies >38 Hz, and lower frequency EEG responses (<38 Hz) were stronger during slower tempo music. The Alpha band was the most sensitive band to auditory stimuli (especially in the parietal lobe) and in both the Alpha and Beta bands, the effects of the tempo of music were stronger than cognition of music.

In the text below, first, we discuss the use of cardiac synchronized EEGs and the sensitivity of different EEGs in different frequency bands to the three phases of cardiac cycles. Then, the findings of two components of tempo and cognition of music in brain electrical responses in different frequency bands are presented and compared, and finally, the consistently observed changes during all audio stimuli, regardless of their type, structure or familiarity are discussed.

2.4.1 Cardiac synchronized EEGs

According to statistical scores and average percent changes (Tables 2.1-2.4, 2.7), for all four features used in the total band, Pr3 had the highest statistical scores and percent changes. Also, when EEGs were band-passed filtered between 0.5-100 Hz, or between 0.5-125 Hz, or when the mean of five largest eigenvalues was used instead of using FLE, Pr3 still had the highest scores and mean percent changes for all four features. This shows that Pr3 of cardiac-synchronized EEGs has the highest potential to reflect the changes triggered in the EEG by auditory stimuli. This higher potential of Pr3 in showing these changes is highly possible to be rooted in being the farthest portion from the peak of cardiac electrical activity (R-peak). In all the three lobes, Pr1 had the smallest MCI. In temporal and parietal lobes, Pr3 had the largest average MCI over all EEGs. This difference was seen in both LH and RH as well where MCI of Pr3>Pr2>Pr1. This observation is consistent with the higher PVS, ESS, and percent change of four used features during Pr3 than their corresponding values in the other two portions. The Pr3 contains data from the farthest time instants between two consecutive heartbeats, while it is tempting to attribute these observations to settling of perfusion surge caused by cardiac systole since Pr1 did not have higher scores it is not clear why Pr3 seems to be most informative.

2.4.2 Cardiac sensitivity of brain electrical response

According to cardiac sensitivity of MCI, among frequency bands in all of the EEGs, Beta band, and among the lobes, in frequencies<38 Hz, these indexes from the temporal lobe were the most sensitive ones to cardiac portions, both during silence and listening to music. This shows the differences in observed complexity of brain electrical response during different cardiac cycles were more pronounced in frequencies <38 Hz, specifically over temporal EEGs and over the Beta band in all EEGs, while the sensitivity indices in frequencies >38 Hz in all of the EEGs were small, which shows less sensitivity of brain electrical activity in higher frequency bands to phases of cardiac activity. This difference in sensitivity of low-frequency bands (<38 Hz) compared to high-frequency bands (>38 Hz) to phases of cardiac cycles is possibly rooted in the concentration of major components of heart electrical activity in less than 40 Hz range [59, 60]. This observation was also confirmed by the cardiac sensitivity of FLE. According to cardiac sensitivity of FLE, the frequency bands which include components with frequency range of cardiac electrical activity had larger cardiac sensitivity indices. Delta, Theta, Beta, and total bands had large sensitivity to cardiac portions. CSI of both MCI and FLE confirms low sensitivity of frequencies >38 Hz to cardiac portions.

2.4.3 Effects of Cognition of music

The subjects' favorite song increased the average complexity of brain electrical response over all EEGs and caused the most complex brain response compared to other songs. However, this increase was more significant in the temporal lobe. The favorite song was chosen by each subject and it was a song that they liked the most and had listened to many times before the experiment, so memory and cognitive response of the brain were both expected, which makes this higher brain complexity predictable. Listening to the LPR version of the favorite song triggered a smaller MCI than listening to its original version. This drop of MCI for favorite-LPR was larger in RH than LH. It is, therefore, possible that the increased complexity of brain response seen during the favorite song was rooted more in the structure of the song such as specific harmonies of sounds. After the LPR process, by which those specific harmonies of sounds of the favorite songs were perturbed, a less complex response resulted, even though all the subjects knew they were listening to their favorite song, specifically in T4. As shown in Figure 3, the LPR process caused different effects in the MCI of an unknown song (fast song) and a very well-known song (favorite song) in T4. During LPR-favorite, the MCI decreased significantly in T4 (not in other locations) while during LPR-fast song, MCI increased in T4. This significant difference in change of MCI after LPR process on a very familiar song and on an unknown song shows the importance of cognition of music in evoking a more complex brain response in T4, as all the subjects recognized the original version of LPR-favorite song, which was their favorite song, but they did not recognize the original version of LPR-fast, which was the fast song. The fast tempo song was chosen in a way that was unknown for all of the subjects and was played before LPR-fast and all subjects were listening to it for their first time. The effect of the LPR process on the Gamma band was also the same as was observed in Figure 2.3 for the total band. The LPR process on the favorite song triggered a reduction in MCI, compared to the favorite song, while the LPR process on the unknown song (fast song) caused an increase in MCI, compared to the fast song. This suggests that electrical brain oscillations which reflect this music cognitive processes of the brain contain higher frequency components which are within the Gamma band. This observation was also supported by ESS and percent change of Mean-FLE of Gamma band.

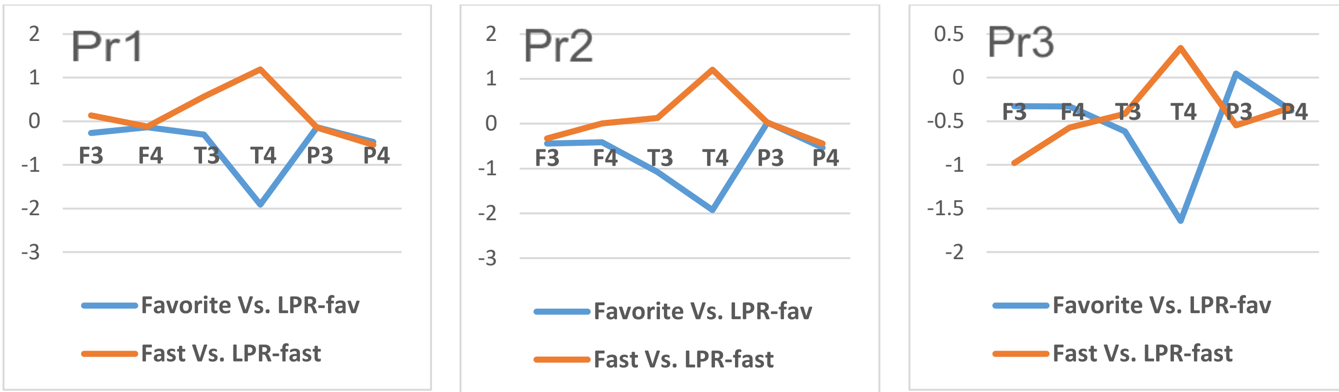


Figure 2.3 Effect of LPR process on EEGs of different cardiac portions: Difference of MCI between LPR songs and their original versions

As done previously [15], here, "cognition" is referred to the effects of music not directly from structural features of music, i.e. sensory effects, but those that may occur from other factors such as memory recall and its associated effects. The difference of ESS of fast and LPR-fast songs in frequencies >42 Hz was 0.046 (average over three portions) while this number for favorite and LPR-favorite was 0.17. The differences in responses between favorite song and its LPR version suggest that structure of music such as specific harmony of sounds, may have a determinative role in producing larger effects, and when it was the distorted size of effects was smaller, even though subjects knew which song they were listening to. The difference between LPR-fast and fast songs was small, possibly because the subjects were listening to the fast song for the first time, and their level of cognition towards the song and its composite structure was less than that of the favorite song, so the size of change during LPR-fast song was not very different than of fast song.

2.4.4 Effects of Tempo

The increase of tempo of song caused an increase in average complexity of brain electrical response in all EEGs in the total band. In the parietal lobe, the fast and slow tempo songs had the largest and the smallest MCI, respectively which shows how this lobe responds to the tempo of song.

Slow tempo song triggered the smallest MCI in all three portions over all EEGs, which was even smaller than during control. Also, the slow tempo song had the smallest ESS in Delta, Gamma1, Gamma2, Gamma and total bands and lowest average ESS over all frequency bands compared to all other songs in all three portions. On the other hand, the fast song caused the largest average ESS over all frequency bands and in all three portions, and it had a larger ESS than the slow song in each of the individual frequency bands. These results indicate that brain response to slow songs is less complex and the triggered changes were smaller compared to fast or favorite songs, possibly one of the reasons for the calming effect of slow songs which are used during music therapy [28, 30]. On the other hand, as subjects' favorite song and fast song caused the largest MCI and the largest average effect size score, therefore, these may not be good candidates to be used for inducing calming effect or music therapy, to avoid triggering cognition and memory-based responses and arousal effects. Besides, according to changes in Mean-FLE, slow tempo song induced the smallest changes in frequencies >38 Hz, which indicates the less ability of slow tempo song in triggering changes in higher frequency bands of EEGs.

2.4.5 Cognition versus tempo

In the temporal lobe, the favorite song caused the largest MCI, and the drop of MCI by LPR-favorite was much larger than the amount of drop in the parietal lobe in which the fast and slow tempo songs had the largest and smallest MCI, respectively. These observations indicate that in the temporal lobe effects of cognition of song were larger than tempo, and in the parietal lobe effects of tempo were larger than cognition.

In brain EEG frequency response <38 Hz, the sum of PVSs of Mean-FLE for slow, fast, and favorite songs was 9.67, 8.83, and 2.67, respectively; while the sum of this score for frequency response >38 Hz were 4.83, 10.67, and 15.33, respectively. This shows higher frequency brain electrical response (>38 Hz) to cognition of songs and lower frequency brain electrical response to the slower tempo of the music.

In the Beta band, slow song triggered significant reductions in MCI of all EEGs and cardiac portions and fast tempo song caused larger MCI while all the MCIs for the favorite songs were NS. These observations suggest a strong effect of tempo and a weak effect of cognition of song in the Beta band. This stronger effect of tempo than cognition of song on the Beta band was also supported by larger ESSs of slow and fast songs compared to favorite and LPR-favorite songs (Table 2.5).

In the Alpha band, the average percent changes of Mean-FLE for slow and fast tempo songs were larger than all other songs which indicates the Alpha band can get affected by the tempo of song in a significant way. This was also supported by larger ESS of slow and fast tempo songs in this band than other songs. In [18] it was shown that rhythmic aspects of music, including tempo, are the major determinants of physiological measures to music than other aspects. However, in [18] EEGs were not measured. In the present study, our result shows the effects of the tempo of music on the Alpha and Beta bands of EEGs were also larger than cognition of song, consistent with their observations.

2.4.6 Brain electrical response to auditory stimuli

The larger changes in RH in temporal and parietal lobes in frequencies>38 Hz for each individual song could possibly be explained by the larger involvement of RH for the processing of music [61]. In terms of the complexity of the response, both cognition and tempo caused a more complex response in RH than LH, which again underlines the responsibility of RH in processing music [61].

The complexity of response of temporal EEGs, both during silence and music, was larger than other lobes, and the changes triggered by songs were more significant in the temporal lobe than others. These results indicate that the EEGs from the temporal lobe carry more information about responses to music.

The larger MCI from the Gamma band showed that this band carried more information than other bands both during control and listening to music, even more than the total band. Also, the MCI of the Gamma band of P4 was significantly affected almost by all the songs and its average changes was larger than the average changes of all other EEGs which suggests the Gamma band of P4 can be a good candidate to evaluate the effects of auditory stimuli.

Comparing the four features investigated in this study, Mean-FLE had the largest sum of PVS and the largest average ESS in each of frequency bands, especially in Alpha and all Gamma bands. This shows that this feature has a higher potential in reflecting the changes triggered by auditory stimuli in different frequency bands of EEGs than other features, especially in higher frequency ranges (>38 Hz).

According to statistical scores (Tables 2.3 to 2.5), the Alpha band was the most sensitive band to auditory stimuli since its PVS for all the used features and its ESS of Mean-FLE were significantly larger than other bands. Disregarding of tempo, cognition, and phase sequence of songs, the Alpha band of parietal EEGs were significantly affected by almost all the songs, and their PVS for each of the four used features was the largest compared to other EEGs. Despite the higher sensitivity of the Alpha band to auditory stimuli, according to Tables 2 and 6, this band has less sensitivity to phases of the cardiac cycle than other bands. Delta, Theta, and Beta bands were not affected significantly by any of the auditory stimuli in any of the EEGs.

CHAPTER 3. EFFECTS OF BREATHING PATHWAY ON THE PROCESSING OF EMOTIONS AND CORRELATION OF MUSICAL FEATURES AND EMOTIONS

3.1 Introduction

The autonomic breathing drive, which is created by conditional bursting pacemaker neurons of the brainstem [62, 63] does not have a fixed pace and some emotional and cognitive states such as anxiety [64], exploratory behavior [65-67] and stress [68] can all adjust the rhythm and depth of respiration. Thereby, the final respiratory output is affected by a complex network between the brainstem and higher cortical structures including the limbic system which is responsible to process emotions. The connection between emotional states and respiration is investigated in some studies; it is reported that focused breathing causes positive responses to neutral picture slides while unfocused breathing causes significantly more negative responses to the same slides [69]. Also, this relation between emotion and respiration was used for automatic emotion recognition with deep learning [70]. In another study [71], by using both EEG-based features and respiratory-based features, meditation state was detected more accurately rather than using EEG-only or respiration-only features vector.

Breathing patterns can be impacted by changes in emotions such as happiness, fear, anxiety, or sadness [72]. The alternative hypothesis, that the respiratory attributes, such as the breathing pathway, can impact the processing of emotion is not recognized. It is shown that human cognitive response is more accurate and faster when respiration was performed by nose than by mouth [73]. This shows the respiratory-pathway-related oscillations are present in areas responsible for cognition such as limbic regions which is also supported by their results. They reported respirational entrainment of brain local field potential changes in the limbic region in patients with medically intractable epilepsy using intracranial EEG (iEEG) data and showed that normal breathing synchronizes oscillations in the human olfactory cortex and limbic-related brain areas such as amygdala and hippocampus. They also showed these oscillations are more significant during nasal breathing than oral breathing. Some of these results are also supported by animal studies. In rats and small animals, the low-frequency oscillations in the brain are reported at the rate of breathing (~2–12 Hz) even in absence of odor stimuli [74-77]. These dynamic fluctuations are thought to induce cortical excitability and trigger network interactions within the brain.

The remained key questions are whether the respiratory pathway affects other performances of the limbic region than cognition such as processing emotion and whether the respiratory pathway affects the breathing synchronized oscillations in EEGs of healthy humans in normal and emotional states. Emotions play a central role in physical health such as negative emotions contribute to coronary heart disease [78], Alzheimer's [79], and premature mortality [80]. Providing preventing role in emotion-related diseases by controlling emotions in a more effective way and bringing the emotional state into the region of positive emotional states to people which is aimed to do so always has been of great importance.

The primary aim of this study was to see whether the respiratory pathway affects feeling different music-induced emotions or not, and if yes, how big its effects are and how they are correlated with the structural features of pieces of music which triggered the emotions. The other aim of this study was to know whether the effects of the respiratory pathway contribute to any differences in some physiological variables and to see whether they are reflected in surface EEGs recorded from scalps of healthy humans during rest with no external stimuli and in presence of emotions. To meet this end, two trials of purely nasal and purely oral breathing were compared during rest and for various emotions, which were triggered by different pieces of music.

3.2 Materials and Methods

3.2.1 Participants

There were 12 subjects (6 males) who participated in this study. The study was approved by the Institutional Review Board (IRB) at the University of Kentucky. All subjects gave written informed consent before participating in the study. The exclusion criteria were having any of these conditions: under 18 years or over 35 years of age, having a history of regular loud snoring, nasal obstruction, sleep complaints, pregnancy, high blood pressure, having a history of epilepsy or seizures.

3.2.2 Data Collection

During each experiment, these data were recorded: 8 channels of EEG (Fp1, Fp2, F3, F4, P3, P4, T3 and T4, OpenBCI), ECG (Lead II, Biopac), and respiration using thoracic and abdominal inductance bands (Inductotrace). The EEGs were digitized using OpenBCI software at a sampling rate of 125 samples/second, and the rest of the data (ECG and respiratory data) were digitized at a rate of 1000 samples/second using a commercial data acquisition system (Dataq).

3.2.3 Study Procedure

After providing written consent, subjects were asked to provide their demographic details and then were instructed to sit on a comfortable chair. To rule out subjects with overt hearing loss a short online hearing acuity test [70] was administered at the beginning of each experiment. After this test, subjects were instrumented to start the measurements. All the trials were repeated two times: one for pure oral breathing (OB) and one for pure nasal breathing (NB). A nose clip was used to block the nasal cavity and to guarantee oral breathing and a mouth strip of the type, that is used to prevent snoring, was used to guarantee nasal breathing. Subjects were asked to let experimenters know if felt any sort of discomfort while using the nose clip or the mouth strip to stop the study.

After starting recording data, the first part of the experiment was control, when there was no music presented (silence). One five-minute control was recorded with NB and one with OB. The second part was listening to three two-minute songs (one happy, one peaceful, and one sad song [81]) one time with OB, and one time with NB. We used the same 30-second songs as used in [82] and with their musical features evaluated by expert musicians as reported in [18]. Between each song, there was a two-minute pause. The third part was listening to twelve 30-second songs one time with OB and one time with NB. Between each song, there was a 30-second pause. In each part, the sequence of songs and whether NB or OB happens first were different in each experiment. The only order, which was constant in all the experiments, was that in part two the peaceful song was always played as the second song so the subject experience a more moderate state before transitioning from the sad to the happy song or vice versa. The name of the songs used in this study is listed in Table 3.1.

3.2.4 Evaluation of Emotions

There are few models to evaluate human emotion, the two of which are commonly used in various studies are discreet and dimensional models [83]. The discreet model asserts that all emotions can be extracted from a set of basic emotions and subjects rate each emotion separately [84, 85]. In the dimensional model, emotion is presented based on two core dimensions in affective space which are valence and arousal [86]. In this study, we used the dimensional model. Subjects were asked to state how they perceived emotions from each piece of music after listening to it by using a 10-point Likert-type scale anchored by 0 (*not at all*) and 9 (*very much so*) for 9 different emotions for different quadrants in Thayer's model for the emotional plane [87] (Quadrant 1: happy, excited; Quadrant 2: fear, angry, frustrated; Quadrant 3: bored, sad; Quadrant 4: relaxed, sleepy). For the two representing the main axis of the model (arousal, valence) subjects were asked to rate based on how they felt those from listening to the songs.

3.2.5 Data Analysis

The peaks of the R waves from the ECGs were detected by the adaptive threshold method [88] from which heartrate and RR intervals were computed. All the detections were visually verified by investigators. The beat-by-beat RR interval values were assumed to stay constant during each beat to extract piece-wise RR time series. The thoracic and abdominal inductotrace respiratory signals were added to generate the respiratory signal. The envelopes of the EEGs were extracted by *envelope* function in *MATLAB.* The respiratory signal, RR time series, and EEG envelopes were low-pass filtered at a cutoff frequency of 5 Hz, and then, down-sampled to a rate of 10 samples/second. These down-sampled data were employed for further analyses. Welch's method was used to compute auto, $S_{xx}(f)$, and cross spectra, $S_{xy}(f)$, with ten-second segments of Hanning window with 50 % overlap. The ratio of the squared cross-spectrum divided by the two auto spectra was computed to extract mean squared coherence (MSC) between two signals shown in Eq.3.1. Frequency width (Fw) of the respiratory signal was calculated based on the amount of deviation from respiratory rate (r_m) that presents most of the power (here we considered 70%) of respiratory auto spectra in 0-0.5 range which is shown in Eq. 3.2.

$$MSC = \frac{|S_{xy}(f)|^2}{S_{xx}(f)S_{yy}(f)} \qquad \text{Eq. 3.1}$$

$$F_w = \min(d), \quad d = \sum_{r_m-d}^{r_m+d} S_{xx}(f) > 0.7*\sum_{0}^{0.5} S_{xx}(f) \qquad \text{Eq. 3.2}$$

Table 3.1 List of Musical Selection

Musical Selection	**Composer**	**Composition**	**Duration**
1 (Happy song)	J. Strauss	Unter Donner und Blitz, Op. 324	2 minutes
2 (Peaceful song)	G. Bizet	Carmen Suite No. 1 - Intermezzo	2 minutes
3 (Sad song)	Chopin	FUNERAL MARCH, Op. 72 No. 2	2 minutes
4	Offenbach	Rosenthal, Cancan	30 seconds
5	A. Ponchielli	La Gioconda - Dance of the Hours	30 seconds
6	E. Serra	Le Grand Bleu - Spaghetti del mare	30 seconds
7	G. Holst	The Planets, Venus	30 seconds
8	R. Strauss	Also sprach Zarathustra - Von den Freuden und Leidenschaften	30 seconds
9	A. Dvorak	Symphony No. 9 - Largo	30 seconds
10	E. Elgar	Enigma Variations - Romanza	30 seconds
11	Gandalf	From Source to Sea - Refuge Island	30 seconds
12	Manowar	Hail to England - Black Arrows	30 seconds
13	D. Borgir	Puritanical Euphoric Misanthropia - Fear and Wonder	30 seconds
14	G. Mahler	Symphony Nro. 5 - Adagietto	30 seconds
15	M. Ravel	Piano Concerto in G major - Adagio Assai	30 seconds

A paired t-test was used to measure statistical significance, and a difference was considered significant for $p<0.05$. To find the relation between emotion rates and musical features, the *corrcoef* function in *MATLAB* was used. The structural musical features of the songs were used from [18] which are melodic direction, pitch range, rhythm, tempo, accentuation, rhythmic articulation, pitch level, harmonic complexity, and consonance.

3.3 Results

3.3.1 Emotion rates and breathing pathway

The average rates for valence, arousal level, and different emotions during OB and NB for all the songs are listed in Table 3.2. The emotions which were felt differently during NB than OB in a statistically significant way or close to significance level are shown in Figure 1. Totally, the average of rates during NB was larger than OB (p=0.059).

The most significant difference in emotion rates during NB than OB was the average relaxed rates and subjects found songs more relaxing during NB than OB (p=0.00013). In 14 out of 15 songs, the average relaxed rates was higher in NB than OB 10 of which were also statistically significant (p<0.05) or close to significance level (0.05<p<0.1).

During NB and listening to songs, subjects felt more aroused than during OB (p=0.036). Also, during NB and listening to songs, subjects found the songs happier (p= 0.069), more exciting (p=0.063), and less boring (p=0.082) than during OB.

Table 3.2 Average rates for valence, arousal, and different emotions during NB and OB for different songs

Emotion	Breathing Pathway	Musical Selection														
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Valence	**Oral**	6.1	7.1	5.8	5.8	5.7	5.9	5.3	4.5	6	6	5.9	1.2	5.3	6.5	5.1
	± std	1.7	1.7	1.4	1.9	1.8	2.5	1.9	1.7	1.7	1.9	2.2	1.7	2.2	1.9	1.7

	Nasal	6.2	7.1	5.3	5.5	5.8	5.7	6	4.8	6.4	6.3	6.3	1.3	6.1	5.8	6.3
	± std	1.7	1.4	1.9	2.1	1.7	2.6	1.8	1.5	2.2	1.5	2	1.7	1.7	1.8	1.6
Arousal	**Oral**	5.8	3.7	3.3	6.6	5.8	5.3	3.6	4.7	2.9	3.2	3.7	3.8	4.5	2.9	2.6
	± std	1.5	2.1	2.7	2.1	2.2	2.6	2.7	2.4	2.1	1.7	1.6	2.6	2.9	1.9	2.4
	Nasal	6.5	3.6	3.6	6.4	6.2	5.3	3.3	5.3	2.7	3.3	4.1	4.1	5.2	2.8	2.5
	± std	1.8	2.3	2.8	2	1.7	2.7	2.2	2.4	1.9	2.1	2.4	2.6	2.6	2.4	2.9
Happy	**Oral**	5.8	5	1.7	5.8	5.6	6	2.8	1.7	3.1	4.1	3.7	1	1.2	3	1.1
	± std	1.9	2.4	2.1	2.1	2.2	2.6	2.5	1.9	2.8	1.8	2	1.5	1.3	2.5	1.5
	Nasal	6.3	4.5	2	6.2	5.9	6.5	3.2	2	3.4	4	3.7	0.8	1.5	2.2	1.8
	± std	1.9	2.7	1.6	1.7	1.9	1.8	2.3	2	3	2.9	1.7	1.6	2.4	1.5	2.3
Relaxed	**Oral**	2.3	6.2	3.8	1.1	1.8	3.3	3.3	0.7	5.5	4.8	3.7	0	1	5.8	4.8
	± std	2.1	2.8	2.9	1.6	2.1	2.6	2.6	1.4	2.6	2.2	2.3	0	1.3	2.3	2
	Nasal	4.1	7.3	3.9	1.7	2.3	4	4.9	1	6.2	6	5.1	0.3	2.1	5.2	6.2
	± std	2.6	1.8	2.4	2	2.3	2.4	2.4	2.3	2.7	2.3	2.2	0.6	2.8	2.5	2.5
Sleepy	**Oral**	0.8	4.1	3.3	0.6	1	1.4	2.9	1	4	3.4	1.8	0.8	1.7	3.3	4
	± std	1.9	2.9	2.9	1.5	1.8	1.9	2	1.8	3.1	2.6	2.2	1.9	2.3	2.4	2.8
	Nasal	1.4	3.3	3.2	0.3	0.8	1.5	4	1.5	4	2.8	2.6	0.4	1	3.3	4.3
	± std	2.1	3.2	3	0.7	1.8	2.4	2.2	2.2	3.3	2.9	2.7	1.2	1.9	3.2	3.5
Bored	**Oral**	0.9	1.8	2.1	0.8	0.9	0.8	2.1	0.8	2.3	2.5	1.6	1.8	0.8	1.4	2.8
	± std	1.5	2.4	2.4	1.6	1.5	1.4	2.7	1.4	2.4	2.3	2	2.1	1.4	1.8	2.9
	Nasal	0.8	1.4	2	0.8	0.8	1.8	2.2	0.8	1.3	1.7	1	1.3	0.8	1.8	2.1
	± std	1.1	2	2.9	1.4	1.4	2.8	1.5	1.8	1.7	2.2	1.9	2.3	1	2.2	1.8
Sad	**Oral**	0.3	2.1	5.7	0.3	0.9	0.1	2.7	1.6	2.9	1.8	1.5	1.3	3.4	3.3	4.3
	± std	0.9	2.4	2.1	0.7	1.6	0.3	2.4	1.6	2.8	1.8	2.2	1.8	2.5	2.6	2.5
	Nasal	0.8	1.5	4.6	0.4	0.5	0.3	2.9	3.3	3.5	1.8	1.6	1.8	2.3	3.8	4.8
	± std	0.9	2.4	2.8	0.7	1	0.5	2.5	2.7	2.5	1.9	1.6	2.1	1.7	3	3
Frustrated	**Oral**	1.5	1.4	2.7	1.9	1.2	0.7	2	1.8	0.9	1	1.3	4.2	3.1	0.5	2.1
	± std	1.7	2.5	2.9	2.1	1.8	1.2	2.2	2.8	1.6	1.5	2.3	3.4	2.5	1.2	2.6
	Nasal	0.9	0.7	2.4	1.6	1	0.5	1.8	3.2	0.6	1.3	1.3	5.6	1.6	1.8	1.2
	± std	1.2	1.2	3.1	2.5	1.6	1.2	2	3	1.1	2.2	1.9	3.3	2.8	2.4	1.6
	Oral	5.4	1.4	0.8	6.4	5.3	3.5	1.5	3.4	1.8	1.8	2.9	3.9	2.8	1	0.3

Excited	± std	2.4	1.2	1.1	2.2	2.2	2.6	1.9	2.6	2.1	1.8	2.3	3.1	2.2	1	0.7
	Nasal	5.7	2.5	1.3	6.2	5.3	4.8	1.8	3.8	1	1.9	2.6	4.1	3.1	0.9	0.4
	± std	2.6	1.7	1.7	2.4	2.1	2.7	2	2.8	1.3	2.6	2.2	3	2.1	1.2	0.9
Angry	Oral	1.2	0.1	1.1	1.2	0.3	0.2	0.3	3	0.2	0.7	0.3	6	2.7	0.3	0.3
	± std	1.9	0.3	1.6	1.9	0.6	0.6	0.9	2.9	0.4	1.2	0.9	2.9	2.8	0.6	0.9
	Nasal	0.6	0.1	1.3	1.3	0.8	0.3	0.8	2.3	0.2	0.5	0.4	5.3	1.6	0.5	0.4
	± std	1.4	0.3	2.6	2.2	1.3	0.9	1.6	2.6	0.4	1.2	0.8	2.9	2.2	1	1
Fear	Oral	1.3	1.2	1.3	1.3	0.6	0.1	2.1	4.6	0.2	0.7	1.3	2.6	6.3	0.3	0.4
	± std	2	2.3	1.3	1.8	1	0.3	2.3	3.1	0.6	1	2.3	3	2.5	0.7	1.2
	Nasal	1.3	0.4	2.3	1.3	1.1	0	1.6	5.1	0.4	0.8	1.3	3.3	5.3	1.5	0.4
	± std	2.3	1	2.5	2.2	2.2	0	2.5	2.7	0.8	1.4	2.4	3.1	3.1	2.1	0.7

P<0.001 | P<0.01 | P<0.05 | P<0.1 — Comparisons are between NB and OB

3.3.2 Physiological variables and breathing pathway

Table 3.3 shows changes in physiological parameters for both OB and NB during control. As shown in the table, during silence with NB, subjects had significantly lower heartrate ($p<0.001$) and higher respiratory rate ($0.05< p <0.1$) than during silence with OB. Also, RR-respiratory coherence was significantly larger during NB than during OB ($p<0.05$).

Table 3.4 shows changes in physiological parameters for both OB and NB during listening to music. As shown in the table, during listening to music with NB, the average respiratory rate ($p<0.001$) was higher than during listening to music with OB, heartrate was also higher during listening to music with NB ($p<0.05$) but the change was very minimal.

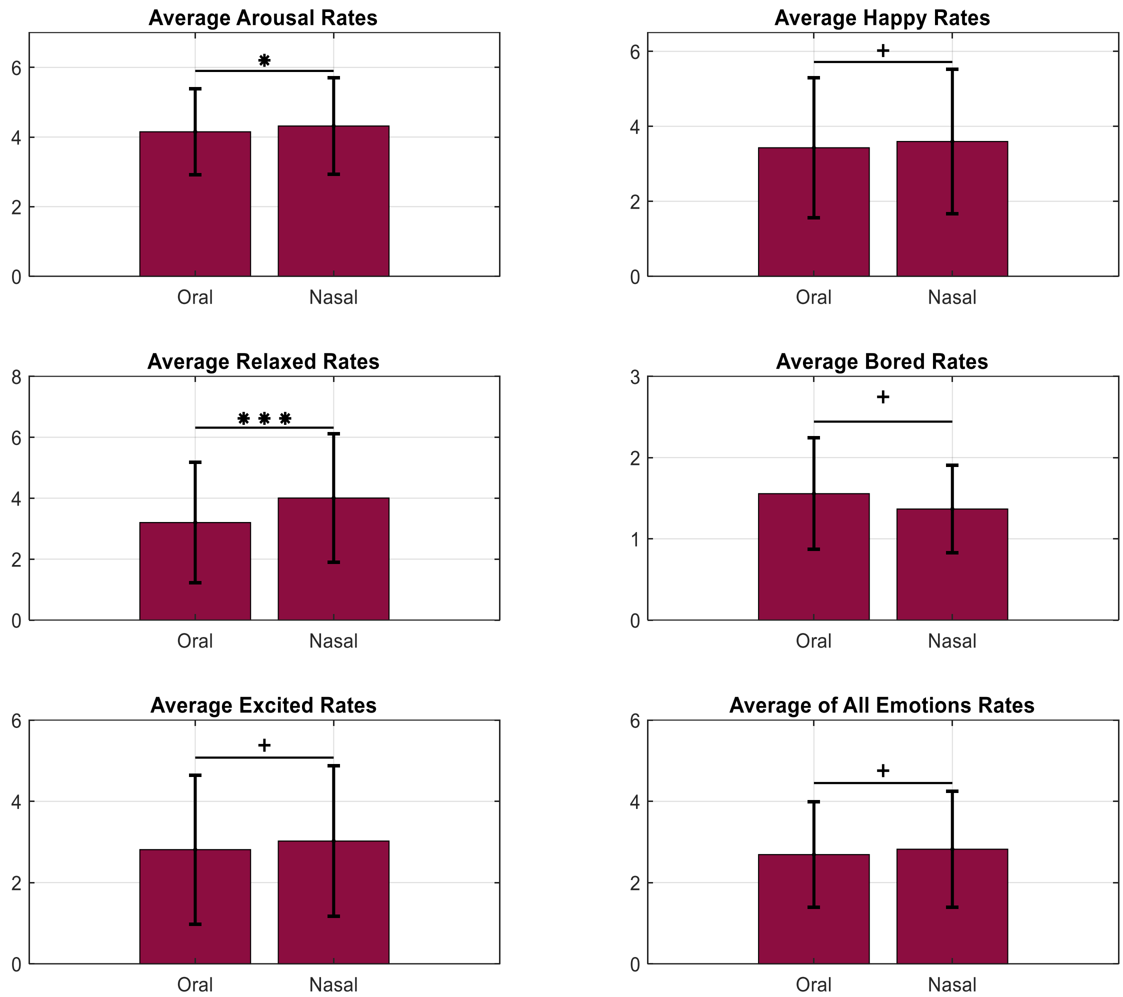


Figure 3.1 The average emotion rates during NB and OB which were significantly different. +: 0.05<p<0.1, *: 0.01<p<0.05, **: 0.001p<0.01, ***: p<0.001

Table 3.3 Changes in physiological parameters for OB and NB during control (± SEM)

Heartrate**		**Respiratory Rate**+		**Fw of Respiratory**		**RR-Respiratory coherence (0-0.5 Hz)***	
Oral	Nasal	Oral	Nasal	Oral	Nasal	Oral	Nasal
73.83	71.58	0.29	0.32	0.14	0.16	0.47	0.58
±2.27	±2.46	±0.02	±0.02	±0.01	±0.01	±0.04	±0.04

+: 0.05<p<0.1, *: 0.01<p<0.05, **: 0.001p<0.01, ***: p<0.001

Table 3.4 Changes in physiological parameters for OB and NB during listening to music (± SEM)

Heartrate*		**Respiratory Rate*****		**Fw of Respiratory**+		**RR-Respiratory coherence (0-0.5 Hz)**	
Oral	Nasal	Oral	Nasal	Oral	Nasal	Oral	Nasal
71.24	71.79	0.32	0.38	0.15	0.16	0.55	0.56
±2.43	±2.09	±0.02	±0.02	±0.01	±0.01	±0.04	±0.04

+: 0.05<p<0.1, *: 0.01<p<0.05, **: 0.001p<0.01, ***: p<0.001

The coherences of respiratory and RR interval time series with all the eight channels of EEGs both for OB and NB during control and listening to music are shown in Figure 2. All the coherences in which the differences between NB and OB were statistically significant, the coherence value for NB was larger than for OB, and in the rest of them which were non-significant still the coherence values for NB were larger than OB or values were almost equal.

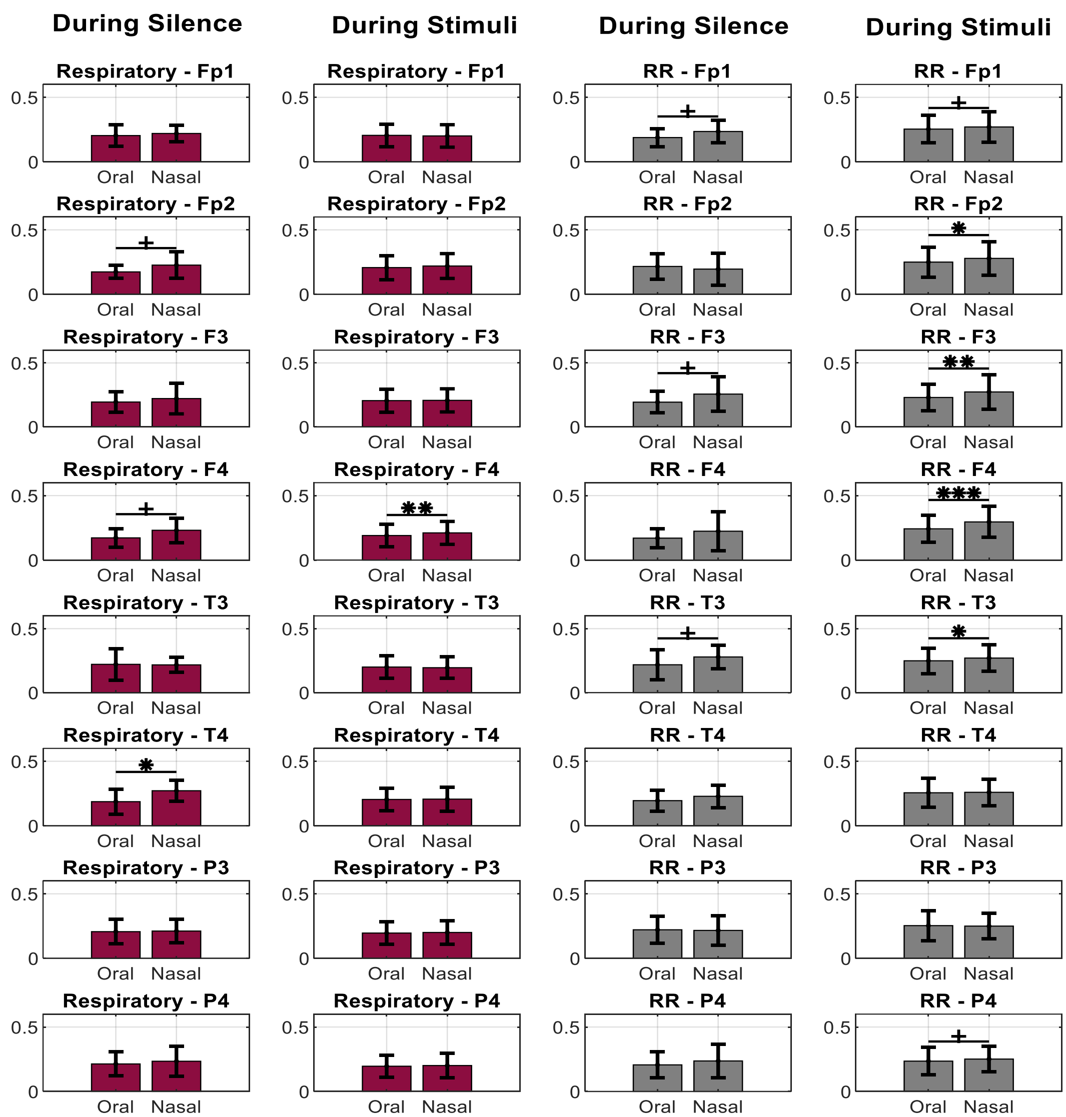


Figure 3.2 Coherence of respiratory and RR interval series with EEGs both for OB and NB during control (silence) and listening to music: +: 0.05<p<0.1, *: 0.01<p<0.05, **: 0.001p<0.01, ***: p<0.001

3.3.3 Correlation of musical features with rates of emotions

None of the correlations between melodic direction and emotion both during NB and OB were significant. During OB, none of the emotions had significant correlations with pitch range and rhythm. During NB, being bored had a negative correlation with pitch range (-0.64, $p=0.026$), and rhythm had a negative correlation with valence (-0.53, $p=0.07$) and being frustrated (0.66, $p=0.2$). Mode had only a high correlation with the average fear rate which was negative (<-0.69, $p<0.05$). Since these musical features did not show consistent correlations they were not listed in Table 3.5.

During both NB and OB, the tempo of songs had a high correlation with average arousal rates ($=0.69$ (both OB and NB), $p<0.05$) and average excited rates ($=0.83$ (both OB and NB), $p<0.001$) and high negative correlation with feeling relaxed (<-0.71, $p<0.01$), sleepy (<-0.78, $p<0.01$), sad (<-0.64, $p<0.05$). The average of correlation of emotion ratings with the tempo was higher during NB than OB.

The complexity of songs had a high correlation with the average rate of fear (>0.71, $p<0.01$) and a high negative correlation with feeling happy (<-0.59, $p<0.05$). The average of correlation of emotion ratings with complexity was higher during NB than OB.

Consonance was the musical feature which had the highest correlation with the average valence of the songs (>0.72, $p<0.01$). Consonance had a high positive correlation with feeling happy (>0.58, $p<0.05$) and relaxed (>0.53, NB: $p<0.05$, OB: NS). Also, it had a high negative correlation with being frustrated (<-0.54, NB: $p<0.001$, OB: NS), angry (<-0.78, $p<0.001$), and fear (<-0.62, $p<0.05$). The average of correlation of emotion ratings with consonance was higher during NB than OB.

Rhythmic articulation was the only musical feature that had a high negative correlation with average arousal rates (<-0.81, $p<0.01$) and average excited rates (<-0.87, $p<0.001$). It also had a high negative correlation with average happy rates (<0.75, $p<0.01$) and had a high positive correlation with average sad rates (>0.86, $p<0.001$) and average sleepy rates (>0.69, p<0.05). The average of correlation of emotion ratings with consonance during NB was equal to OB.

Accentuation of songs had a high correlation with average arousal rates (>0.68, p<0.05) and average excited rates (>0.83, p<0.001) and high negative correlation with average relaxed rates (<-0.69, p<0.05), average sleepy rates (<-0.76, p<0.01), and average sad rates (<-0.62, p<0.05). The average of correlation of emotion ratings with accentuation was higher during NB than OB.

Pitch level had a high positive correlation with valence (>0.68, p<0.05) and a high negative correlation with average angry rates (<-0.69, p<0.05).

Table 3.5 Correlation of musical features with different emotion rates

Emotion	Breathing Pathway	Tempo	Accentuation	Rhythmic Articulation	Pitch level	Harmonic Complexity	Consonance
Valence	Oral	-0.53	-0.45	0.048***	0.69*	-0.37*	0.72**
	Nasal	-0.65*	-0.62*	0.22*	0.68*	-0.38*	0.74**
Arousal	Oral	0.69*	0.71**	-0.88***	0.21*	-0.09*	0.08**
	Nasal	0.69*	0.68*	-0.81**	0.13*	0.02*	-0.05**
Happy	Oral	0.31*	0.36**	-0.75**	0.53	-0.59*	0.58*
	Nasal	0.32*	0.35*	-0.77**	0.53	-0.63*	0.62*
Relaxed	Oral	-0.71**	-0.69*	0.51	0.32	-0.39*	0.53
	Nasal	-0.75**	-0.76**	0.51	0.38	-0.46*	0.59*
Sleepy	Oral	-0.78**	-0.76**	0.76**	0.12	-0.16*	0.37
	Nasal	-0.8**	-0.78**	0.69*	0.2	-0.2*	0.34*
Bored	Oral	-0.43**	-0.46**	0.57	-0.04	-0.21*	0.23
	Nasal	-0.5**	-0.51	0.36*	0.08	-0.19*	0.11*
	Oral	-0.77**	-0.76**	0.92***	0.04	0.2*	0.06

Sad	**Nasal**	-0.64*	-0.62*	0.86***	-0.19	0.35*	-0.15*
Frustrated	**Oral**	0.33**	0.27**	0.05***	-0.46	0.37*	-0.54
	Nasal	0.49*	0.48*	-0.02***	-0.67*	0.6*	-0.84***
Excited	**Oral**	0.83***	0.85***	-0.87***	0.06	-0.1*	0.001
	Nasal	0.83***	0.83***	-0.91***	0.03*	-0.06*	-0.09***
Angry	**Oral**	0.51	0.47***	-0.03***	-0.76**	0.62*	-0.83***
	Nasal	0.62*	0.58*	-0.15***	-0.69*	0.51	-0.78**
Fear	**Oral**	0.02	0.02***	0.17***	-0.38**	0.71**	-0.62*
	Nasal	0.12*	0.14*	0.17***	-0.48*	0.82**	-0.75**
Average +	**Oral**	0.54	0.53	0.5	0.33	0.35	0.41
	Nasal	0.58	0.58	0.5	0.37	0.38	0.46

***P<0.001 **P<0.01 *P<0.05

+ Average of absolute values

3.4 Discussion

The results of this study suggest that during NB subjects felt more aroused from various types of music and found songs more relaxing, happier, and more exciting, but during OB, they found the sad song sadder and gave larger rates to bored and frustrated emotions. During NB trials, the average synchronizations of respiratory time series with EEGs and heartrate variation were larger compared to OB trials. The average respiratory rate in all the OB trials, including OB control, was significantly lower than the during NB trials which can be related to more effective breathing by mouth compared to nose [89]. Higher consonance of songs had higher positive and negative correlations to positive and negative emotions, respectively, while higher complexity of songs had a positive correlation with negative emotions.

3.4.1 Breathing pathway and emotions

The average of subjects' rates over all emotions was higher during NB than OB and the level of activation by songs was higher during NB since their rate for arousal was higher in NB than OB. During NB, the subjects found songs much more relaxing than during OB.

The subjects perceived the happy song to be happier during NB and the sad song to be sadder during OB, and their average perception of happiness and excitement from the songs were larger during NB than OB during which the average perceived boringness of songs was larger than NB. Briefly, during NB the rates for more positive emotions were larger: larger average happy rates for the happy song and larger average happy rates over all songs and larger average relaxed rates over all songs; and during OB the average rates to more negative emotions was larger: larger average of sad rates for the sad song, and larger average of bored and frustrated rates over all songs.

3.4.2 Physiological reasoning

Autonomic breathing is vital in maintaining physiological homeostasis and constantly reacts to emotional changes. The olfactory receptor cells are located in the nasal cavity and are activated during nasal breathing even in absence of odor stimuli and consequently, activates the olfactory tract and bulb. The fact that the limbic brain regions mediating emotion are closely linked with the olfactory bulb, whose performance is significantly improved during inspiration and nasal respiration causing our sense of smell to be improved [72], suggests that nasal respiration could form rhythmic electrical activity in the limbic region with corresponding effects on processing emotion and cognitive function. This, also, possibly could form rhythmic electrical activity even in its neighboring cortices such as the primary auditory cortex resulting in different effects triggered by auditory stimuli and the correspond resulting emotions. In [73] it is shown that during nasal breathing memory performance is more accurate and cognitive response is faster than during oral breathing. The air that periodically enters the nose at the rate of breathing triggers rhythmic neural oscillations that propagate within the limbic region which is responsible for memory and emotion. These results suggest that this phenomenon affects the process of emotion as well, which can be the reason for difference in emotion ratings to the same piece of music during NB compared to OB and was the primary physiological reason for raising questions that resulted in conducting this study.

3.4.3 Physiological variations during NB and OB

During silence with NB, the average heartrate was lower than during silence with OB, and during listening to music the heart rate was more or less similar (very slightly higher) during NB than OB, possibly reflecting the overall feeling of being more relaxed during NB. Breathing rates were lower during OB in both silence and while listening to music, as stated before, a possible consequence of more effective breathing through the mouth.

Furthermore, the Fw of the respiratory was also slightly less during OB compared to NB, both during control and during listening to songs, showing that during OB the variation of respiratory frequency was less.

It was observed the higher synchronization of respiratory rhythm with heartrate variations (RR interval time series) during NB compared to OB both during control and listening to music. Also, the coherences of respiratory with different EEGs were slightly higher during NB than during OB or in some cases were equal. This was the same for coherences of RR intervals with various EEGs. These higher synchronizations of respiratory with different EEGs can be explained by physiological reasoning explained in section 3.4.2 and is consistent with findings reported in [73], where a higher temporal correlation of the mean respiratory signal with low-pass filtered intracranial EEGs was observed during NB than OB.

3.4.4 Correlation of musical features with emotions

According to Table 3.4, the average of correlations of all musical features over all emotion rates was higher during NB than OB, except for rhythmic articulation they were equal. The pattern of correlations (values and statistical significance) for tempo and accentuation with different rates of emotions were similar while both features had an opposite pattern of correlations with rates of emotion than the correlation pattern of rhythmic articulation with rates of emotion.

Average valence rates had a high correlation with consonance and a high negative correlation with tempo and accentuation, all of which were higher for NB than OB.

Average arousal and excited rates had a large positive correlation with tempo and accentuation and a large negative correlation with rhythmic articulation, and their correlations with other features were small.

Average relaxed and sleepy rates had a large positive correlation with consonance and rhythmic articulation, and they had large negative correlations with tempo and accentuation. These can be useful as guidance in choosing songs for music therapy.

The only large positive correlation with average sad rates was with the rhythmic articulation of songs and both tempo and accentuation had a large negative correlation with average sad rates. This pattern of correlations for average sad rates was the opposite of for average arousal and excited rates.

Average angry and fear rates had a positive correlation with the complexity of songs and a large negative correlation with the mode and consonance rate of songs. Average angry rates had a large correlation with tempo and accentuation which were significantly higher during NB than OB.

Average happy rates had a large positive correlation with consonance and a large negative correlation with rhythmic articulation and complexity of songs. All of these correlations were higher in NB than OB.

Average bored rates did not have a large correlation with any of the musical features.

Higher consonance of songs not only can help to trigger higher relaxed states but also can help to trigger higher happiness in the listener and for both of these emotions the correlation was even larger during NB than during OB. Consonance, also, had large negative correlations with negative emotions such as average angry, frustrated, and fear rates. On the other hand, the complexity of songs only had a large positive correlation with negative emotions such as average angry, frustrated, and fear rates. These results show that songs with higher consonance can help to reach more positive states and stay away from more negative emotional states while during songs with higher complexity listeners gave higher average rates to more negative emotions, all of which can provide preventing role in emotion-related diseases by better controlling emotional states resulted from music.

The musical feature which had the largest correlation values with various emotion rates, most of which were also statistically significant, was rhythmic articulation. Rhythmic articulation had the largest positive correlation with average sad rates and had large negative correlations with each of average excited, arousal, and happy rates.

CHAPTER 4. DISCUSSION

4.1 Study overview and objectives

In this dissertation, the aims we pursued are divided into two categories each of which is elaborated in chapter 2 and chapter 3, respectively. In chapter 2, using cardiac synchronized EEG segments we explored which cardiac synchronized EEG portions reflect the changes triggered by music in the most pronounced way and which frequency band of cardiac synchronized EEGs has more variation over different portions of a cardiac cycle. Also, we investigated the effects of tempo and cognition of music on the complexity of brain response, strength and localization of their effects, and their targeted frequency bands. Answering these questions has the potential to improve our understanding of how the effects of music come about and also show the time intervals in the cardiac cycle during which stronger influence of music can be observed in EEGs. The latter information would not only be useful in investigating the impacts of music on the brain but also may have the same potential for looking for impacts of other types of internal or external stimuli and pave the way for use of cardiac synchronous EEG in such studies.

With evidence of the presence of respiratory entrainment of local field potential activity in human limbic brain networks and the importance of nasal airflow in shaping this entrainment [73], the effects of breathing pathway (nasal vs. oral) on the processing of various emotions, which happens in the limbic region, is not yet well-understood. In chapter 3, we investigated to see whether the breathing pathway affects feeling different emotions or not and if yes, to see the strength of effect of the breathing pathway on feeling emotions and how they are correlated with the structural features of music. The other aim was pursued there was to know whether the effects of respiratory pathway contribute to any differences in physiological variables of healthy humans during rest both with no external stimuli and with external stimuli triggering various emotions.

Experiencing negative emotions is inevitable for humans and at times can be helpful. However, when negative emotions are being felt in an extreme way over a long period of time, they can cause various problems for individuals and society. Anxiety and fear with stress (acute and chronic) can cause problems for the immune system [90]. Anger and its resulting improper management have been associated with heart disease [36, 91, 92] and in some cases, with cancers [93, 94]. In some cases, grief and sadness may initiate unipolar depression [95], and in severe cases, can lead to loss of work productivity [96], immunosuppression [90], and suicide [97]. All the possible adverse consequences of negative emotions led to strong literature focusing on negative emotions like anger, sadness, anxiety, and fear than on positive emotions like happiness and contentment [34]. Here one can argue that this makes sense and understanding positive emotions should be postponed while researchers focus more on negative emotions to learn preventing and treating measures for the diseases triggered by them. But at the same time, we can find ways to trigger positive emotions and consequently suppress negative emotions. This study provides some information about triggering positive emotions and musical features that correlate with positive and negative emotions which could be useful in designing behavioral interventions that are used to modify the processing of emotions.

4.2 Significant findings

In chapter 2, we investigated the effects of cognition and tempo of music using cardiac-synchronized EEG portions to determine which portion reflects those changes better. Our analysis approach showed that the portion farthest from the R-wave of cardiac cycles (Pr3) has the most potential to capture those changes, and it may have the same potential to reveal effects of other causes such as emotion triggering stimuli or odor stimuli and is a promising approach to extract information from EEGs. The physiological reason for this observation is that the fact that Pr3 carries data series from the farthest time instants between two ventricular depolarization, which can cause an electrical artifact in brain electrical signals; while during Pr1 atrial depolarization and part of ventricular depolarization happen, and during Pr2, part of ventricular depolarization and repolarization happen. The slow tempo song caused the lowest complexity in EEG response, even less than during control, and triggered the smallest effect size in EEGs as well, suggesting a possible reason for why slow songs are perceived to have calming effects. Furthermore, we found an increase in complexity of EEG response during increased tempo and increased cognition of music specifically in the parietal and the temporal lobe, respectively. Alpha and Beta bands were the most sensitive bands to auditory stimuli and cardiac phases, respectively, and in both of them, effects of tempo were larger than cognition of music. In the total band and frequency bands <38 Hz, we observed higher sensitivity to cardiac phases and stronger response to slower tempo music, and in frequency bands >38 Hz, we observed stronger response to cognition of music. The subjects' favorite song amplified the average complexity of brain electrical response over all EEGs and resulted in the most complex brain response compared to other songs. However, this increase was more significant in the temporal lobe, particularly in T4. The LPR process caused very different effects in MCI of an unknown song and a very well-known song (subject's favorite song) in T4. Larger changes in RH in temporal and parietal lobes in frequencies>38 Hz were observed for each individual song which can be explained by the larger association of RH for processing of music Also, both tempo and cognition of songs produced a more complex response in RH than LH, which again underlines involvement of RH in processing music [61].

In chapter 3, our findings suggest that during NB compared to OB, subjects gave higher rates to positive emotions, and they found songs more relaxing and the average level of felt arousal was higher. Also, during NB, subjects found songs to be happier and more exciting, than during OB, while during OB, subjects found the sad song sadder and gave larger rates to bored and frustrated emotions. During NB trials, the average of synchronizations between respiratory time series and EEGs and between respiratory time series and heartrate variation were larger compared to OB trials. The average respiratory rate in all the OB trials, including OB control, was significantly less than during NB trials probably reflecting more effective inhalation by mouth than by nose [89]. Additionally, the Fw of the respiration was also lower during OB compared to NB, both during listening to music and during control. This shows that during OB the variation of respiratory rate was less, and subjects tended to breath slower during OB trials than NB trials. We found that higher consonance had a positive correlation with positive emotions and a negative correlation with negative emotions while higher complexity of songs was positively correlated with more negative emotions. These results suggest that the respiratory pathway can be a playing factor in emotion-focused therapy (EFT) [98], and show that the breathing pathway, as well as some musical features, may be used as a controlling factor in employing emotion modification via music in human functions such as information processing and action readiness which improves human well-being and adapt people to their environments. Our results suggest that both breathing pathway and some musical features may help to bring one's emotional states to a more positive region and stay away from negative emotions which can be useful in better tailoring music therapy for overall health and wellbeing.

4.3 Study limitations

In investigating effects of tempo and cognition of music, as part of investigating effects of acoustical features of music, only effects of tempo were evaluated as it was assumed that this feature would have the most pronounced effect on physiological responses. Also, we reported that the Pr3 has the most potential to reflect the changes triggered by music because of being the farthest time instants from R-peak which cause the largest contamination from electrical cardiac activity but did not investigate whether this portion has the same potential to reflect the changes triggered by other types of stimuli. We acknowledge that the experimental approach (LPR) that we used to gain insight into the cognitive component vs purely sensory component of effects of music was not ideal. Perhaps studies that utilize more quantitative measures of the acoustical structure of music to find a song that has acoustical features similar to that of the favorite song would allow for more clear insight into these effects. Considering other structural characteristics of music, like spectral, timbre, and tonality features might also provide additional information. The menstrual cycle has been shown to impact autonomic function [99], however, this factor was not accounted for in this study.

4.4 Future work

In the study related to the use of cardiac synchronized EEGs to investigate the effects of music, we observed that the Pr3 of cardiac synchronized EEGs has the most potential to reflect the changes triggered by music possibly because of being the farthest time instants from R-peak and the settling of perfusion swell caused by events in a cardiac cycle. We did not investigate whether the same portion of Pr3 has a good potential to reveal the changes triggered by other types of stimuli. The physiological reasoning behind why Pr3 has this better potential can be used in investigating effects of other stimuli like odor, emotion or detecting drowsiness or neural disorders.

In the study for investigating effects of breathing pathway on processing emotions and physiological variables, considering phases of the respiratory cycle (inspiratory phase and expiratory phase) is a good candidate for further investigations, like seeing the difference of the effects during inspiratory interval versus expiratory interval. Also, the fact that the limbic brain regions mediating emotion are closely linked with the olfactory bulb, whose performance is significantly improved during inspiration and nasal respiration causing our sense of smell to be improved [72], suggests that nasal respiration could form rhythmic electrical activity in the limbic region with corresponding effects on processing emotion and cognitive function. This opens a door to investigate the effects of odor on the processing of emotion and cognition.

REFERENCES

[1] H. Bringman, K. Giesecke, A. Thorne, S. Bringman, "Relaxing music as pre-medication before surgery: a randomised controlled trial," *Acta Anaesthesiol Scand*, 2009, 53(6), pp. 759-64.

[2] C. Gelinas, C. Arbour, C. Michaud, L. Robar, J. Cote, "Patients and ICU nurses' perspectives of non-pharmacological interventions for pain management," *Nurs Crit Care*, 2013, 18(6), pp. 307-18.

[3] H. J. Trappe, "Role of music in intensive care medicine," *Int J Crit Illn Inj Sci*, 2012, 2(1), pp. 27-31.

[4] P. J. Mansky, D. B. Wallerstedt, "Complementary medicine in palliative care and cancer symptom management," *The Cancer Journal*, 2006, 12(5), pp. 425-31.

[5] T. Särkämö, M. Tervaniemi, S. Laitinen, A. Forsblom, S. Soinila, M. Mikkonen, et al., "Music listening enhances cognitive recovery and mood after middle cerebral artery stroke," *Brain*, 2008, 131(3), pp. 866-76.

[6] L. Bernardi, C. Porta, G. Casucci, R. Balsamo, N. F. Bernardi, R. Fogari, et al., "Dynamic interactions between musical, cardiovascular, and cerebral rhythms in humans," *Circulation*, 2009, 119(25), pp. 3171-80.

[7] L. Bernardi, C. Porta, P. Sleight, "Cardiovascular, cerebrovascular, and respiratory changes induced by different types of music in musicians and non-musicians: the importance of silence," *Heart*, 2006, 92(4), pp. 445-52.

[8] S. B. Hanser, S. E. Mandel, "The effects of music therapy in cardiac healthcare," *Cardiology in review*, 2005, 13(1), pp. 18-23.

[9] M. V. Pitzalis, F. Mastropasqua, A. Passantino, F. Massari, L. Ligurgo, C. Forleo, et al., "Comparison between noninvasive indices of baroreceptor sensitivity and the phenylephrine method in post–myocardial infarction patients," *Circulation*, 1998, 97(14), pp. 1362-7.

[10] K. Okada, A. Kurita, B. Takase, T. Otsuka, E. Kodani, Y. Kusama, et al., "Effects of music therapy on autonomic nervous system activity, incidence of heart failure events, and plasma cytokine and catecholamine levels in elderly patients with cerebrovascular disease and dementia," *International heart journal*, 2009, 50(1), pp. 95-110.

[11] V. N. Salimpoor, M. Benovoy, G. Longo, J. R. Cooperstock, R. J. Zatorre, "The rewarding aspects of music listening are related to degree of emotional arousal," *PloS one*, 2009, 4(10), pp. e7487.

[12] R. J. Zatorre, V. N. Salimpoor, "From perception to pleasure: music and its neural substrates," *Proceedings of the National Academy of Sciences*, 2013, 110(Supplement 2), pp. 10430-7.

[13] R. J. Ellis, J. F. Thayer, "Music and autonomic nervous system (dys) function," *Music Perception: An Interdisciplinary Journal*, 2010, 27(4), pp. 317-26.

[14] P. Fries, "A mechanism for cognitive dynamics: neuronal communication through neuronal coherence," *Trends in cognitive sciences*, 2005, 9(10), pp. 474-80.

[15] M. Mollakazemi, D. Biswal, S. Elayi, S. Thyagarajan, J. Evans, A. Patwardhan, "Synchronization of Autonomic and Cerebral Rhythms During Listening to Music: Effects of Tempo and Cognition of Songs," *Physiological research*, 2019, 68(6), pp. 1005-19.

[16] F. Haas, S. Distenfeld, K. Axen, "Effects of perceived musical rhythm on respiratory pattern," *Journal of applied physiology*, 1986, 61(3), pp. 1185-91.

[17] J. A. Etzel, E. L. Johnsen, J. Dickerson, D. Tranel, R. Adolphs, "Cardiovascular and respiratory responses during musical mood induction," *International Journal of psychophysiology*, 2006, 61(1), pp. 57-69.

[18] P. Gomez, B. Danuser, "Relationships between musical structure and psychophysiological measures of emotion," *Emotion*, 2007, 7(2), pp. 377.

[19] A. M. Croom, "Music, neuroscience, and the psychology of well-being: a précis," *Frontiers in psychology*, 2012, 2pp. 393.

[20] P. N. Juslin, P. Laukka, "Expression, perception, and induction of musical emotions: A review and a questionnaire study of everyday listening," *Journal of new music research*, 2004, 33(3), pp. 217-38.

[21] J. A. Sloboda, S. A. O’neill, "Emotions in everyday listening to music," *Music and emotion: Theory and research*, 2001, 8pp. 415-29.

[22] J. A. Sloboda, P. N. Juslin, "Psychological perspectives on music and emotion," *Music and emotion: Theory and research*, 2001, pp. 71-104.

[23] D. Sammler, M. Grigutsch, T. Fritz, S. Koelsch, "Music and emotion: electrophysiological correlates of the processing of pleasant and unpleasant music," *Psychophysiology*, 2007, 44(2), pp. 293-304.

[24] K. S. Moore, "A systematic review on the neural effects of music on emotion regulation: implications for music therapy practice," *Journal of music therapy*, 2013, 50(3), pp. 198-242.

[25] V. J. Konečni, "Does music induce emotion? A theoretical and methodological analysis," *Psychology of Aesthetics, Creativity, and the Arts*, 2008, 2(2), pp. 115.

[26] P. N. Juslin, "Communicating emotion in music performance: A review and a theoretical framework," 2001, pp.

[27] L. Bunt, M. Pavlicevic, "Music and emotion: Perspectives from music therapy," 2001, pp.

[28] U. Nilsson, N. Rawal, M. J. A. Unosson, "A comparison of intra-operative or postoperative exposure to music–a controlled trial of the effects on postoperative pain," 2003, 58(7), pp. 699-703.

[29] P. Berbel, J. Moix, S. Quintana, "Music versus diazepam to reduce preoperative anxiety: a randomized controlled clinical trial," *Revista espanola de anestesiologia y reanimacion*, 2007, 54(6), pp. 355-8.

[30] H. Bringman, K. Giesecke, A. Thörne, S. J. A. A. S. Bringman, "Relaxing music as pre-medication before surgery: a randomised controlled trial," 2009, 53(6), pp. 759-64.

[31] C. Lepage, P. Drolet, M. Girard, Y. Grenier, R. DeGagné, "Music decreases sedative requirements during spinal anesthesia," *Anesthesia & Analgesia*, 2001, 93(4), pp. 912-6.

[32] H.-J. Trappe, "The effects of music on the cardiovascular system and cardiovascular health," *Heart*, 2010, 96(23), pp. 1868-71.

[33] K. L. Phan, T. Wager, S. F. Taylor, I. Liberzon, "Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI," *Neuroimage*, 2002, 16(2), pp. 331-48.

[34] B. L. Fredrickson, "Cultivating positive emotions to optimize health and well-being," *Prevention & treatment*, 2000, 3(1), pp. 1a.

[35] B. L. Fredrickson, R. A. Mancuso, C. Branigan, M. M. Tugade, "The undoing effect of positive emotions," *Motivation and emotion*, 2000, 24(4), pp. 237-58.

[36] B. L. Fredrickson, K. E. Maynard, M. J. Helms, T. L. Haney, I. C. Siegler, J. C. Barefoot, "Hostility predicts magnitude and duration of blood pressure response to anger," *Journal of Behavioral Medicine*, 2000, 23(3), pp. 229-43.

[37] S. Pérez Lloret, J. J. Diez, M. N. Domé, A. Alvarez Delvenne, N. Braidot, D. P. Cardinali, et al., "Effects of different" relaxing" music styles on the autonomic nervous system," 2014, pp.

[38] C. Bernard, "Lecture on the physiology of the heart and its connections with the brain, delivered at the Sorbonne, the 27th March, 1865." Savannah,: Purse; 1867. 47 p. p.

[39] J. F. Thayer, R. D. Lane, "Claude Bernard and the heart-brain connection: further elaboration of a model of neurovisceral integration," *Neurosci Biobehav Rev*, 2009, 33(2), pp. 81-8.

[40] M. Kern, A. Aertsen, A. Schulze-Bonhage, T. Ball, "Heart cycle-related effects on event-related potentials, spectral power changes, and connectivity patterns in the human ECoG," *Neuroimage*, 2013, 81pp. 178-90.

[41] R. Schandry, R. Weitkunat, "Enhancement of heartbeat-related brain potentials through cardiac awareness training," *International Journal of Neuroscience*, 1990, 53(2-4), pp. 243-53.

[42] G. Dirlich, L. Vogl, M. Plaschke, F. Strian, "Cardiac field effects on the EEG," *Electroencephalography and clinical neurophysiology*, 1997, 102(4), pp. 307-15.

[43] M. A. Gray, P. Taggart, P. M. Sutton, D. Groves, D. R. Holdright, D. Bradbury, et al., "A cortical potential reflecting cardiac function," *Proceedings of the National Academy of Sciences*, 2007, 104(16), pp. 6818-23.

[44] R. Schandry, P. Montoya, "Event-related brain potentials and the processing of cardiac activity," *Biological psychology*, 1996, 42(1-2), pp. 75-85.

[45] H. Fukushima, Y. Terasawa, S. Umeda, "Association between interoception and empathy: evidence from heartbeat-evoked brain potential," *International Journal of Psychophysiology*, 2011, 79(2), pp. 259-65.

[46] P. Montoya, R. Schandry, A. Müller, "Heartbeat evoked potentials (HEP): topography and influence of cardiac awareness and focus of attention," *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 1993, 88(3), pp. 163-72.

[47] E. Al, F. Iliopoulos, N. Forschack, T. Nierhaus, M. Grund, P. Motyka, et al., "Heart–brain interactions shape somatosensory perception and evoked potentials," *Proceedings of the National Academy of Sciences*, 2020, 117(19), pp. 10575-84.

[48] M. F. Larra, J. B. Finke, E. Wascher, H. Schächinger, "Disentangling sensorimotor and cognitive cardioafferent effects: A cardiac-cycle-time study on spatial stimulus-response compatibility," *Scientific reports*, 2020, 10(1), pp. 1-10.

[49] J. A. Filosa, H. W. Morrison, J. A. Iddings, W. Du, K. J. Kim, "Beyond neurovascular coupling, role of astrocytes in the regulation of vascular tone," *Neuroscience*, 2016, 323pp. 96-109.

[50] F. Silvio Taccone, S. Scolletta, F. Franchi, K. Donadello, M. Oddo, "Brain perfusion in sepsis," *Current vascular pharmacology*, 2013, 11(2), pp. 170-86.

[51] M. Iwanaga, A. Kobayashi, C. Kawasaki, "Heart rate variability with repetitive exposure to music," *Biological psychology*, 2005, 70(1), pp. 61-6.

[52] R. U. Krabs, R. Enk, N. Teich, S. Koelsch, "Autonomic effects of music in health and Crohn's disease: the impact of isochronicity, emotional valence, and tempo," *PloS one*, 2015, 10(5), pp. e0126224.

[53] S. Kume, Y. Nishimura, K. Mizuno, N. Sakimoto, H. Hori, Y. Tamura, et al., "Music improves subjective feelings leading to cardiac autonomic nervous modulation: a pilot study," *Frontiers in neuroscience*, 2017, 11pp. 108.

[54] M. J. Mollakazemi, D. Biswal, J. Evans, A. Patwardhan, "Eigen Decomposition of Cardiac Synchronous EEGs for Investigation of Neural Effects of Tempo and Cognition of Songs," in *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* 2018, IEEE.

[55] M. J. Mollakazemi, D. Biswal, A. Patwardhan, "Target Frequency Band of Cognition and Tempo of Music: Cardiac Synchronous EEG," in *2018 IEEE International Symposium on Signal Processing and Information Technology (ISSPIT)* 2018, IEEE.

[56] D. Biswal, M. J. Mollakazemi, S. Thyagarajan, J. Evans, A. Patwardhan, "Baroreflex Sensitivity During Listening to Music Computed from Time Domain Sequences and Frequency Domain Transfer Function," in *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* 2018, IEEE.

[57] M. J. Mollakazemi, D. Biswal, A. Patwardhan, "Interaction Among Musical, Cerebral and Autonomous Rhythms," in *2020 IEEE International Conference on Consumer Electronics (ICCE)* 2020, IEEE.

[58] M. J. Mollakazemi, D. Biswal, S. Sunderam, A. Patwardhan, "EEG segments synchronized to be temporally farthest from the R-waves in ECG are more informative during listening to music," *Biomedical Signal Processing and Control*, https://doi.org/10.1016/j.bspc.2021.102660, 2021

[59] Y. Hu, J. Mak, H. Liu, K. D. Luk, "ECG cancellation for surface electromyography measurement using independent component analysis," in *2007 IEEE International Symposium on Circuits and Systems* 2007, IEEE.

[60] S. Mahmoodabadi, A. Ahmadian, M. Abolhasani, "ECG feature extraction using Daubechies wavelets," in *Proceedings of the fifth IASTED International conference on Visualization, Imaging and Image Processing* 2005.

[61] D. Schön, C. Magne, M. J. P. Besson, "The music of speech: Music training facilitates pitch processing in both music and language," 2004, 41(3), pp. 341-9.

[62] J. C. Smith, A. P. Abdala, I. A. Rybak, J. F. Paton, "Structural and functional architecture of respiratory networks in the mammalian brainstem," *Philosophical Transactions of the Royal Society B: Biological Sciences*, 2009, 364(1529), pp. 2577-87.

[63] J. C. Smith, H. H. Ellenberger, K. Ballanyi, D. W. Richter, J. L. Feldman, "Pre-Botzinger complex: a brainstem region that may generate respiratory rhythm in mammals," *Science*, 1991, 254(5032), pp. 726-9.

[64] F. A. Boiten, "The effects of emotional behaviour on components of the respiratory cycle," *Biological psychology*, 1998, 49(1-2), pp. 29-51.

[65] K. C. Evans, D. D. Dougherty, A. M. Schmid, E. Scannell, A. McCallister, H. Benson, et al., "Modulation of spontaneous breathing via limbic/paralimbic–bulbar circuitry: An event-related fMRI study," *Neuroimage*, 2009, 47(3), pp. 961-71.

[66] W. Huijbers, C. Pennartz, E. Beldzik, A. Domagalik, M. Vinck, W. F. Hofman, et al., "Respiration phase-locks to fast stimulus presentations: Implications for the interpretation of posterior midline “deactivations”," *Human brain mapping*, 2014, 35(9), pp. 4932-43.

[67] E. Vlemincx, J. Taelman, S. De Peuter, I. Van Diest, O. Van Den Bergh, "Sigh rate and respiratory variability during mental load and sustained attention," *Psychophysiology*, 2011, 48(1), pp. 117-20.

[68] W. M. Suess, A. B. Alexander, D. D. Smith, H. W. Sweeney, R. J. Marion, "The effects of psychological stress on respiration: a preliminary study of anxiety and hyperventilation," *Psychophysiology*, 1980, 17(6), pp. 535-40.

[69] J. J. Arch, M. G. Craske, "Mechanisms of mindfulness: Emotion regulation following a focused breathing induction," *Behaviour research and therapy*, 2006, 44(12), pp. 1849-58.

[70] Q. Zhang, X. Chen, Q. Zhan, T. Yang, S. Xia, "Respiration-based emotion recognition with deep learning," *Computers in Industry*, 2017, 92pp. 84-90.

[71] A. Ahani, H. Wahbeh, H. Nezamfar, M. Miller, D. Erdogmus, B. Oken, "Quantitative change of EEG and respiration signals during mindfulness meditation," *Journal of neuroengineering and rehabilitation*, 2014, 11(1), pp. 1-11.

[72] I. Homma, Y. Masaoka, "Breathing rhythms and emotions," *Experimental physiology*, 2008, 93(9), pp. 1011-21.

[73] C. Zelano, H. Jiang, G. Zhou, N. Arora, S. Schuele, J. Rosenow, et al., "Nasal respiration entrains human limbic oscillations and modulates cognitive function," *Journal of Neuroscience*, 2016, 36(49), pp. 12448-67.

[74] D. P. Calderon, N. Leverkova, A. Peinado, "Gq/11-induced and spontaneous waves of coordinated network activation in developing frontal cortex," *Journal of Neuroscience*, 2005, 25(7), pp. 1737-49.

[75] O. Garaschuk, J. Linn, J. Eilers, A. Konnerth, "Large-scale oscillatory calcium waves in the immature cortex," *Nature neuroscience*, 2000, 3(5), pp. 452.

[76] H. Onimaru, I. Homma, "Spontaneous oscillatory burst activity in the piriform–amygdala region and its relation to in vitro respiratory activity in newborn rats," *Neuroscience*, 2007, 144(1), pp. 387-94.

[77] A. Peinado, "Traveling slow waves of neural activity: a novel form of network activity in developing neocortex," *J Neurosci*, 2000, 20(RC54), pp.

[78] B. C. Sirois, M. M. Burg, "Negative emotion and coronary heart disease: A review," *Behavior modification*, 2003, 27(1), pp. 83-102.

[79] I. Lavenu, F. Pasquier, F. Lebert, H. Petit, M. Van der Linden, "Perception of emotion in frontotemporal dementia and Alzheimer disease," *Alzheimer disease and associated disorders*, 1999, pp.

[80] T. W. Smith, K. Glazer, J. M. Ruiz, L. C. Gallo, "Hostility, anger, aggressiveness, and coronary heart disease: An interpersonal perspective on personality, emotion, and health," *Journal of personality*, 2004, 72(6), pp. 1217-70.

[81] N. N. Vempala, F. A. Russo, "Predicting emotion from music audio features using neural networks," in *Proceedings of the 9th International Symposium on Computer Music Modeling and Retrieval (CMMR)* 2012, Lecture Notes in Computer Science London, UK.

[82] P. Gomez, B. Danuser, "Affective and physiological responses to environmental noises and music," *International Journal of psychophysiology*, 2004, 53(2), pp. 91-103.

[83] T. Eerola, J. K. Vuoskoski, "A review of music and emotion studies: Approaches, emotion models, and stimuli," *Music Perception: An Interdisciplinary Journal*, 2012, 30(3), pp. 307-40.

[84] P. Ekman, "An argument for basic emotions," *Cognition & emotion*, 1992, 6(3-4), pp. 169-200.

[85] J. Panksepp, "Affective neuroscience: The foundations of human and animal emotions," Oxford university press; 2004.

[86] J. A. Russell, "A circumplex model of affect," *Journal of personality and social psychology*, 1980, 39(6), pp. 1161.

[87] R. E. Thayer, "The biopsychology of mood and arousal," Oxford University Press; 1990.

[88] M. J. Mollakazemi, S. A. Atyabi, A. Ghaffari, "Heart beat detection using a multimodal data coupling method," *Physiological measurement*, 2015, 36(8), pp. 1729.

[89] W. W. James, S. Hastings. Discussion on mouth-breathing and nasal obstruction. SAGE Publications; 1932.

[90] A. O'leary, "Stress, emotion, and human immune function," *Psychological bulletin*, 1990, 108(3), pp. 363.

[91] J. C. Barefoot, W. G. Dahlstrom, R. B. Williams, "Hostility, CHD incidence, and total mortality: A 25-yr follow-up study of 255 physicians," *Psychosomatic medicine*, 1983, pp.

[92] R. B. Williams, T. L. Haney, K. L. Lee, Y.-H. Kong, J. A. Blumenthal, R. E. Whalen, "Type A behavior, hostility, and coronary atherosclerosis," *psychosomatic Medicine*, 1980, pp.

[93] H. J. Eysenck, "Cancer, personality and stress: prediction and prevention," *Advances in behaviour research and therapy*, 1994, 16(3), pp. 167-215.

[94] S. Greer, T. Morris, "Psychological attributes of women who develop breast cancer: A controlled study," *Journal of Psychosomatic Research*, 1975, 19(2), pp. 147-53.

[95] S. Nolen-Hoeksema, J. Morrow, B. L. Fredrickson, "Response styles and the duration of episodes of depressed mood," *Journal of abnormal psychology*, 1993, 102(1), pp. 20.

[96] W. Coryell, W. Scheftner, M. Keller, J. Endicott, J. Maser, G. L. Klerman, "The enduring psychosocial consequences of mania and depression," *The American journal of psychiatry*, 1993, pp.

[97] Y.-W. Chen, S. C. Dilsaver, "Lifetime rates of suicide attempts among subjects with bipolar and unipolar disorders relative to subjects with other Axis I disorders," *Biological psychiatry,* 1996, 39(10), pp. 896-9.

[98] L. S. Greenberg, "Emotion–focused therapy," *Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice*, 2004, 11(1), pp. 3-16.

[99] X. Bai, J. Li, L. Zhou, X. Li, "Influence of the menstrual cycle on nonlinear properties of heart rate variability in young women," *American Journal of Physiology-Heart and Circulatory Physiology*, 2009, 297(2), pp. H765-H74.

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Publications

Journal papers:

1. **Mohammad Javad Mollakazemi,** D. Biswal, S. C. Elayi, S. Thyagarajan, J. Evans, and A. Patwardhan. "Synchronization of Autonomic and Cerebral Rhythms During Listening to Music: Effects of Tempo and Cognition of Songs." *Physiological research* 68, no. 6 (2019).

2. **Mohammad Javad Mollakazemi,** D. Biswal, S. Sunderam, and A. Patwardhan. " EEG segments synchronized to be temporally farthest from the R-waves in ECG are more informative during listening to music". Biomedical Signal Processing and Control, https://doi.org/10.1016/j.bspc.2021.102660, (2021).

3. **Mohammad Javad Mollakazemi,** D. Biswal, B. Place, and A. Patwardhan. " Effects of breathing pathway on processing of emotions: correlation of musical features and emotions" – *Ready for Submission* (2021).

4. **Mohammad Javad Mollakazemi**, S. Abbas Atyabi, and Ali Ghaffari. "Heart beat detection using a multimodal data coupling method." *Physiological measurement* 36, no. 8 (2015): 1729.

5. Mostafa Abdollahpur, Ali Ghaffari, Shadi Ghiasi, and **Mohammad Javad Mollakazemi**. "Detection of pathological heart sounds." *Physiological measurement* 38, no. 8 (2017): 1616.

6. Ali Ghaffari, **Mohammad Javad Mollakazemi**, Seyyed Abbas Atyabi, and Mohammad Niknazar. "Robust fetal QRS detection from noninvasive abdominal electrocardiogram based on channel selection and simultaneous multichannel processing." *Australasian physical & engineering sciences in medicine* 38, no. 4 (2015): 581-592.

7. **Mohammad Javad Mollakazemi**, Farhad Asadi, and Aref Ghafouri. "The evaluation of the performance of different filtering approaches in tracking problem and the effect of noise variance." *International Journal of Mathematical and Computational Sciences,* 8(10), 1369-1374 (2015).

8. **Mohammad Javad Mollakazemi**, Farhad Asadi, Mahsa Tajnesaei, and Ali Ghaffari. "Fetal QRS Detection in Noninvasive Abdominal Electrocardiograms Using Principal Component Analysis and Discrete Wavelet Transforms with Signal Quality Estimation." *Journal of Biomedical Physics and Engineering, 11(2), 197-204* (2021)

9. **Mohammad Javad Mollakazemi,** and Farhad Asadi "Real Time Adaptive Obstacle Avoidance in Dynamic Environments with Different D-S", *International Journal of Mechanical and Mechatronics Engineering,* Vol: 8, No: 10, 1794-99, 2015.

10. Farhad Asadi, and **Mohammad Javad Mollakazemi**, "Investigation on performance of change point algorithm in time series dynamical regimes and effect of data characteristics", *International Journal of Bioengineering and Life Sciences,* 1(10), 1787-93, 2014.

11. Farhad Asadi, **Mohammad Javad Mollakazemi**, and Aref Ghafouri, "Influence of parameters of modeling and data distribution for optimal condition on locally weighted projection regression method", *International Journal of Mathematical and Computational Sciences,* Vol:8, No:10, 1800-7, 2015.

Conference papers:

1. **Mohammad Javad Mollakazemi,** Dibyajyoti Biswal, and Abhijit Patwardhan. "Interaction Among Musical, Cerebral and Autonomous Rhythms." In *2020 IEEE International Conference on Consumer Electronics (ICCE)*. IEEE, 2020.

2. **Mohammad Javad Mollakazemi,** Dibyajyoti Biswal, and Abhijit Patwardhan. "Target Frequency Band of Cognition and Tempo of Music: Cardiac Synchronous EEG." In *2018 IEEE International Symposium on Signal Processing and Information Technology (ISSPIT)*, pp. 696-700. IEEE, 2018.

3. **Mohammad Javad Mollakazemi**, Dibyajyoti Biswal, Joyce Evans, and Abhijit Patwardhan. "Eigen Decomposition of Cardiac Synchronous EEGs for Investigation of Neural Effects of Tempo and Cognition of Songs." In *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 2402-2405. IEEE, 2018.

4. Dibyajyoti Biswal, **Mohammad Javad Mollakazemi**, Sridevi Thyagarajan, Joyce Evans, and Abhijit Patwardhan. "Baroreflex Sensitivity During Listening to Music Computed from Time Domain Sequences and Frequency Domain Transfer Function." In *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 2776-2779. IEEE, 2018.

5. Biswal, Dibyajyoti, **Mohammad Javad Mollakazemi**, and Abhijit Patwardhan. "Changes in coherent activity between EEG and Various Frequency Components of Music while listening to Familiar and Unfamiliar Songs." In *6th IEEE International Symposium on Smart Electronic Systems (IEEE-iSES)*, IEEE, 2020.

6. Biswal, Dibyajyoti, **Mohammad Javad Mollakazemi**, and Abhijit Patwardhan. "Heart Rate and Breathing Rate calculated from Cheeks and Lips Using Green and Derived Colors from Video." In 6th IEEE International Symposium on Smart Electronic Systems (IEEE-iSES), IEEE, 2020.

7. **Mohammad Javad Mollakazemi**, Farhad Asadi, Shadi Ghiasi, and S. Hossein Sadati. "Applying quality index criterion for flexible multi-detection of heartbeat using features of multimodal data." In *2016 Computing in Cardiology Conference (CinC)*, pp. 1065-1068. IEEE, 2016.

8. **Mohammad Javad Mollakazemi**, Farhad Asadi, Hamid Ebrahimi Orimi, Seyyed Abbas Atyabi, Ilija Uzelac, and Ali Ghaffari. "Estimation of extent damage tissue by multi resolution analysis of the electrocardiogram and arterial blood pressure." In *2015 Computing in Cardiology Conference (CinC)*, pp. 1113-1116. IEEE, 2015.

9. Farhad Asadi, **Mohammad Javad Mollakazemi**, Shadi Ghiasi, and S. Hossein Sadati. "Enhancement of life-threatening arrhythmia discrimination in the intensive care unit with morphological features and interval feature extraction via random forest classifier." In *2016 Computing in Cardiology Conference (CinC)*, pp. 57-60. IEEE, 2016.

10. Farhad Asadi, **Mohammad Javad Mollakazemi**, I. L. I. J. A. Uzelac, and S. Ali A. Moosavian. "A novel method for arterial blood pressure pulse detection based on a new coupling strategy and discrete wavelet transform." In *2015 Computing in Cardiology Conference (CinC)*, pp. 1081-1084. IEEE, 2015.

11. Farhad Asadi, **Mohammad Javad Mollakazemi**, Seyyed Abbas Atyabi, I. L. I. J. A. Uzelac, and Ali Ghaffari. "Cardiac arrhythmia recognition with robust discrete wavelet-based and geometrical feature extraction via classifiers of SVM and MLP-BP and PNN neural networks." In *2015 Computing in Cardiology Conference (CinC)*, pp. 933-936. IEEE, 2015.

12. Mostafa Abdollahpur, Shadi Ghiasi, **Mohammad Javad Mollakazemi**, and Ali Ghaffari. "Cycle selection and neuro-voting system for classifying heart sound recordings." In *2016 Computing in Cardiology Conference (CinC)*, pp. 1-4. IEEE, 2016.

13. Ali Ghaffari, SeyyedAbbas Atyabi, **Mohammad Javad Mollakazemi**, Mohammad Niknazar, Maryam Niknami, and Ali Soleimani. "PhysioNet/CinC Challenge 2013: a novel noninvasive technique to recognize fetal QRS complexes from noninvasive fetal electrocardiogram signals." In *Computing in Cardiology 2013*, pp. 293-296. IEEE, 2013.

Abstracts:

1. **MJ Mollakazemi**, D Biswal, S Thyagarajan, J Evans, A Patwardhan, "Cerebro-cardiac and Cerebro-respiratory Interactions while Listening to Songs", BMES 2017, October 11-14, 2017, Phoenix, AZ.

2. **MJ Mollakazemi**, D Biswal, S Thyagarajan, J Evans, A Patwardhan, "Effects of Phase Randomization, Tempo and Cognition of Songs in Cardiac Synchronous EEGs", BMES 2018, October 17-20, 2018, Atlanta, GA.

3. **MJ Mollakazemi**, D Biswal, B Palace, A Patwardhan, "Effects of Respiratory Pathway on Processing of Emotions, Autonomic and Brain Response", BMES 2020, October 14-17, 2020, San Diego, CA.

4. **MJ Mollakazemi**, D Biswal, S Thyagarajan, J Evans, A Patwardhan, “Cerebro-cardiac and Cerebro-respiratory Interactions while Listening to Songs”, Cardiovascular Research Day 2017, November 3, 2017, Lexington, KY.

5. **MJ Mollakazemi**, D Biswal, J Evans, A Patwardhan, “Cardiac-synchronized EEG: Effects of Cognition and Tempo of Music”, Cardiovascular Research Day 2018, September 2018, Lexington, KY.

6. **MJ Mollakazemi**, D Biswal, A Patwardhan, “Effects of Cognition and Tempo of Music on Cardiac-synchronized Electrical Response of Brain”, Cardiovascular Research Day 2019, September 2019, Lexington, KY.

7. **MJ Mollakazemi**, D Biswal, A Patwardhan, “Frequency Response of Brain Electrical activity to Cognition and Tempo of Music”, CCTS 2019, April 2019, Lexington, KY.

8. **MJ Mollakazemi**, D Biswal, A Patwardhan, “The Effects of Tempo and Cognition of Songs using Eigenvalue Analysis of Covariance Matrix”, CCTS 2018, April 2018, Lexington, KY.

9. D Biswal, **MJ Mollakazemi**, S Thyagarajan, J Evans, A Patwardhan, “Auditory Entrainment of Autonomic Rhythms”, CCTS 2017, Lexington, KY.

10. **MJ Mollakazemi,** M Rafat, R A Alaee, “Investigation of principals of movement of the piston and dynamical optimization of its effects on the amount of leakage of oil and gas”, *National Conference of internal combustion motors, Semnan, Iran, 2012*.

Books:

One of the co-authors of “Book of the 2014 Year: The Iranian Society of Mechanical Engineers”, 2014

Research/Work Experience

Cardiac Rhythm Lab, University of Kentucky, KY (2016-2021)

Graduate Research Assistant

- Investigating autonomic changes from auditory sensory stimulation
- Designing and conducting experiments on human subjects
- Extensive analysis/recording of EEG, ECG, Blood Pressure and Respiratory data
- Evaluation of human emotion response
- Writing Institutional Review Board (IRB) applications for two different studies

***Cardiovascular Research Group*, K.N.Toosi University of Technology, Tehran, Iran (2012-16)**

Graduate Research Assistant

- *Heart attack prediction*
- *Fetal Electrocardiogram signals analysis*
- *Cardiac Arrhythmia Recognition using artificial intelligence*
- *Heartbeat detection in multimodal data by developing a novel method*
- *ST Segment measurement in adults holter electrocardiogram signals*
- *Frequency analysis of biomedical data series by discrete wavelet transform*
- *Development of an algorithm for change point detection in time series in various conditions*

Teaching Experiences

College of Engineering, University of Kentucky, KY (2018-19)

- *Teaching Assistant: Assisting students in building circuits, Arduino, and MATLAB programming*

Islamic Azad University, Parand Branch, Tehran (2014-16)

- Teaching Assistant of Mathematics (Engineering Mathematics, Differential equation, General Mathematics 1 and 2)

Semnan University, Semnan (2011-12)

- Teaching Assistant of Mathematics (General Mathematics 1 and 2)
- Tutoring Mathematics, Technical Mechanical Engineering courses, and Catia

Leadership Experience

- University of Kentucky:
  - ✓ *President of Biomedical Engineering Society (2019-2020)*
  - ✓ *Representative of Dep. of Biomedical Engineering at Graduate Student Congress*
  - ✓ *Member of Partnership Committee in Science Olympians*
  - ✓ *Member of Award Committee in Graduate Student Congress*
- Leader of two groups of researchers in PhysioNet/CinC Challenges in 2013 and 2016

Computer Skills

- **Computer Programming:** MATLAB - Python - C++
- **Scientific Applications:** Artificial Intelligence - Artificial Neural Networks - Machin Learning - Deep Learning – NLP - SVM - PNN - MLP-BP - RFC - RNN - RBF - Time Series Analysis - FDA - LDA - Computer Vision – Data Mining - Pattern Recognition - Data Visualization - Microsoft Office (Word, Excel, PowerPoint) - MATLAB/Simulink

- **Data Tools:** Pandas – Tensorflow – NumPy – Matplotlib – OpenCV – SciPy
- **Cloud Platforms**: Azure Microsoft
- **Technical and Engineering Designing Software:** Catia, SOLIDWORKS

Certificates

- Computer Numerical Control (CNC)
- Business Entrepreneurship (complete level)
- Production Management
- Job Preparation
- Essential skills in work environment
- Geometrical Dimensions and Tolerances (GD&T)
- CATIA Level 1
- CATIA Level 2
- CATIA Advanced
- SOLIDWORKS
- Geomagic
- Rapidform - Level 1
- Rapidform - Level 2
- Plastic Injection Mold Designing - Level 1
- Plastic Injection Mold Designing - Level 2
- Weld Inspection
- Ecotourism and Nature
- ICDL1
- ICDL2