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Synchronization of Autonomic and Cerebral Rhythms During Listening to Music: Effects of Tempo and Cognition of Songs

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Summary

A large number of studies document cardiorespiratory changes occurring while listening to music. Less is known, however, about the interaction between cardiorespiratory and cerebral electrical rhythms during listening to music and how cognition and acoustic structural aspects of songs influence that interaction. We focused on tempo as a structural feature of songs, since tempo is a major determinant of physiological responses to music, and on familiarity and randomization of phase of local spectra of known and unknown songs for cognition. Our results indicated an overall increase in the degree of synchronization among cardiorespiratory variables (Heart rate (RR), systolic and diastolic blood pressure (SBP, DBP), respiration) and between cardiorespiratory and cerebral (EEG) oscillations during all songs. We also observed a marked decrease in respiratory frequency bandwidth and increase in respiratory rate while listening to songs, and slow song produced the most periodic breathing. Compared with slow tempo, during fast song, DBP and cerebral oscillations became less synchronized with high frequency components of RR suggesting that the processes causing the previously known reduction in vagal activity with increase in tempo also may have caused the decrease in these synchronizations. Cognition of songs affected the SBP coherencies the most. DBP was synchronized with respiration more than all other measured variables in response to auditory stimuli. Results indicate an overall increase in the degree of synchronization among a variety of cerebral electrical and autonomically driven cardiovascular rhythms. It is possible that this significant increase in synchronizations underlies the widely reported pleasurable and palliative effects of listening to music.

Key words

Synchronization • Autonomic and cerebral rhythms • Tempo • Cognition • Music

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Introduction

Listening to music can induce emotional and physiological changes. Increasing recognition of the palliative effects of music (Bringman *et al.* 2009, Gelinas *et al.* 2013, Trappe 2012) has led to its use as an adjuvant therapeutic tool in the treatment of various diseases (Mansky and Wallerstedt 2006, Särkämö *et al.* 2008). Previous studies have shown that the rhythmic components of music do affect and entrain cardiovascular autonomic regulation (Bernardi *et al.* 2009, Bernardi *et al.* 2006), including regulation of BP (Hanser and Mandel 2005, Pitzalis *et al.* 1998). Increase in parasympathetic nervous activity is observed during listening to sedative music or slow tempo songs (Okada *et al.* 2009) while increase in sympathetic nervous activity is observed during listening to pleasurable music (Salimpoor *et al.* 2009, Zatorre and Salimpoor 2013) or songs with higher tempo (Bernardi *et al.* 2006). A review of the effects of music on the autonomic nervous system

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is provided by Ellis *et.al* (Ellis and Thayer 2010). Neuronal coherence, which is hypothesized to serve as a neural communication mechanism, can be dynamically modulated by cognitive demands (Fries 2005). Because of this dynamic modulation of neural coherence and changes in autonomic nervous system induced by music, we used coherence to investigate how neural electrical oscillations and autonomic mediated rhythms in respiratory and cardiovascular regulation change 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 (Haas *et al.* 1986). There are not many studies, however, focusing on respiratory frequency bandwidth (RFB) changes, in addition to those in respiratory frequency during listening to music. The RFB reflects how periodic and less variable the respiratory pattern is.

Several studies have reported that tempo of music is a major determinant of physiological changes induced by music compared to other acoustic features (Etzel *et al.* 2006, Gomez and Danuser 2007). This observation is the reason why one of the features that we focused on in this study was tempo of songs. 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 includes cognitional contribution resulting from memory association and recall. In this study, we attempted to separate the effects induced by an acoustical aspect of music, i.e. the purely sensory component, from that resulting from the cognitional component. 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 memory recall and its associated effects triggered by the music. In the present study, 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 way that LPR of the favorite song is recognizable for the subjects but is not recognizable for the unknown song even though the subjects had heard it before hearing its LPR. In summary, our study was designed to answer the following questions: Does the coherence among autonomic mediated cardiorespiratory rhythms and cerebral electrical oscillations change during listening to music? How do the tempo and cognition of songs alter these coherencies? And how do these affect respiratory frequency and bandwidth?

Methods

All study procedures were approved by the Institutional Review Board (IRB) at the University of Kentucky (IRB protocol number: 16-0140-P3H).

Participants

A total of healthy 14 subjects participated in the study (7 males and 7 females, ages 18-37 years). Table 1 includes details of subject demographics. Subjects gave written informed consent prior to participation in the study. The consent form was also approved by the IRB at the University of Kentucky. The exclusion criteria were: age<18 years or >37 years, pregnancy; hypertension; history of epilepsy or seizures; photosensitivity; adverse reaction after listening to certain music, songs or sounds; psychotropic drug use that could affect alertness or cognitive functions.

Measurements:

The following measurements were made: 6 channels of EEG (locations F3, F4, P3, P4, T3 and T4, Biopac), ECG (Lead II, Spacelabs), non-invasive finger plethysmographic continuous BP (Finapres/Portapres), and respiration using thoracic and abdominal inductance bands (Inductotrace). These data were digitized on line at a rate of 1000 samples/second using a commercial data acquisition system (Dataq). A synchronization pulse was also digitized along with these data to align them with the music that was played at a much higher rate (22050 samples/second, mono) using a different computer. Subjects listened to the music through a pair of circumaural headphones. The volume was set to a level that was comfortable to the subject.

Table 1. Subject demographics

Number of subjects	14 (7 female)
Age (years)	27.33 ± 4.25
Body Mass Index (kg/m^2)	22.77 ± 2.75*

* Two subjects were a few pounds overweight (26<BMI<27)

Study design and setting

On the day of study, subjects were seated in a comfortable chair with a slight recline in a room with normal indoor temperature and humidity levels used in the building. A short internet-based hearing acuity test ('Online Hearing Test and Audiogram Printout') was administered to each subject to rule out overt hearing loss. After this test, subjects were instrumented to make measurements. Before the experiment, subjects were asked to provide a song of their choice that "moved" them the most and was their favorite song. The fast and slow tempo vocal songs were selected in Italian language since none of the subjects understood Italian. Mindful of the total study duration, the fast song was chosen in a way that was unknown to all subjects, so it played the role of both fast song and unknown song. For cognitive evaluation, the favorite song and the unknown song (fast song) were processed for local phase randomization (LPR, as described below) to generate LPR-favorite and LPR-fast songs. After subjects listened to the LPR songs, they were asked whether they realized the original version of the song or not. Therefore, a total of five songs (S1-S5) were played for each subject: slow tempo, fast tempo, favorite, LPR-fast and LPR-favorite. The sequence of songs was randomized among subjects and in 12 subjects the protocol was repeated. There was a 10-min control (no music with no headphone over ears) at the beginning and at the end of the study. The subjects were asked to keep their eyes closed during listening to songs and while recording controls. The total study duration, including instrumentating the subjects, was about 2 hours. The schematic of the study protocol is shown in Fig. 1.

Data analysis

The peaks of the R waves from the ECGs were identified from which RR intervals were computed. The peaks and nadirs related to beat by beat systolic and diastolic (SBP and DBP) pressures were also detected. In all trials, the R-peak, SBP, and DBP detections were manually verified to avoid possible errors in computations. The beat by beat RR intervals, SBP and DBP values were assumed to remain constant during that particular beat to generate piece-wise constant RR interval, SBP and DBP time series. The abdominal and thoracic inductotrace signals were added to create a single respiratory signal. The *envelope* function in *Matlab* was used to compute the envelopes of the EEGs. The envelopes, respiration and piecewise constant RR, SBP, and DBP were low-pass filtered with a cutoff frequency of 5 Hz and sub-sampled at a rate of 10 samples/second. These sub-sampled time series were used for further analyses. Whenever a segment of the study was repeated, the data from both segments were included in the analysis. Auto and cross spectra were computed using Welch's method with 100 second segments, a Hanning window and 50 % overlap. Mean squared coherence (MSC) was computed as the ratio of the squared cross spectrum divided by the two autospectra. Respiratory bandwidths were computed as the width of a symmetric band centered at the peak of the repsiratory spectrum and within which 80 % of the respiratory spectral power was contained.

Statistical analysis

A paired t test was used to test for statistical significance, a difference was considered significant for $p<0.05$. To measure the effect of size of each song on coherencies, Cohen's d effect size was also computed, and $d=0.2$, 0.5 and 0.8 were considered small, medium and large effect sizes.

Local phase randomization for the songs

Digitized songs (mono), sampled at 22,050 samples/second, were divided into 3-sec long segments with 50 % overlapping tapered windows. The windows were selected such that the sum of the windows within the overlap was unity which ensured that when the phase randomized segments were patched together using overlap and add to reconstruct the song in the time domain, there was no variation in amplitude between segments. Each segment was converted to the frequency domain and its phase component was randomized while the maginitude was unchanged. Appropriate symmetry was maintained in the frequency domain. The phase

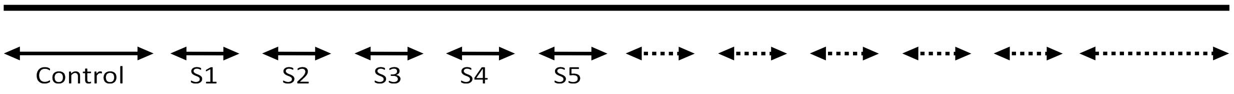

Fig. 1. Schematic of the experimental protocol. Data were collected during 10 minutes of control and during 5 periods (S1-S5) when subjects listened to five different types of songs; slow tempo, fast tempo, a song of the subjects' choosing, and phase randomized versions of the fast tempo and the subjects' selected songs. In 12 subjects (out of 14) the song sequences, including the control, were repeated as shown by dashed lines. An approximate 2-minute period occurred between songs and between control and songs. The sequence of songs was randomized among subjects.

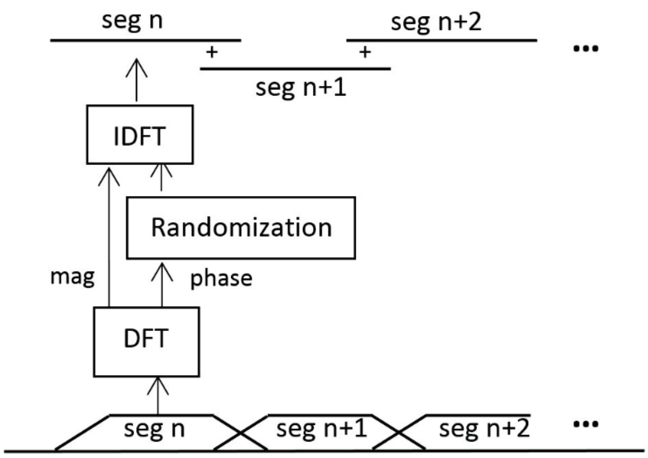

Fig. 2. Schematic of the local phase randomization (LPR) process used for songs. The process consisted of transferring each segment (seg) from time domain to frequency domain by Digital Fourier Transform (DFT), randomizing the phase while keeping the magnitude (mag) the same and transferring back to the time domain by inverse DFT (IDFT).

Table 2. Mean values computed from the entire duration of control and of each song of all subjects (n=14)

	Control	Slow	Fast	Favorite	LPR-Fast	LPR-Favorite
Heart Rate (bpm)	73	73	74	74	74	74
Systolic Blood Pressure (mmHg)	136	130	124	134	126	131
Diastolic Blood Pressure (mmHg)	77	73	70	77	73*	75
Respiratory frequency (Hz)	0.31	0.32*	0.33*	0.33*	0.31	0.32*
Respiratory bandwidth (Fw)	0.16	0.068*	0.09*	0.087*	0.112	0.088*

*denotes that the mean was significantly ($p<0.05$) different from Control. The reported values are the mean values over both periods, e.g. in subjects where the study was repeated the mean values reported during Control are the average of the two Control periods.

Fig. 3. Schematic of cognitive responses during four auditory stimuli. This construct was used when comparing the effects of all these four songs together.

randomized frequency domain segments were converted back into the time domain and the segments were patched together to create the local phase randomized (LPR) version of the songs which were played through the media player on the computer. Fig. 2 shows a schematic of the randomization process.

Results

Table 2 shows the mean values of the following measurements for all subjects: HR, SBP, DBP, respiratory rate and respiratory bandwidths during different parts of the study. For ease of visualization of the results within the overall framework of the study, a schematic that depicts the different cognitive responses is shown in Fig. 3. An increase in respiratory frequency was seen when subjects listened to all songs except during the fast randomized song. A pronounced reduction in respiratory bandwidths was seen when subjects listened to songs, all reductions except during the fast randomized song were statistically significant at a level of $p<0.05$. The table shows that in most cases the bandwidths were smaller by about 50 %. Fig. 4 shows examples of respiratory spectra from a subject during control, slow and fast tempo songs. The figure shows that respiration was more regular (less variable) while listening to songs.

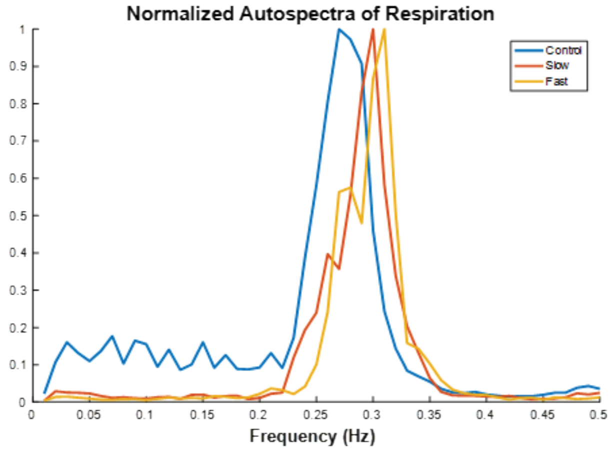

Fig. 4. An example of change in respiratory frequency and narrowing of respiratory bandwidths from one subject.

RR and systolic blood pressure interaction

Compared to control, all songs caused significant increases of between 28 % and 46 % in coherence between RR-SBP integrated over 0-0.4 Hz band ($p<0.058$), shown in Fig. 5. However, the changes within the individual LF (0.01-0.15 Hz) and HF (0.15-0.4 Hz) bands were not significant except for LPR of the fast song. LPR of the fast tempo song (LPR-fast) caused an increase in mean RR-SBP coherence over LF region (38 % increase, $p=0.022$) compared to the fast song. This increase also resulted in a 51 % increase in LF/HF ratio (from 1.19 to 1.8, $p=0.024$). On the other hand, the change during LPR of the favorite song (LPR-favorite) was different from LPR-fast. LPR-favorite compared to its original version caused non-significant changes: in opposite direction than of LPR-fast over LF (4.7 % decrease, NS) and very small change for LF/HF ratio (0.19 %, NS).

RR and diastolic blood pressure interaction

The fast tempo song caused a significant decrease in RR-DBP coherence over HF band (24 %, $p<0.05$) compared to the slow tempo song. Among all songs, the slow tempo and LPR- favorite songs caused the most significant increase over total band (0-0.4Hz) RR-DBP coherence (change>53 %, $p<0.04$). The average coherencies between RR intervals and blood pressure are shown in Fig. 5.

RR-respiratory rhythm interaction

All the songs caused significant increase in RR-Respiration coherence over the total band. These increases in descending order were: LPR-favorite song (51 %, $p<0.005$), fast tempo (47 %, $p=0.02$), slow tempo (45 %, $p=0.009$), favorite song (37 %, $p=0.006$), LPR-fast song (26 %, $p=0.042$). None of the changes within individual LF and HF bands were significant. The average coherencies are shown in Fig. 6. As seen from the figure, the pronounced changes in coherence were due to a change in respiratory frequency and the corresponding shift in the peak of coherence.

SBP-respiratory rhythm interaction

All songs caused significant increases in SBP-respiration coherence over the LF band (change >48 %, $p<0.05$). Comparing the favorite song and its LPR version, SBP-respiration coherencies in the LF region were similar (change=0.5 %, $p=0.48$) but within the HF band, the coherence was 18 % higher for favorite song ($p=0.014$) and consequently, the LF/HF ratio in coherence was 37 % lower for favorite compared to its LPR version ($p=0.045$).

DBP-respiratory rhythm interaction

All songs resulted in significant increases in DBP-respiration coherence over the LF, HF and total bands (LF and HF together). Eleven out of fifteen (5 songs x 3 frequency bands) comparisons were significant ($P<0.05$) and the other four were close to significance ($0.05<p<0.069$) with changes ranging between 29 % and 110 %. While listening to music, DBP became coherent with respiration more than all other variables.

Cerebro-RR interaction

During listening to all songs, cerebro-RR coherencies in the HF band increased when compared with control. Out of 30 comparisons (5 songs x 6 EEGs), 27 of these increases were statistically significant (change >32 %, $p<0.037$). Comparing slow and fast tempo songs, the slow song had higher cerebro-RR coherence in HF band in all EEG locations, but the change was statistically significant only in frontal lobe (change >32 %, $p<0.039$). It is possible that decrease in cerebro-RR coherencies in HF band during fast tempo song is a result of reduced parasympathetic dominance when the song is faster in tempo (Bernardi *et al.* 2006).

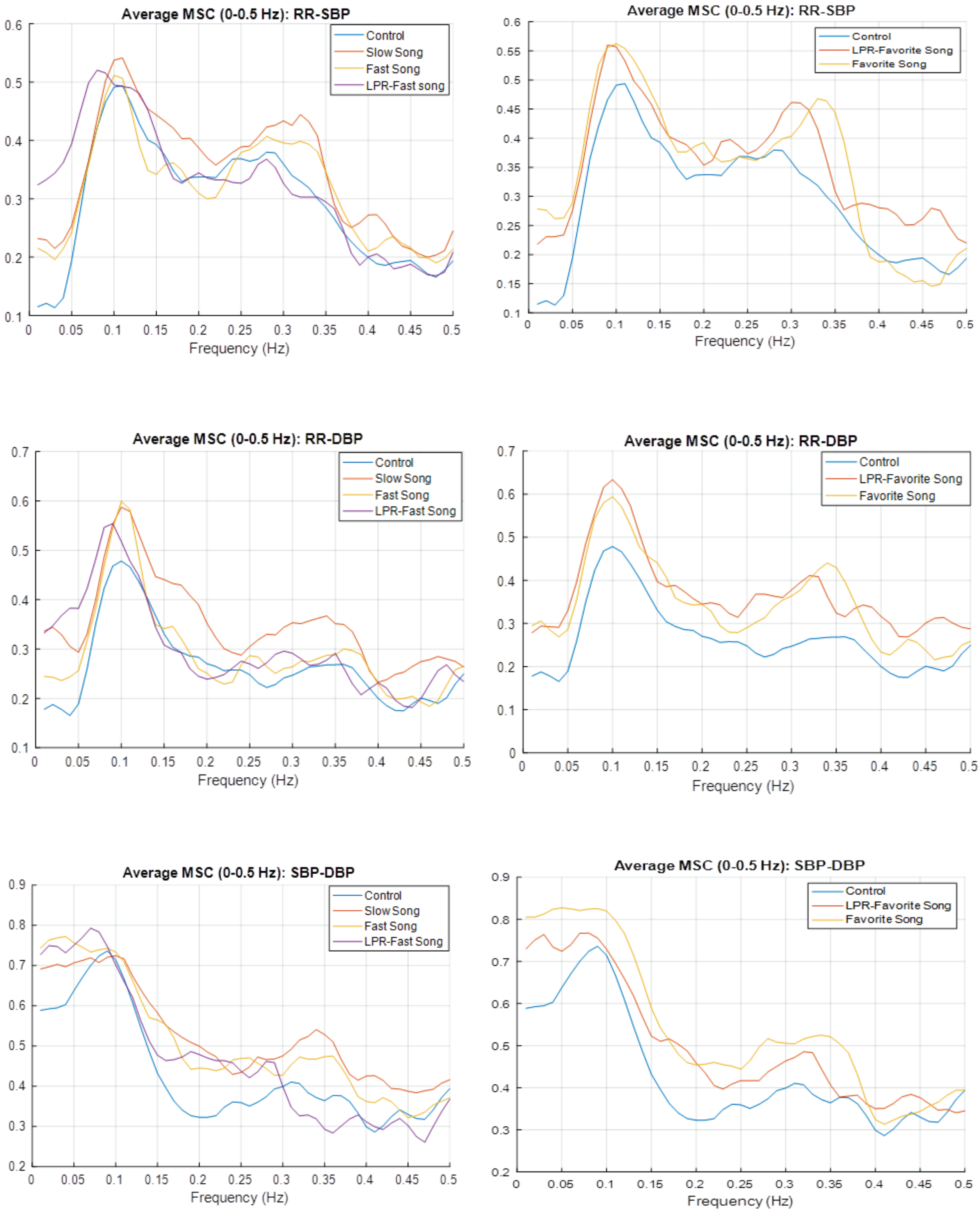

Fig. 5. Average coherencies among RR interval, SBP and DBP while listening to music: results on the left are for slow tempo, fast and fast randomized songs all of which were unknown to the subjects; On the right are coherencies for the subjects' favorite song and its phase randomized version. In case of the LPR-fast songs, coherence was only computed from 11 subjects because it was added to the experiment protocol after experiment number 3.

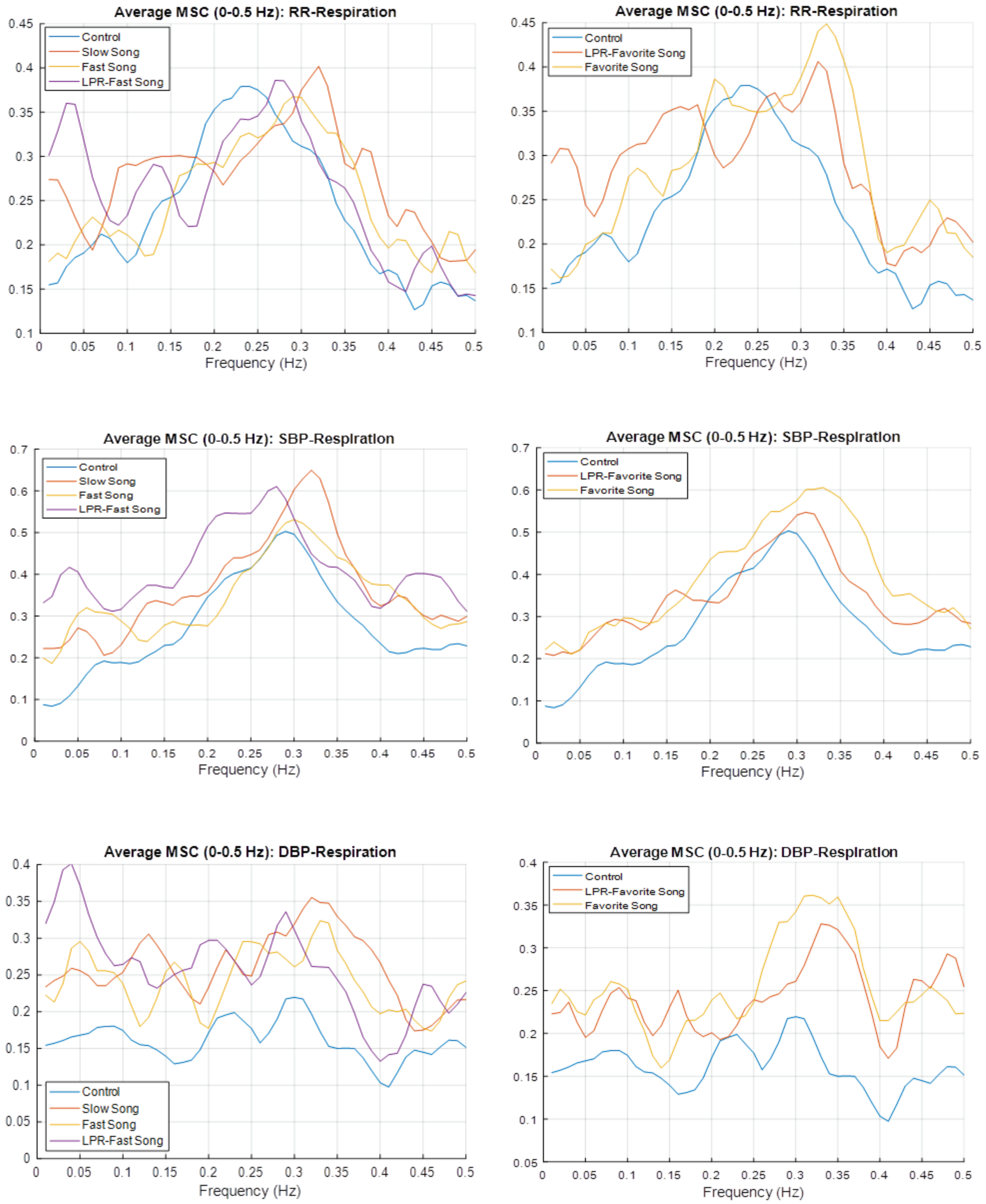

Fig. 6. Average coherencies between RR, SBP and DBP and respiration while listening to music: results on the left are for slow tempo, fast and fast randomized songs all of which were unknown to the subjects; On the right are coherencies for the subjects' favorite song and its phase randomized version. In case of the LPR-fast songs, coherence was only computed from 11 subjects because it was added to the experiment protocol after experiment number 3.

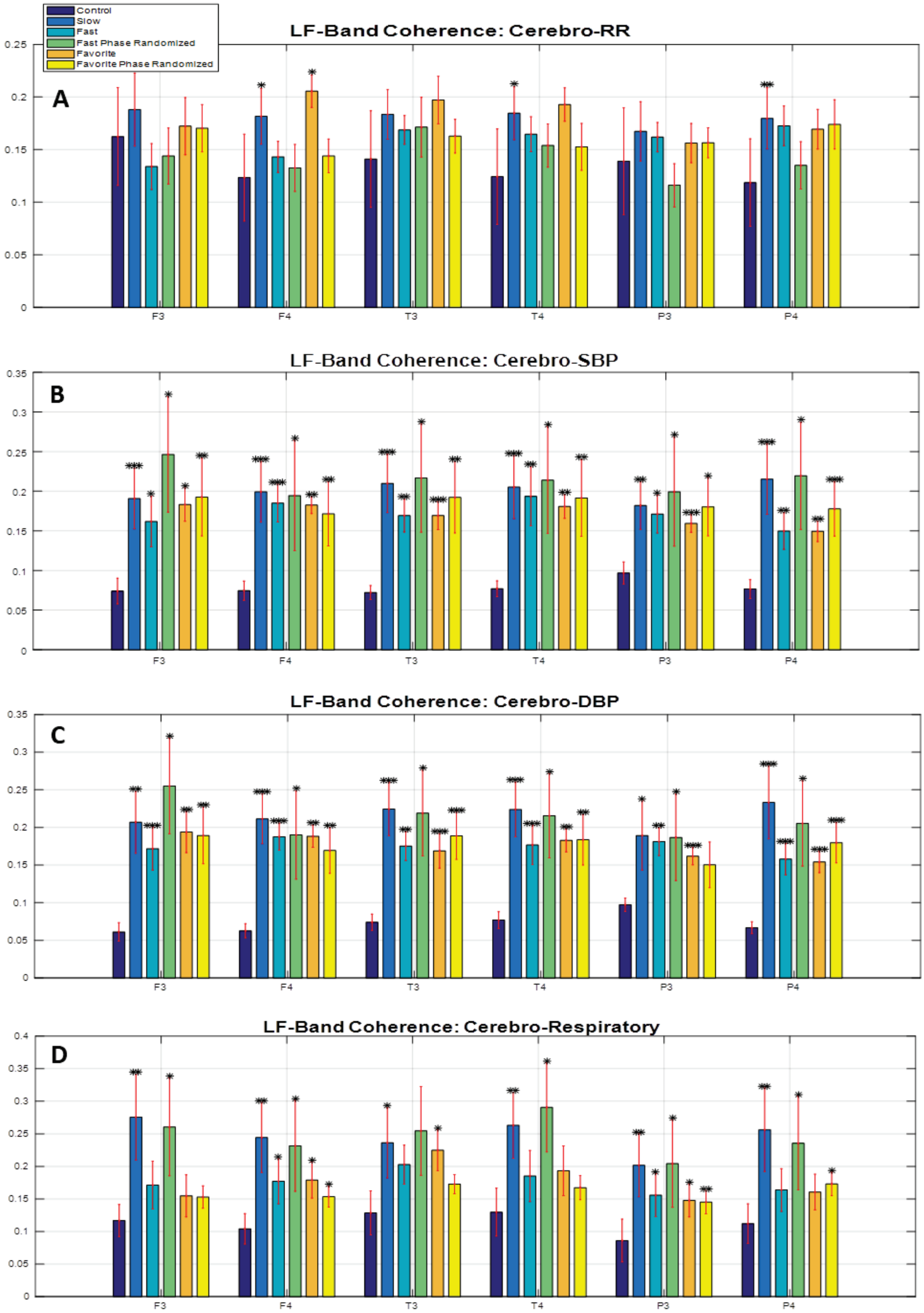

Fig. 7. Average coherencies in LF band in cerebral electrical oscillations with RR, SBP and DBP while listening to music (***: p<0.001, **: p<0.01, *: p<0.05).

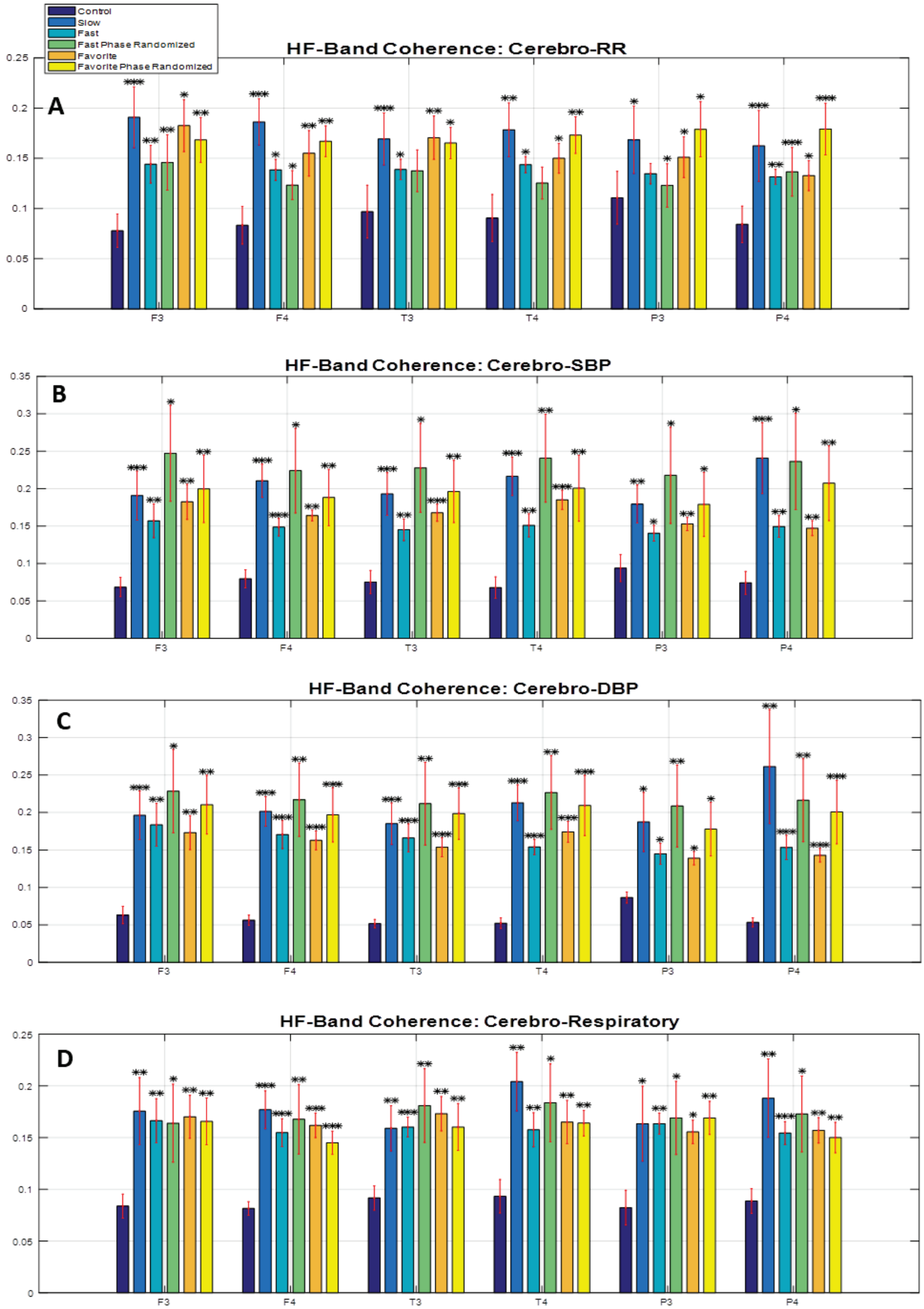

Fig. 8. Average coherencies in HF band of cerebral electrical oscillations with RR, SBP and DBP while listening to music (***: $p<0.001$, **: $p<0.01$, *: $p<0.05$).

Most changes of cerebro-RR coherencies in LF band were not significant, except for the slow and favorite songs. The slow song caused a significant increase in coherence within EEGs recorded from the right hemisphere (change >47 %, p<0.043). The largest change in cerebro-RR coherencies over LF band was for the favorite song in F4 (change=66 %, p=0.033). There were no significant differences between LPR songs and their original versions over both LF and HF bands, except that the LPR-favorite song caused a significant increase in the HF band in EEG from P4; but this increase was not seen when comparing unknown (fast) song and its LPR version, possibly explained by a lack of recognition of that particular song.

Cerebro-SBP interaction

For all EEGs, over the LF and HF bands, all songs caused significant increase in cerebro-SBP coherence. These changes are shown in Fig. 7B and 8B. By comparing fast and slow songs, the effect of tempo was seen in all EEGs (except from F3) within the HF band: with an increase in tempo (slow to fast) the cerebro-SBP coherence in the HF band decreased (decrease >27 %, p<0.032). The effect of LPR was not significant for the favorite song, but it caused a significant increase in cerebro-SBP coherencies in the HF band for the fast song in all EEGs (change >68 %, p<0.065). The similar synchronization of SBP with EEG oscillations while listening to favorite and LPR-favorite songs and totally different synchronization of SBP with EEG oscillations while listening to the fast and LPR-fast songs could be a consequence of recognition of the original version of LPR-favorite song, but not of LPR-fast song.

Cerebro-DBP interaction

Similar to cerebro-SBP coherence, all songs caused significant increase in cerebro-DBP coherence, for all EEGs, over both LF and HF bands. These results are shown in Fig. 7C and 8C. The effect of tempo was observed by comparing fast and slow songs: during the slow song, cerebro-DBP coherence over HF band in EEG from T4 was higher (change =38 %, p=0.035) and from P4 (change =70 %, p=0.04) compared with the coherence during the fast song.

Cerebro-Respiratory interaction

For all EEGs, over the HF band, all songs caused a significant increase in cerebro-respiratory coherencies as shown in Fig. 8D. For LF band, only the slow song caused significant increase in all EEGs (change >83 %, p<0.031).

Effect size

For all the coherencies shown in Figs. 5 to 8, the Cohen's d effect size was computed, and the computed d are listed in Table 3 to show how much was the size of effect of each song over LF, HF and total bands. The effect sizes show that most of the increases in coherencies triggered by songs had medium or large effect size. In most of synchronizations with EEGs (106 out of 120 coherencies) the effect size over LF band was smaller than HF band while for most of parameters other than EEGs (21 out of 30 coherencies) the effect sizes of LF band were larger than HF band. In addition, the average effect size of the slow song was larger than all other songs and the LPR-fast song had the smallest size effect on average.

Discussion

The main observation of our study was an overall increase in coherence, which indicates degree of synchronization, among cerebral, cardiovascular and respiratory rhythms while listening to music. Further, we observed that listening to music decreased RFB, showing that the respiratory pattern becomes less variable and more uniform than silence. Systolic and diastolic blood pressures were not significantly changed during listeing to music but significant changes in their synchronization with other rhythms were obsereved.

The leading acoustical feature of msuic, which is known to have a pronounced effect on physiological variables, is tempo of the songs (Gomez and Danuser 2007), which led us to select two songs with different tempo (fast and slow). To investigate effects of cognition, we used LPR of a song that was very well known to the subjects and of a song that was not known to them and their originl versions. In consideration of the total study duration, we decided to choose fast song in a way that was unknown for all subjects and used LPR-fast as LPR of the unknown song. We were aware that humans do a fairly good job of compensating for phase variations and thus did not expect substantial differences between a song and its LPR version. However, the LPR approach provided a signal analysis based and objective approach to alter the songs while keeping their amplitude spectrum constant to alter cognitive response rather than

Table 3. Effect sizes of each song on all measured coherencies over low frequency band (LF: 0.01-0.15 Hz), high frequency band (HF: 0.15-0.4 Hz) and total band (TB: 0.01-0.4 Hz). d<0.5: small effect size, 0.5<d<0.8: medium effect size (in yellow), d>0.8: large effect size (in green). *Averages of six effects sizes in each category of MSCs for each song and frequency band.

Song	**Slow**			**Fast**			**Favorite**			**LPR-Favorite**			**LPR-Fast**		
MSC coherence	**LF**	**HF**	**TB**	**LF**	**HF**	**TB**	**LF**	**HF**	**TB**	**LF**	**HF**	**TB**	**LF**	**HF**	**TB**
RR_SBP	0.28	0.27	0.72	0.01	0.1	0.5	0.57	0.25	0.64	0.4	0.27	0.67	0.43	0.15	0.41
RR_DBP	0.55	0.47	0.68	0.3	0.11	0.3	0.61	0.47	0.5	0.77	0.49	0.61	0.21	0.05	0.19
SBP_DBP	0.44	0.58	0.55	0.39	0.46	0.4	1.05	0.55	0.48	0.41	0.37	0.4	0.34	0.93	0.94
RR_Resp	0.47	0.14	0.59	0	0.08	0.57	0.32	0.4	0.49	0.61	0.22	0.59	0.66	0.02	0.46
SBP_Resp	0.77	0.39	0.66	0.66	0.16	0.66	0.74	0.6	0.65	0.69	0.24	0.8	0.93	0.3	0.49
DBP_Resp	0.92	0.93	1.1	0.67	0.77	1	0.52	0.96	0.97	0.47	0.62	1.25	0.7	0.67	0.83
Average*	**0.57**	**0.46**	**0.72**	**0.34**	**0.28**	**0.57**	**0.63**	**0.54**	**0.62**	**0.56**	**0.37**	**0.72**	**0.55**	**0.35**	**0.55**
RR_F3	0.15	1.07	1.15	0.2	0.83	0.93	0.06	0.79	0.89	0.05	0.87	0.92	0.1	0.62	0.77
RR_F4	0.54	1.26	1.93	0.2	0.85	1.67	0.71	0.9	1.28	0.21	1.07	1.47	0.06	0.61	1.33
RR_T3	0.38	0.85	1.64	0.23	0.65	1.43	0.51	0.84	1.36	0.2	0.75	1.23	0.26	0.44	1.13
RR_T4	0.54	0.95	1.76	0.36	0.83	1.53	0.6	0.78	1.24	0.26	0.95	1.38	0.25	0.42	1.38
RR_P3	0.23	0.53	0.73	0.2	0.26	0.5	0.15	0.35	0.61	0.15	0.6	0.72	0.17	0.38	1.07
RR_P4	0.56	0.91	1.68	0.52	0.94	1.75	0.45	0.73	1.28	0.5	1.22	1.53	0.19	0.72	1.29
Average*	**0.4**	**0.93**	**1.48**	**0.28**	**0.73**	**1.3**	**0.41**	**0.73**	**1.11**	**0.23**	**0.91**	**1.21**	**0.17**	**0.53**	**1.16**
SBP_F3	1.02	1.19	1.41	0.81	0.95	1.13	0.88	1.06	1.14	0.79	0.97	1.22	0.69	0.83	1.03
SBP_F4	1.45	1.99	2.89	1.75	1.43	2.66	1.2	1.13	1.65	1.08	1.24	2.14	0.69	1.08	1.94
SBP_T3	1.7	1.57	2.6	1.23	1.41	2.14	1.93	1.66	2.23	1.2	1.24	2.13	0.84	1.02	1.68
SBP_T4	1.46	2.05	2.58	1.29	1.58	2.08	1.45	1.69	1.66	1.11	1.35	1.81	0.83	1.17	1.74
SBP_P3	0.93	0.99	1.04	0.81	0.59	0.72	0.69	0.75	0.82	0.82	0.73	0.87	0.76	0.9	1.61
SBP_P4	1.4	1.61	2.61	1.25	1.42	2.17	1.45	1.3	1.92	1.28	1.16	1.89	0.85	1	1.71
Average*	**1.33**	**1.57**	**2.19**	**1.19**	**1.23**	**1.82**	**1.27**	**1.27**	**1.57**	**1.05**	**1.11**	**1.68**	**0.78**	**1**	**1.62**
DBP_F3	1.23	1.32	1.42	1.16	1.18	1.14	1.08	1.14	1.19	0.96	1.2	1.25	0.92	0.88	1.01
DBP_F4	1.89	2.6	2.78	2.28	2.09	2.34	1.36	1.71	1.82	1.48	1.66	2.33	0.91	1.41	1.98
DBP_T3	1.87	1.85	2.56	1.31	2.27	2.21	1.66	2.39	2.47	1.61	1.75	2.24	1.03	1.2	1.86
DBP_T4	1.65	2.26	2.36	1.51	2.05	1.87	1.55	1.82	1.68	1.36	1.67	2.11	1.03	1.43	2.02
DBP_P3	0.72	0.86	0.88	0.81	0.62	0.62	0.59	0.59	0.61	0.49	0.8	0.7	0.88	1.17	1.78
DBP_P4	1.62	1.32	2.28	1.7	2.43	2.52	1.83	1.95	2.06	1.76	1.56	2.38	1.04	1.21	1.98
Average*	**1.5**	**1.7**	**2.05**	**1.46**	**1.78**	**1.78**	**1.35**	**1.6**	**1.64**	**1.28**	**1.44**	**1.83**	**0.97**	**1.22**	**1.77**
Resp_F3	0.83	0.92	1.1	0.43	0.75	0.88	0.31	0.75	0.93	0.31	0.83	0.98	0.64	0.71	0.92
Resp_F4	1.11	1.89	2.21	0.79	1.34	1.67	0.88	1.3	1.61	0.63	1.39	2.09	0.79	1.18	1.87
Resp_T3	0.8	1.17	1.26	0.69	1.61	1.19	0.89	1.23	1.27	0.45	1.14	1.44	0.72	1.07	1.07
Resp_T4	1	1.43	1.51	0.48	1.21	1.08	0.53	1.12	1.17	0.39	1.26	1.5	0.92	1	1.04
Resp_P3	0.93	0.96	1.33	0.71	1.36	1.13	0.65	1.03	1.19	0.69	1.26	1.39	0.67	0.94	0.94
Resp_P4	0.96	1.15	1.48	0.5	1.5	1.22	0.47	1.31	1.36	0.57	1.18	1.49	0.75	1	1.33
Average*	**0.94**	**1.25**	**1.48**	**0.6**	**1.29**	**1.19**	**0.62**	**1.12**	**1.25**	**0.51**	**1.18**	**1.48**	**0.75**	**0.99**	**1.19**
Average over all coherencies	**0.95**	**1.18**	**1.58**	**0.77**	**1.06**	**1.33**	**0.86**	**1.05**	**1.24**	**0.72**	**1**	**1.38**	**0.64**	**0.82**	**1.26**

a subjective selection of a different song with comparable acoustic features. Upon speaking with the subjects, it appeared that most of the subjects could tell that it was their favorite song while listening to LPR-favorite, albeit in a distorted manner, but none of the subjects recognized the LPR-fast song even though fast tempo song was played before its LPR version (Fig. 3). Under this scenario, different auditory stimuli can induce the same cognitive response in one case and a different cognitive response in another. This provided us the chance to evaluate the effects of cognition, which here is referred to effects of music not directly resulting from structural aspect of music.

All songs, except LPR-fast, increased respiratory frequency. The higher tempo song resulted in higher respiratory frequency, similar to what has been reported before (Bernardi *et al.* 2006, Brownley *et al.* 1995, Haas *et al.* 1986). Also, the higher tempo song had higher RFB, i.e. the RFB during fast song also decreased from control, but the decrease among all songs where respiratory frequency increased was least for the fast song. All songs decreased RFB with slow song resulting in the smallest RFB. This means that in presence of auditory stimuli the breathing pattern was much more periodic than during silence and the slow tempo song caused the most periodic breathing pattern. It was interesting to note that the LPR versions, for both songs, seemed to have blunted the increase in respiratory frequency and the reduction in RFB that was observed while listening to their original versions. This blunting shows the importance of meaningful acoustical musical features, which are mostly repeated periodically throughout the songs, in inducing changes in periodic patterns of breathing. While the decrease in RFB is not as widely reported as the increase in breathing frequencies, the reduction is consistent with the observations of Haas et al (Haas *et al.* 1986). The reduction in respiratory variability while listening to songs suggests that the inputs to the respiratory pattern generator that cause the rate to change on a breath by breath basis were either diminished or had less influence when listening to songs, and somewhat less diminished when listening to the LPR versions of them. Because the increase (relative to non LPR version) in RFB caused by the LPR process was very small for the LPR-favorite song (1.1 %) and large for the LPR-fast song (24.4 %), it is possible that processes which decrease RFB may be related to cognition of songs, since all subjects recognized the original version of the LPR-favorite song, but not the original version of the LPR-fast song.

A remarkable observation from our study was that during listening to *all songs*, including LPR versions, most measures of synchronization, i.e. coherencies, increased. Out of the 225 coherencies that we computed (45 pairwise combinations between 10 parameters for each of 5 songs), in the total band (0-0.4 Hz), only three coherencies decreased by small and nonsignificant amounts but increased in the rest. 169 of these increases were not only statistically significant but were consistently seen in almost all 14 subjects. The effect sizes for these differences were either medium or large, which further supports these observations (only 6 out of 150 coherencies listed in Table 3 did not have medium or large effect sizes over any bands). As neuronal coherence is shown to serve as neuronal communication mechanism (Fries 2005), this widespread increase indicates the increase in neural communication during listening to auditory stimuli. It was interesting that not only the slow song caused the most periodic breathing pattern, but it also caused the largest average effect sizes over all coherencies, in each of LF band, HF band and TB, compared to other songs. The effect size for HF band, which encompasses respiratory frequencies and thus captures periodicity or regularity of respiration, was larger than LF band in most of coherencies with EEGs. This further shows the important mediatory role of respiration in all of these increases in synchronization.

Importantly, our findings also highlight that effects of cognition of music, which here is refered to the effects of music not directly resulting from the structural aspect of music, made significant changes on systolic blood pressure coherencies. The synchronization of SBP with RR and with EEGs was not different between favorite and LPR-favorite songs, but was significantly different between fast and LPR-fast songs. There was a significant reduction in the RR-DBP coherence in the HF band from slow to fast tempo song. As HF band of frequency spectrum of RR reflects cardiac vagal tone, synchronization of oscillations of other physiological variables with RR over this frequency band could be considered a consequence of changes in vagal activity, especially when the stimuli used are expected to change vagal tone in same direction as in synchronization and over the same expected frequency band. This reason was also the motivation for dividing coherencies within LF and HF bands and computation of LF/HF ratios because this ratio for RR autospectra is widely thought to reflect the sympathovagal balance. These divisions enabled us to visualize RR and BP spectral based measures in the context of their known or hypothesized autonomic origins. In those cases, where the LF/HF ratios in coherence showed meaningful and relatively larger change, these ratios were reported, especially when one of the variables in computation of the coherence was RR intervals. It has been previously shown that the increase in tempo of song causes a decrease in heart rate variability and an increase in self-reported valence and arousal (Ellis 2009). This increase in arousal level of music has been reported to be associated with a decrease in parasympathetic activity (Ellis and Thayer 2010) which could be a reason for the diminished RR-DBP coherencies that we observed over HF band during fast tempo song. A decrease in parasympathetic activity when the song had a faster tempo was also previously reported by Bernardi *et al.* (2006).

Coherencies between SBP and respiration increased in the total band (0-0.4 Hz) in all cases. Even when one of the variables in computation of coherence was not respiration, the peak of these coherencies within the HF band occurred at or close to the respiratory frequency (Fig. 5). This observation shows the important common role of respiration in variations of all of the measured physiological parameters. SBP-respiratory coherencies, in the LF band, increased significantly during listening to all songs suggesting a high sensitivity of this parameter to auditory stimuli. The very similar effect of LPR songs and their original versions on SBP-respiratory coherence in the LF band suggests that this interaction is affected by auditory stimulus strength and less by its phase or cognition. DBP-respiratory coherencies, in both LF and HF bands, increased significantly during listening to all songs. Compared to other parameters, DBP became more coherent with respiration than all other cardiac and cerebral parameters in response to auditory stimuli.

All songs caused highly consistent increases in cerebro-RR coherencies in the HF band. 27 out of 30 of coherencies were statistically significant (change >32 %, p<0.037). As the HF components of cardiac variability reflect vagal tone, i.e. parasympathetic influence, it is tempting to interpret that the HF synchronization of brain electrical oscillations with cardiac variability may also be a consequence of the same processes that increase parasympathetic activity. The slow tempo song induced higher cerebro-RR coherencies in the HF band than the fast tempo song, probably due to higher parasympathetic activation during the slower tempo song (compared to the fast tempo song) as also reported previously by Bernardi *et al.* (2006). Our results suggest that this hypothesized effect, consistent with parasympathetic activation, was more significant in the frontal lobe. The slow song also induced a significant increase in cerebro-RR coherencies in the LF band in EEGs recorded from the right hemisphere (F4, T4, P4), with larger effect sizes than left hemisphere, quite possibly because one would predict that the changes induced by music should be larger there (Schön *et al.* 2004).

All songs showed significant increase in both cerebro-SBP and cerebro-DBP coherencies over both LF and HF bands in all EEGs, and all of these effects sizes were either medium or large (Table 3). By comparing fast and slow songs, higher HF coherence for the slow song was seen for both SBP and DBP, while this synchronization was more significant for HF electrical oscillations recorded from the right hemisphere which is responsible to process music (Schön *et al.* 2004). If HF synchronization of SBP and DBP with EEGs can be interpreted like HF synchronization of cardiac variability for vagal tone, then a decrease in parasympathetic activity with increased tempo of the song is consistent with reports in the literature (Bernardi *et al.* 2006), and is likely the reason for these changes. Regulation of peripheral blood pressure is mediated by sympathetic alpha-adrenergic receptors; therefore, these changes show that sympathetic outflow was more coupled and in phase with low frequency cerebral oscillations from right hemisphere.

All songs caused significant increases in cerebro-respiratory coherence in the HF band in all EEGs. Similar significant increases, during all songs, in all EEGs, were also seen for DBP-respiratory coherencies in the HF band. These results suggest that oscillations in the envelopes of EEG become more coherent with those in respiration, RR intervals, SBP and DBP. The increase is indicative of consistency between neuronal activation and rhythms mediated by the autonomic system. Furthermore, these increases in coherencies were seen more widely in the HF band, which is more respiratory mediated, again suggesting that respiration plays a central role in increased entrainment of these rhythms in response to auditory stimuli.

Study limitations

We computed coherence between various physiological parameters which shows interactions in terms of similarity of phase between two parameters but does not inform about the sequence of changes, i.e. which parameter drives the other. As acoustic 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. 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 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. Menstrual cycle has been shown to impact autonomic function (Bai *et al.* 2009), however this factor was not accounted for in this study.

Conclusions

The present findings suggest that during listening to music coherence between cerebral electrical activation and cardiac and respiratory rhythms increases, and respiration becomes more periodic. That is, there is an overall increase in uniformity of rhythmic activity. Systolic blood pressure synchronizations and RFB are significantly affected by cognition of music. During listening to all auditory stimuli, diastolic blood pressure synchronization with respiration was more pronounced than all other variables. 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.

Conflict of Interest

There is no conflict of interest.

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