Dynamic Interactions Between Musical, Cardiovascular, and Cerebral Rhythms in Humans

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***Background*—**Reactions to music are considered subjective, but previous studies suggested that cardiorespiratory variables increase with faster tempo independent of individual preference. We tested whether compositions characterized by variable emphasis could produce parallel instantaneous cardiovascular/respiratory responses and whether these changes mirrored music profiles.

***Methods and Results*—**Twenty-four young healthy subjects, 12 musicians (choristers) and 12 nonmusician control subjects, listened (in random order) to music with vocal (Puccini's "Turandot") or orchestral (Beethoven's 9th Symphony adagio) progressive crescendos, more uniform emphasis (Bach cantata), 10-second period (ie, similar to Mayer waves) rhythmic phrases (Giuseppe Verdi's arias "Va pensiero" and "Libiam nei lieti calici"), or silence while heart rate, respiration, blood pressures, middle cerebral artery flow velocity, and skin vasomotion were recorded. Common responses were recognized by averaging instantaneous cardiorespiratory responses regressed against changes in music profiles and by coherence analysis during rhythmic phrases. Vocal and orchestral crescendos produced significant ($P=0.05$ or better) correlations between cardiovascular or respiratory signals and music profile, particularly skin vasoconstriction and blood pressures, proportional to crescendo, in contrast to uniform emphasis, which induced skin vasodilation and reduction in blood pressures. Correlations were significant both in individual and group-averaged signals. Phrases at 10-second periods by Verdi entrained the cardiovascular autonomic variables. No qualitative differences in recorded measurements were seen between musicians and nonmusicians.

***Conclusions*—**Music emphasis and rhythmic phrases are tracked consistently by physiological variables. Autonomic responses are synchronized with music, which might therefore convey emotions through autonomic arousal during crescendos or rhythmic phrases. **(*Circulation*. 2009;119:3171-3180.)**

Key Words: blood pressure ■ heart rate ■ ultrasonography, Doppler, transcranial ■ arousal ■ therapy, music

There has been considerable recent interest in the cardiovascular, respiratory, and neurophysiological effects of listening to music, including the brain areas involved, which appear to be similar to those involved in arousal.[1,2] Responses to music appear to be personal, particularly when skin tingling or "chills" occur,[3–5] which suggests individual reactions to music that are dependent on individual preferences, mood, or emotion. However, our previous study[6] showed consistent cardiovascular and respiratory responses to music with different styles (raga/techno/classical) in most subjects, in whom arousal was related to tempo and was associated with faster breathing. The responses were qualitatively similar in musicians and nonmusicians and apparently were not influenced by music preferences, although musicians responded more. That original study concerned average responses to music rather than to dynamic changes during a track, because we used artificial tracks with 2 or 4 minutes of consistent style and tempo. Changes in tempo and emphasis were less evident, which is important for originating "chills."

Clinical Perspective on p 3180

We did not then study the entrainment of spontaneous cardiovascular rhythms, the 6 cycles/min (10-second period, 0.1 Hz) Mayer waves of blood pressure that result from imperfect baroreflex control because of the interaction between a fast (vagal) response in heart rate and a slow (sympathetic) vascular response.[7] These responses are readily entrained and enhanced by slow respiration at 6 cycles/min.[8,9] Interestingly, several famous operatic arias, particularly by Giuseppe Verdi, contain phrases close to 6 cycles/min. Some of these have special emotional emphasis, for example, "Va pensiero" from the slaves' chorus in *Nabucco* (recently proposed as the National Anthem of Italy and also used by

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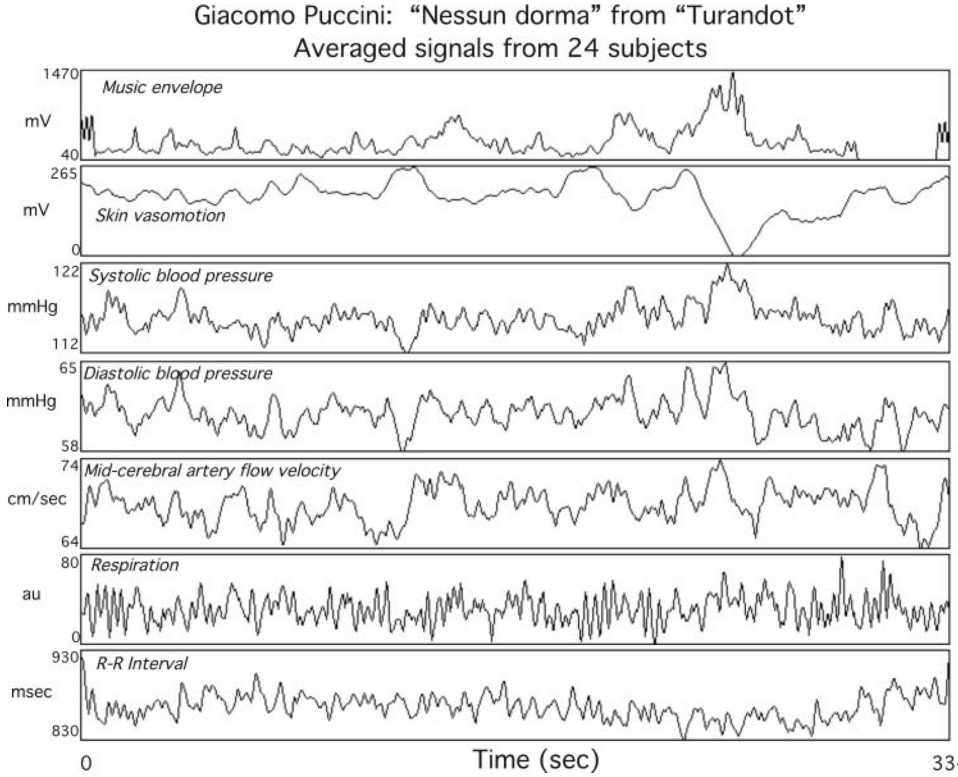

Figure 1. Average cardiovascular and respiratory data obtained in the 24 subjects while listening to "Nessun dorma." Top, Music envelope, with the 3 synchronization bursts at start and finish. Note the synchronous tachycardia, increases in blood pressures and cerebral blood flow velocity, and skin vasoconstriction after the lyrical crescendo toward the end of the aria.

British Airways). Another example is the drinking song "Libiam nei lieti calici" from Verdi's *La Traviata.*

Music is increasingly used in treating cardiovascular, neurological, and respiratory diseases.[10–16] If music induces similar physiological effects in different subjects, standard therapeutic interventions would be possible. We examined the dynamic cardiovascular responses to variations in phrasing and emphasis using real compositions, selected for different emotional characteristics, to determine the following: (1) Whether variable musical emphasis (eg, crescendo versus stable emphasis) could produce similar instantaneous cardiovascular/respiratory responses among different subjects; (2) whether phrases at approximately 6 cycles/min could entrain the cardiovascular and respiratory responses; and (3) whether these responses were influenced by music training.

We recorded cardiovascular/respiratory variables in musicians (choristers) and nonmusicians, identifying patterns common to all subjects by synchronization between individual biological responses and music phrases. We compared both individual responses and the responses averaged over the different groups studied with the music profile. Common patterns of response, if present, would then appear and could be related to specific points in the music.

Methods

Subjects

We studied 24 healthy white subjects, 25±1 years of age, matched for age and sex; 12 (25±2 years old, 9 females) were experienced choristers (at least 3 years). The 12 control subjects (24±1 years old, 7 women) had no previous music training.

Study Protocol

All subjects gave informed consent to the protocol (approved by the local ethics committee). All tests were performed with subjects in the supine position in comfortable temperature, humidity, and light. The subjects (eyes closed) wore headphones[17] and avoided tapping with a finger or a foot (to avoid artifactual entrainment), which was confirmed by continuous visual monitoring.[18] We monitored an ECG (by chest leads); noninvasive beat-to-beat blood pressure by radial artery applanation tonometry (Pilot, Colin, San Antonio, Tex)[19]; middle cerebral artery flow velocity by a 2-MHz transcranial Doppler probe at a depth of 35 to 55 mm, through the temporal window of the nondominant side (DWL, Sipplingen, Germany); respiratory movements by an inductive plethysmograph built and validated in our laboratory against a pneumotachograph[6]; skin vasomotion (left index fingertip) by a previously described and validated skin photoplethysmograph[20,21]; and continuous end-tidal carbon dioxide by a nasal cannula (COSMOplus, Novametrics, Wallingford, Conn).

Baseline recordings were taken for 5 minutes. Then, in random order, the following tracks were presented: (1) A well-known orchestral piece (adagio from Beethoven's *Ninth Symphony*); (2) an emotional and lyrical operatic aria ("Nessun dorma" from Puccini's *Turandot*); (3) a more "intellectual" piece of solo singing from Bach (Cantata BWV 169, "Gott soll allein mein Herze haben"); 2 Verdi arias with rhythmic phrases: (4) "Va pensiero" (from *Nabucco*) and (5) "Libiam Nei Lieti Calici" (from *La Traviata*); and (6) 2-minute silence (see online-only Data Supplement material for details). Individual reactions to the music tracks were collected immediately after the experimental session in structured oral interviews based on a widely accepted model of emotions[22]; subjects rated the intensity of emotion and the novelty and pleasantness of the piece on 1-to-5

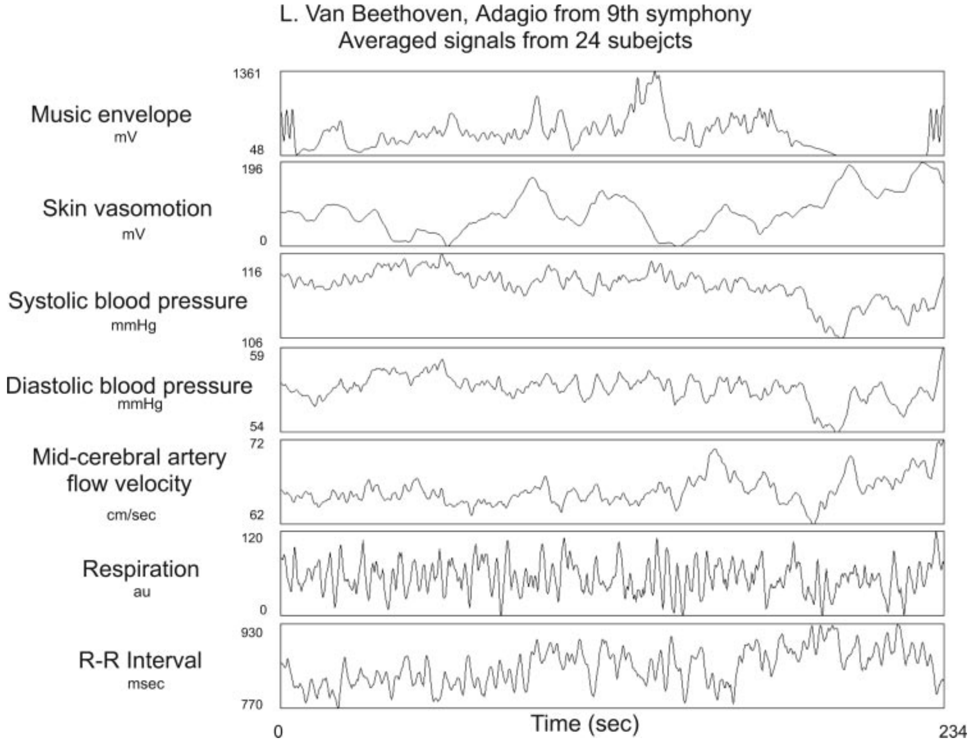

Figure 2. Average cardiovascular and respiratory data obtained in the 24 subjects while listening to Beethoven's *Ninth Symphony*. Note a lesser response to the orchestral crescendo (vertical line) from Beethoven's *Ninth Symphony* than to the vocal fortissimo in Figure 1.

(1=very low, 5=very high) Likert scales. The subjects were also asked to report whether they felt any chills or other strong feelings in response to each music track.

Music Profile and Synchronization in Different Subjects

A low-frequency signal proportional to the amplitude of the audio signal was obtained by feeding the music through an envelope generator (see online-only Data Supplement material).

Data Acquisition and Analysis

The peaks of the R waves of the ECG were identified, together with the sequences of systolic and diastolic blood pressures and the sequence of the mean (during each heart period) middle cerebral artery flow velocity and skin vasomotion. These discontinuous signals were interpolated and resampled at 4 Hz.[23] Continuous data (respiration and music envelope) were also resampled at 4 Hz. In addition, the recordings obtained for each signal in each subject were synchronized and averaged by use of 3 starting and 3 ending reference markers (online-only Data Supplement, Figure I). We thus obtained the average for the 12 control subjects, the 12 musicians, and all 24 subjects together. Figures 1 through 4 and online-only Data Supplement Figures II and III show the averaged data obtained, together with the music envelope. To analyze the respiratory signal, we obtained a continuous profile of the respiratory power by the instantaneous power spectrum of the respiratory signal, obtained by a continuous (time-varying) spectral algorithm (Wigner-Ville).[21,24]

The synchronization between different signals and the music envelope during rhythmic phrases by Verdi was tested by coherence analysis in both individual and averaged data. The coherence function was evaluated by an autoregressive bivariate method with a model order of 12.[25] The autoregressive method is particularly useful for short-term data, allowing a better frequency resolution than simpler Fourier-based approaches under these conditions.[25] To evaluate the coherence changes over time, we used a recursive method, with a moving window of 200 points (50 seconds). The coherence function could then be seen as a continuous function after the first 100 points (25 seconds) and until the last 100 points before the end of the recordings (Figures 5 and 6; online-only Data Supplement Figures IV through VI). The frequency at which peak coherence occurred was plotted against time together with the peak coherence and its phase.

Baroreflex sensitivity was measured by the sequence method.[26] Briefly, sequences of 3 or more pulses during spontaneous rises or falls in systolic blood pressure were related to changes in RR interval by linear regression, and the baroreflex sensitivity was calculated as the average of the positive or negative slopes.

Statistical Analysis

Numeric data are presented as mean±SEM. Differences between baseline and music responses were tested by repeated-measures ANOVA (online-only Data Supplement Table I). To test the appropriateness of the analysis on averaged data, linear correlations between music envelope and cardiovascular data were tested in individual data by unbiased linear regression analysis with varying time lags (to find the maximal correlation and the delay at which it occurred). Individual correlation coefficients then underwent the *r*-to-*z* transformation[27] to normalize their distribution. To assess whether transformed correlation coefficients were significantly and consistently different from 0 at the group level, we used the *t* test (1-group test, testing differences versus 0) and the Wilcoxon rank sum test, respectively. The Wilcoxon rank sum test was also used to test consistency among different subjects in correlation lags (online-only Data Supplement Table II). The relation of the biological signals to the music envelope was also tested on the averaged data by regression analysis with varying time lags. During the most important crescendos, we compared (by linear regression) the instantaneous peak spectral power in the respiratory frequency range (0.15 to 0.35 Hz) with the music envelope.

To test entrainment between the music envelope and cardiovascular/respiratory signals during the tracks by Verdi, coherence analysis between the music envelope and each signal was performed

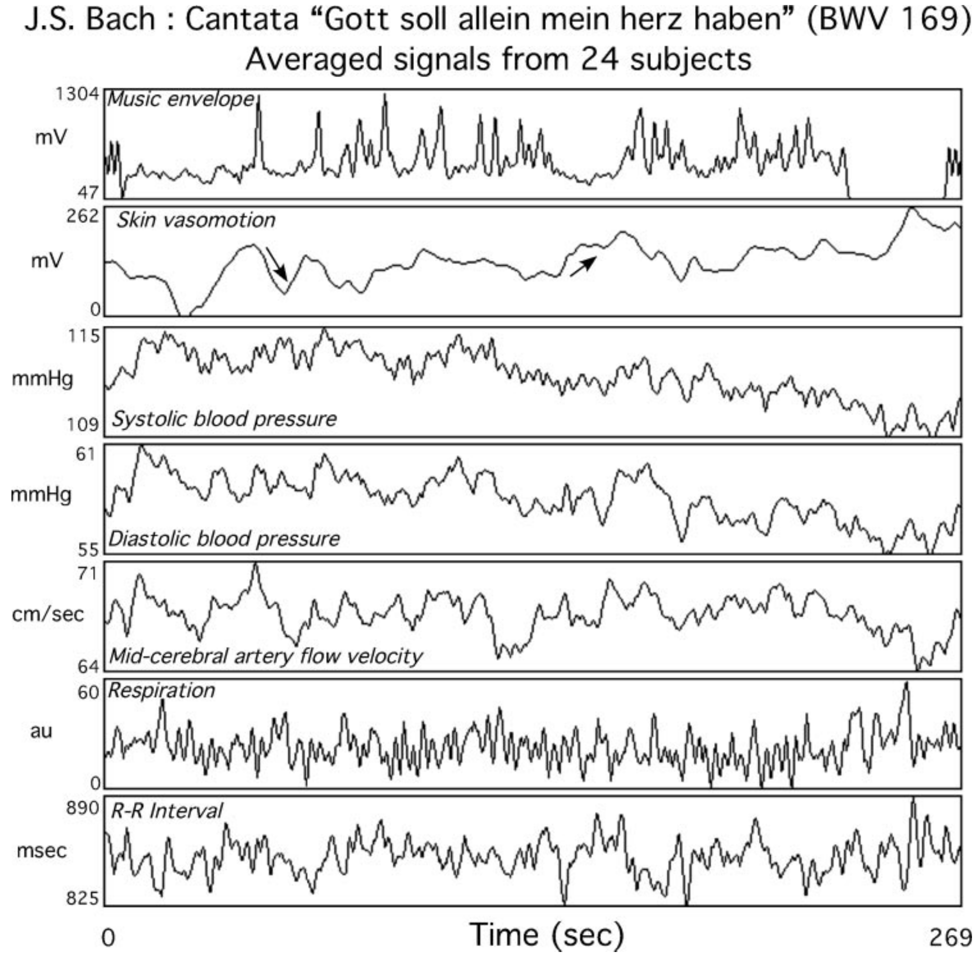

Figure 3. Average cardiovascular and respiratory data obtained in the 24 subjects while listening to Bach's cantata. This music shows a general "relaxation": Gradual skin vasodilation and lower blood pressures (in contrast to the responses to the more arousing crescendos of the previous Figures). Note the more frequent and close peaks in the music envelope. The only spaced peak is the first one, coincident with the first note by the singer. This in fact corresponds to a clear skin vasoconstriction (marked by an arrow). Conversely, the vocal pause in the middle of the track (only orchestral music) coincides with a further upward deflection (vasodilatation, marked by the arrow).

in each subject, and the instantaneous peak coherences±SEM were plotted against time. The same analysis was performed on the averaged data (online-only Data Supplement Figures IV and V). A coherence ≥0.5 traditionally indicates that 2 biological signals are statistically associated at a given frequency; however, to show the trend better, we reported in graphical terms the entire coherence function over time using a 3D scheme (Figures 5 and 6; online-only Data Supplement Figure VI). To grade coherence levels, we used different colors: Yellow, >0.8; red, between >0.6 and 0.8; light blue, between >0.4 and 0.6; dark blue, between >0.2 and 0.4; and black, between 0 and 0.2. In addition, we plotted the trend of phase in the 0.1-Hz band with respect to the music envelope. Although coherence could be consistently high, the phase should also be stable in different time segments to demonstrate entrainment.

Results

Subjective Reactions to Music

Likert scale scores ranged from 1 to 3, with no definite preference for any track. There was absent (or only moderate) emotional involvement in music, with "calm" and "no particular emotions" as the most frequently reported answers, and "interesting" or "stimulating" given as an answer by 5 musicians and 3 control subjects. None of the subjects reported the occurrence of "chills" according to a standard definition[3–5] or of other strong emotions.

Differences Between Baseline and Music

See online-only Data Supplement material and online-only Data Supplement Table I.

Individual Versus Averaged Signals From Different Subjects

Correlation coefficients between the music envelope and individual signals were significantly and consistently different from 0 for most signals, particularly skin vasomotion and blood pressures. By averaging the signals obtained in individual subjects, larger correlation coefficients were observed (online-only Data Supplement Table II).

Cardiovascular Responses to Music

The results for the different tracks are shown in Figures 1 through 4 and online-only Data Supplement Figures II and

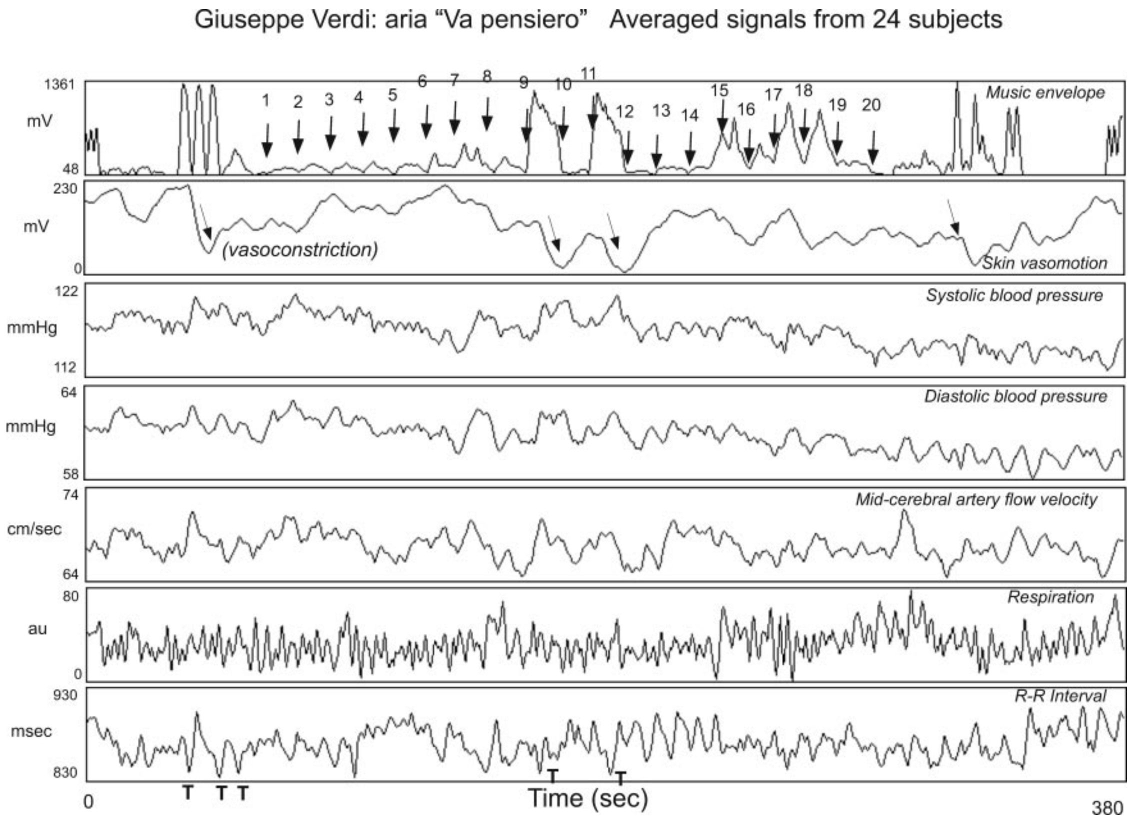

Figure 4. Average cardiovascular and respiratory data obtained in the 24 subjects while listening to "Va pensiero." Top, Music envelope. The music envelope, after the 3 orchestral initial fortissimi, shows a regular rhythm, (11.48-second period). The arrows with numbers in the music envelope mark the beginning of each phrase. Some examples: (1) "Va pensiero sull'ali dorate," and (9) "arpa d'or dei magnifici vati." All cardiovascular signals show systematic changes related to both rhythm and emphasis. The arrows in the skin vasomotion panel mark the main vasoconstrictions (downward slope) that occurred in coincidence with changes in the music profile. The "T" marks downward deflections in R-R interval (tachycardia), in connection with increases in blood pressures and skin vasoconstriction, which occurred with the peaks of the music envelope.

III. Consistent dynamic cardiovascular and respiratory responses to music were observed. Almost every music crescendo or emphasis induced progressive skin vasoconstriction (downward deflection), along with increases in blood pressures and heart rate. This consistency would not have been possible if individual subjects had responded differently. Conversely, during the silent pause (and baseline), the changes were minor, with progressive skin vasodilation and reductions in heart rate and blood pressure (online-only Data Supplement Figure III). The degree of change in the cardiovascular variables paralleled those in the music envelope, with highly significant correlations, the most with skin vasomotion and the least with RR interval (Figure 7; online-only Data Supplement Table II). The maximum correlation was delayed

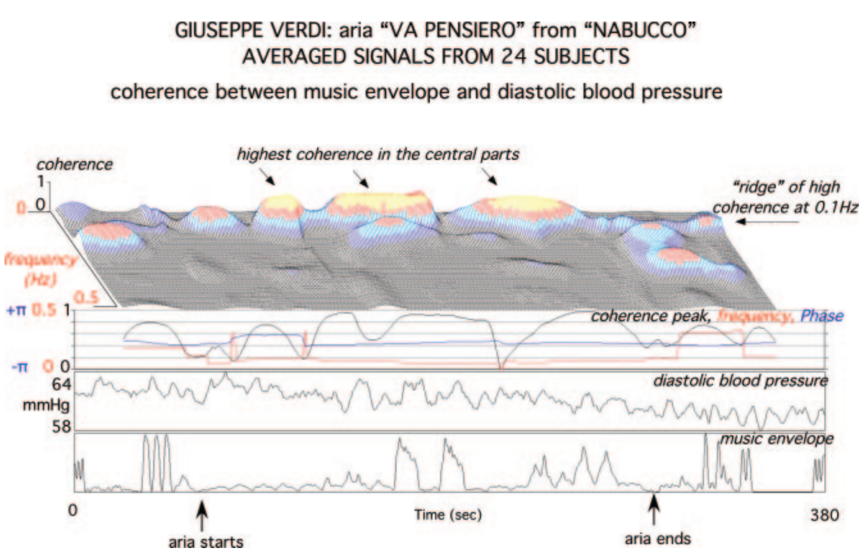

Figure 5. Continuous coherence between the music envelope and diastolic blood pressure obtained in the 24 subjects while listening to "Va pensiero." The peak coherence (in black), the frequency at which the peak coherence occurred (in red), and the phase in the 0.1-Hz region (in blue) are represented in the top 2-dimensional panel. The complete coherence function (y axis) is represented in the 3-dimensional panel as a function of both time (x axis) and frequency (z axis). The color scheme represents the level of significance of the coherence value (see Methods). With the beginning of the aria, the coherence increased and remained high (with stable phase) after the end of the aria. The peak coherence was between 0.08 and 0.09 Hz (the same rhythm as the musical phrase, 0.087 Hz), which indicates that while listening to the central part of the track (ie, during the aria), the subjects synchronized their Mayer waves with the rhythm of the music.

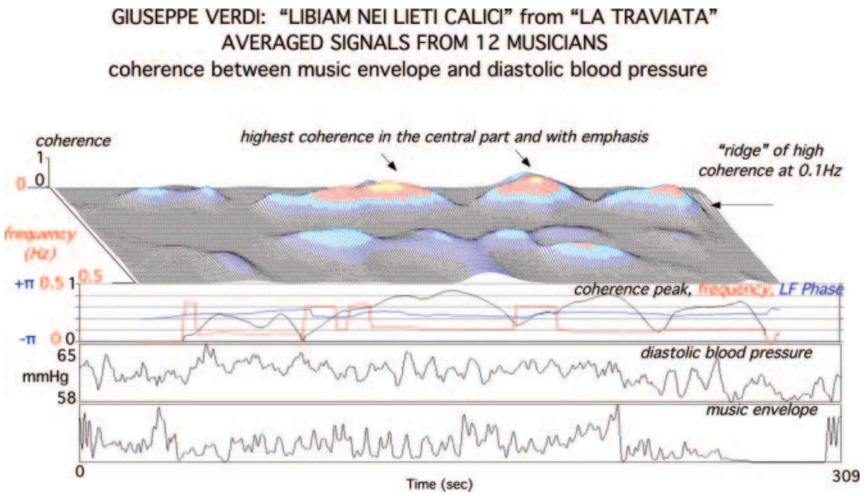

Figure 6. Continuous coherence between the music envelope and diastolic blood pressure (bottom) obtained in the 12 musicians while listening to "Libiam nei lieti calici." Same conventions as in Figure 5. The frequency of the peak coherence was almost constantly at 0.1 Hz (with stable phase). Owing to multiple coherence peaks, the peak in coherence occasionally occurred at a higher frequency (see red graphic in the top 2-dimensional panel), but in the 3-dimensional panel, significant coherence was still present at 0.1 Hz.

in relation to the music profile. The fastest responses were in RR interval and middle cerebral artery flow velocity, followed by systolic and diastolic blood pressures and skin vasomotion (online-only Data Supplement Table II).

There were also marked differences between the music tracks. The correlations were greatest during "Nessun dorma" (online-only Data Supplement Table II), characterized by a series of increasing crescendos (Figure 1; online-only Data Supplement Figure II). The Beethoven adagio (orchestral music only) also showed significant correlations between cardiovascular variables and music profile (several crescendos of progressively increasing intensity; Figure 2), although to a lesser degree than those seen in "Nessun dorma." In contrast, the Bach cantata was characterized by 2 solo mezzo-soprano phrases with an interposing orchestral part (Figure 3). The voice produced several high but short peaks in the music envelope, probably too close together to elicit responses, and minor changes were observed. Comparing the individual or average data, we observed a progressive arousal during "Nessun dorma" but relaxation during the Bach cantata and the silent pause, with the Beethoven adagio being intermediate (Figures 1 through 3; online-only Data Supplement Figure II). There were no differences between groups.

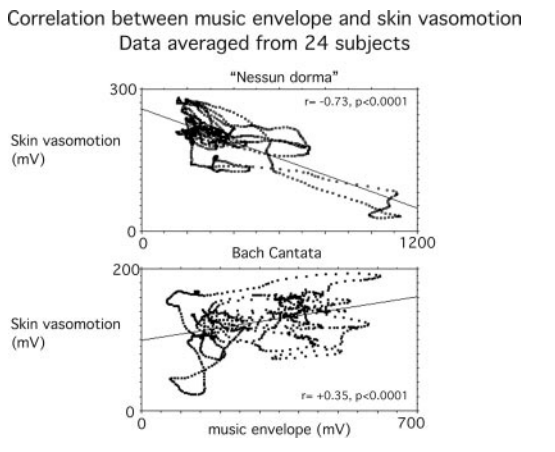

Figure 7. Scattergrams and correlation between music profile and skin vasomotion. In "Nessun dorma," the crescendo induced a proportional vasoconstriction; in the Bach cantata, the crowded peaks in the music envelope ended by creating a progressive vasodilation.

Responses to Rhythmic Phrases (by Verdi)

The envelope of "Va pensiero" (Figure 4) shows the 3 initial markers, then the orchestral introduction, followed by 3 brief orchestral fortissimi. The melody of the aria (phrases indicated by arrows in the Figures) shows regular phrases (11.48 seconds, 0.087 Hz) with a triangular shape (crescendo and decrescendo) until the middle, where 2 chorus fortissimi occur (Figure 4). The chorus resumes triangular phrases until the final crescendo, with vasoconstriction and increases in systolic/diastolic blood pressures and middle cerebral flow velocity; the RR interval changed less, with little change in breathing. Coherence between the music and cardiovascular responses (Figure 5; online-only Data Supplement Figures IV and VI) increased markedly at the beginning of "Va pensiero," remaining high throughout, without major differences between musicians and nonmusicians. The dominant coherence occurred at the frequency of the musical phrase (0.08 Hz), except for 2 central fortissimi in which the large double peaks in the music envelope halved the frequency (0.04 Hz), which indicates continued close tracking of the music. The period of the phrasing of the second Verdi aria, "Libiam nei lieti calici," was 9.04 seconds (0.110 Hz), with similar entrainment of cardiovascular variables at this frequency (Figure 6). These changes occurred consistently both in the individual data and in the averaged data; however, the coherence obtained from averaged data showed greater values (online-only Data Supplement Figures IV and V). The 2 approaches nevertheless showed very similar trends (r=0.755 and 0.601 between the 2 coherences for "Libiam nei lieti calici" and "Va pensiero," respectively; P<0.0001). The phase remained stable during the central phrases of "Va pensiero" (0.22±0.08 radians, mean±SD, equivalent to a delay of 0.3 second) and "Libiam nei lieti calici" (0.39±0.08 radians, equivalent to a delay of 0.6 second).

Effect of Silence

During the silent track (online-only Data Supplement Figure III), we still observed some synchronization between cardio-

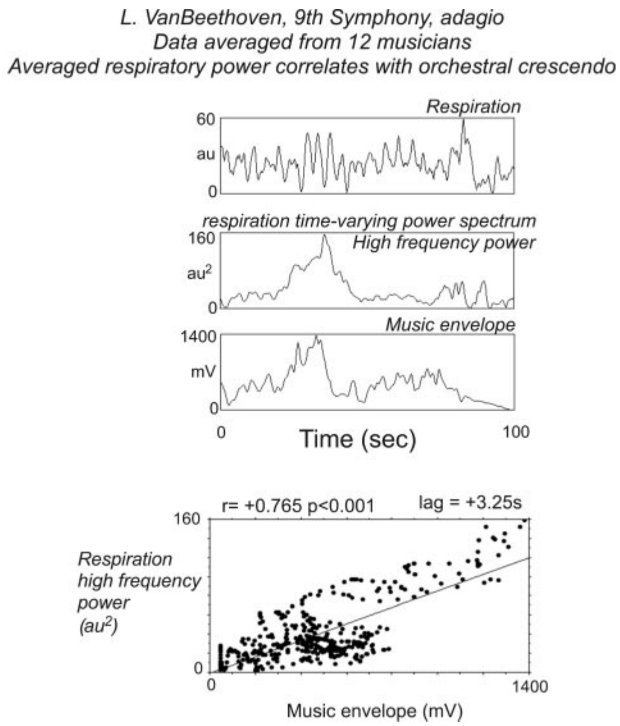

Figure 8. Respiratory modifications during the orchestral crescendo from the adagio from Beethoven's *Ninth Symphony*. There is a clear period of very regular breathing (top) coincident with the crescendo in the music envelope (third panel). The continuous amplitude of respiration (obtained by respiratory spectral power; second panel) closely mirrored the music envelope during the crescendo, which showed that respiration also mirrored the music data. The highest correlation (bottom) was seen when respiration followed the music envelope by 3.25 seconds.

vascular and respiratory signals, perhaps due to some carryover effect. Unlike music, silence and baseline showed progressive reductions in heart rate and other variables, which indicates progressive relaxation.

Respiration

Respiration showed regularization of rhythm and a transitory increase in amplitude with crescendos (Figures 1 through 3), without overall changes in end-tidal carbon dioxide affected by music. When respiratory power was tracked continuously (by use of a time-varying spectral algorithm), there was a clear correlation with the music envelope. During Beethoven's adagio, the instantaneous power of the respiratory signal closely tracked the amplitude of the music envelope, which also indicates that the depth of respiration could be influenced tightly by music, at least during crescendos (Figure 8), similar to what occurred during "Nessun dorma" and even during Bach (online-only Data Supplement Figures VII and VIII). Although for Beethoven, both musicians and control subjects showed a very high correlation between music and breathing (r=0.765 and 0.768, respectively; P<0.0001 for both), for the other tracks, the musicians showed a higher correlation than control subjects ("Nessun dorma": r=0.323 versus r=−0.161, respectively, P<0.0001 for both; Bach cantata: r=0.330 versus r=0.217, respectively, P<0.0001 for both). The delay of the response between the music envelope and respiration was also consistently shorter in musicians than in control subjects (Beethoven 3.25 versus 14.75 seconds; "Nessun dorma" 3.75 versus 7.5 seconds; Bach cantata 4.75 versus 7.5 seconds; "Va pensiero" 2.25 versus 3.00 seconds; and "Libiam nei lieti calici" 3.25 versus 3.5 seconds, respectively; P=0.05, Wilcoxon test). During the tracks by Verdi, respiration correlated highly (P<0.0001) during the crescendos but only minimally (P<0.05) during the rhythmic phrases.

Discussion

This study reveals several novel findings, which are potentially important for the therapeutic use of music and for understanding the underlying physiological mechanisms: (1) The cardiovascular (particularly skin vasomotion) and respiratory fluctuations mirrored the music profile, particularly if it contained a crescendo. (2) Specific music phrases (frequently at a rhythm of 6 cycles/min in famous arias by Verdi) can synchronize inherent cardiovascular rhythms, thus modulating cardiovascular control. This occurs regardless of respiratory modulation, which suggests the possibility of direct entrainment of such rhythms and allows us to speculate that some of the psychological and somatic effects of music could also be mediated by modulation or entrainment of these rhythms. (3) Musicians and nonmusicians showed similar qualitative responses, but musicians showed closer and faster cardiovascular and particularly respiratory modulation induced by the music. (4) Music induces predictable physiological cardiovascular changes even in the absence of conscious reactions, which suggests that these changes may "precede" the psychological appreciation. This finding may explain the apparent discrepancy between individual appreciation (subjective) and physiological reactions (common to all subjects despite different music culture and practice) and provide a rational basis for the use of music in cardiovascular medicine.

Cardiovascular and Respiratory Systems Mirror the Music Profile, Particularly During Crescendos

Although extreme responses to arousing phrases (goose pimples or chills) are associated with conscious emotional arousal,[3] we have found that there are subconscious reflex autonomic responses, involving respiration and cardiovascular parameters, that are common to all subjects, independent of music preferences or previous training. Musical profile was closely mirrored in the skin microvasculature, which suggests a possible lower (subconscious) connection between auditory sensation and cardiovascular reactions. If this is the case, then the subjective presence of a "chill" possibly requires the intensity of this cardiovascular modulation to pass a certain threshold to become perceived consciously. The present findings complement those of Grewe et al,[3] who observed that some subjects occasionally experience the sensation of chills during sudden crescendo, together with cardiovascular changes similar to those of the present study. The present findings also demonstrate that in addition to conscious chills, which typically are experienced by a minority of subjects,[3] there is a common pattern of unconscious response when different subjects listen to the same music.

These autonomic responses were more apparent with lyrical responses from an operatic aria ("Nessun dorma") or a typical exciting orchestral phrase (Beethoven's adagio) than with more "intellectual" solo singing from a Bach cantata, however beautiful. The extent of the response appeared to be dependent on the specific pattern of the music profile. When a sudden crescendo was spaced adequately, or the music profile exhibited a regular or slow change (eg, "Nessun dorma," Beethoven's adagio, or Verdi's arias), then the cardiovascular system tracked the music profile, and skin vasoconstriction was evident. When the music profile changed very rapidly, as in the Bach example, the overall effect was opposite: Skin vasodilation and a reduction in blood pressure (general relaxation). This may be due to the longer time required to constrict the skin microvasculature. The skin microvasculature is indeed sensitive to changes in sympathetic activity, but its modulation can be influenced only by slow stimuli.[20,21] In agreement with those findings, we observed a delay of skin vasomotion with respect to the music profile of 6 to 11 seconds (online-only Data Supplement Table II). In addition to confirming an important influence of music on respiration,[6] we now report a definite respiratory synchronization with increases in musical emphasis among different subjects, particularly during slow crescendos.

Specific Music Phrases, Frequently at a Rhythm of 6 Cycles/Min, as in the Verdi Arias, Can Synchronize With Intrinsic Cardiovascular Rhythms, Causing a Modulation of Cardiovascular Control

In the present study, we have found for the first time that music can synchronize cardiovascular variability as a result of listening to phrases at a frequency close to that of circulatory oscillations. This synchronization apparently occurs regardless of respiratory modulation, which suggests the possibility of a direct central entrainment. The fast responses observed in relation to music suggest the involvement of neural rather than humoral mechanisms, at least in the short term. We therefore speculate that some of the psychological and somatic effects of music could be mediated by modulation or entrainment of inherent cardiovascular rhythms in the brain. It is possible that this effect might be enhanced by special phrases preceding the "entraining" sequence, to generate an arousal or "presetting" effect. This could be obtained by an orchestral fortissimo, as in "Va pensiero," just before the beginning of the chorus (Figures 4 and 5) or by a rapid crescendo followed by a brief pause (as during "Libiam nei lieti calici"; Figure 6; online-only Data Supplement Figure V). These sudden changes produce a consistent arousing effect among different individuals. After this kind of "priming," occurring in all subjects, it might then be more likely that the following phrases might produce a similar pattern of response in all subjects. Although each subject still maintained part of his or her own individual cardiovascular fluctuations, a common response was clearly evident not only in the averaged data (Figure 4) but also in individual signals (online-only Data Supplement Figures I, IV, and V and online-only Data Supplement Table II). This indicates that the averaging technique (albeit overemphasizing the extent of coherences/correlations) is not the result of a technical artifact.

In the Verdi arias, we found that the musical phrases have a period of approximately 10 seconds (0.1 Hz), similar to the Mayer waves of blood pressure. It is well known that this rhythm derives from the autonomic modulation of the cardiovascular system.[28–30] We and others described different cultural methods (yoga, prayers, poetry recitation) to induce positive mental conditions that slowed respiration and resulted in modulation of this basic rhythm.[9,31,32] The present study appears to represent a new example of this phenomenon. It is rather surprising that Verdi used this time interval in arias with different emotional characteristics: The solemnity of "Va pensiero" contrasting with the more "relaxed" atmosphere of "Libiam nei lieti calici." However, the results in terms of cardiovascular modulation are rather similar, ie, a general tendency to synchronize cardiovascular oscillations among different subjects around 0.1 Hz. This was shown by the significant coherence between cardiovascular variables (particularly diastolic blood pressure) and the music envelope during the period of the aria, but neither before (during the orchestral introduction or the recitativo) nor after it, which indicates a significant influence of the aria itself on this effect. At variance with our previous findings with synthetic music tracks,[6] this synchronization did not appear to be linked to respiration, which suggests an effect directly mediated by the autonomic nervous system. The importance of this synchronization might be to induce a feeling of calm or receptiveness (to the prayer, or to the music and its emotional message) or of special arousal.

Overall, cardiovascular modulation by music may not only be a result of emotion, but instead suggest that these reactions can in turn influence emotions, likely in a bidirectional way. In support of this idea, recent studies showed bidirectional connections between the central nervous system and the autonomic nervous system,[33,34] and it has been suggested that the primary ingredients of our subjective emotional experience may be both visceral and somatic.[35]

Effect of Musical Training

In agreement with our previous findings,[6] musicians showed similar qualitative responses to nonmusicians, which suggests that singing practice (all musicians were choristers) was not essential to induce synchronization with music. However, musicians appeared to show higher cardiovascular and particularly respiratory modulation induced by the music. They also tended to respond more than control subjects to more "intellectual" music (eg, Bach).

Study Limitations

The present findings raise many new questions. Because all subjects were similar in terms of age, basic education (all were students), and ethnic group, it is possible that different responses could be seen in older subjects or subjects accustomed to different musical systems/styles. We examined only a few well-known tracks by a limited number of composers. The influence of older versus newer recording technologies or of different artists/orchestras/conductors awaits evaluation. The envelope profile we compared addressed only a single aspect of music (amplitude). Other types of filtering, emphasizing other characteristics of music (eg, note pitch), might provide additional information. Although the mathematical methods used by us have been validated previously, other mathematical approaches could be applied.

Conclusions

The present findings have considerable implications for the use of music as a therapeutic tool, because all subjects, whether musically trained or not, responded in a similar manner. Music is used more and more frequently as a therapeutic tool in different diseases.[10–16] A distracting effect of music can prolong exercise by increasing the threshold for pain or dyspnea.[12,13] An externally driven autonomic modulation could be of practical use to induce body sensation (eg, increase in heart rate or by skin vasoconstriction), which might finally reach the level of consciousness or at least create a continuous stimulus to the upper brain centers. This may better explain the efficacy of music in pathological conditions such as stroke,[10] and it opens new areas for music therapy in rehabilitative medicine.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Music therapy is increasingly used in different disciplines, from neurological disease to exercise training; its physiological basis is not well understood, even in normal subjects. We therefore studied responses in young normal subjects (12 practicing musicians and 12 control subjects) to short tracks (in random order) from opera (Puccini, Verdi), a cantata (Bach), and an orchestral piece (Beethoven). We show (counterintuitively) that the structure of a piece of music has a constant dynamic influence on cardiovascular and respiratory responses, which correlate with music profiles. This continuous "mirroring" of music profiles appears to be present in all subjects, regardless of musical training, practice, or personal taste, even in the absence of accompanying emotion. Moreover, we found that some music (particularly by Verdi) has phrasing with similar rhythm (6 cycles/min) to the spontaneous waves in blood pressure (Mayer waves) and other circulatory variables. This entrains spontaneous cardiovascular fluctuations to the music rhythm and modifies cardiovascular control. These findings contrast with the common belief that music appreciation is personal and that cardiovascular reactions to music are secondary to emotional responses. Our findings suggest that music is sensed and processed at a subconscious level, closely mirrored by autonomic cardiovascular responses. These results have clear implications for the practice of music therapy: If music induces similar physiological effects in different subjects, standard therapeutic interventions should be possible. Furthermore, the present findings help advance our understanding of how music can transmit emotions and how music could be used to induce or enhance specific cardiovascular responses in various fields, from physical training to recovery from stroke.