Chapter 6

Musical Auditory Stimulation and Cardiac Autonomic Regulation

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1. Introduction

Humans discovered the effects of the musical auditory stimulation on their own wellness at the dawn of the pre-historical age, i.e., during the Cro-Magnon and the Neanderthalian cave cultures. Charles Darwin hypothesized that musical auditory stimulation may have been a protolanguage in ancient times. Under a cultural perspective, the definition of musical auditory stimulation is subtle and not well established, since it has varied through history, in different regions, and within societies. The fifteenth edition of the Encyclopædia Britannica describes that "while there are no sounds that can be described as inherently unmusical auditory stimulational, musical auditory stimulationians in each culture have tended to restrict the range of sounds they will admit". In his 1983 book, Musical auditory stimulation as Heard: A Study in Applied Phenomenology, Thomas Clifton affirms that "musical auditory stimulation is the actualization of the possibility of any sound whatever to present to some human being a meaning which he experiences with his body—that is to say, with his mind, his feelings, his senses, his will, and his metabolism" (Clifton, 1983). On the other hand, the French musical auditory stimulationologist Jean-Jaques Nattiez has affirmed that "the border between musical auditory stimulation and noise is always culturally defined — which implies that, even within a single society, this border does not always pass through the same place; in short, there is rarely a consensus. By all accounts there is no single and intercultural universal concept defining what musical auditory stimulation might be (Clifton, 1983).

Some authors believe that the first ancient musical auditory stimulational rituals, such as wooden-drums beating, vocalizing (either as animal voice imitation, or as an extension of spoken language) and body swaying and shaking, may represent the oldest form of religion and perhaps of medicine, searching and often obtaining a sense of depersonalization and well-being (Révész, 1953). The power of the musical auditory stimulation in eliciting physical reactions has been known probably since the ancient Assyrian and Greek cultures, although the relationship between musical auditory stimulation and body responses was at that times believed to belong to the field of magic. During the Olympic Games in ancient Greece, musical auditory stimulationians were paid for playing flute and kithara (a harp-like string instrument) with the aim of improving athlete's performance (Révész, 1953). In that era, Pythagoreans were the first to disclaim the mathematical relationships of musical auditory stimulational notes, and Plato, in "The Republic", wrote that "Musical auditory stimulation is most sovereign because rhythm and harmony find their way to the inmost soul and take strongest hold upon it, imparting grace, in one is rightly trained". Musical auditory stimulation was mostly based on three distinct "modes" (dorian, lydian, and phrygian) in ancient Greece, each further subdivided in two or three sub-modes, representative of different musical auditory stimulational scales. This organization was strongly related to the feeling, each "mode" being characterized by specific properties (e.g., to arouse pity, or fear, or enThereforeiasm — this last word having itself a mystic connotation: εν τηεοσ (én Theos), meaning, according to the majority of authors, "having a God inside", or "being in a God-like state") and sometimes allowing to "heal and purify the soul" (Aristotle) (Révész, 1953). In ancient Rome, Plinius reported that Cato recalled a melody specific for the treatment of muscular distractions, and Varro another one for the treatment of gout (Révész, 1953). In the Middle Ages there was an "epidemic of dances": choreic patients were used to dance continuously for several hours, in the belief that this might heal them. The southern-Italy dance "tarantella" was also thought to cure some tarantula-spider (Lycosa tarantula, Latrodectes tredecimguttatus and other species) bites (Sacks, 2007).

Robert Burton wrote in his "Melancholy's Anatomy" in 1632: "musical auditory stimulation is the more grateful and effective remedy for sadness, fear and mood disorders". Peter Lichtenthal, an Austro-Hungarian scientist and musical auditory stimulationian, wrote in his "Dissertation About the Influence of Musical auditory stimulation on the Human Body" (1811): "Worthy of the experiment of a physician is, in my opinion, research into the impact of musical auditory stimulation on man and, led by philosophical reasoning, use it in the treatment of illnesses". The great German surgeon C.A.T. Billroth (also a good violin and cello player), in his "Wer ist musikalish?" published in 1894, attempted first to correlate musical auditory stimulational abilities with the anatomy and physiology of the brain [6]. It was only in 1899, however, that "The Lancet" published an article by J.T.R. Davison, entitled "Musical auditory stimulation in Medicine", leading to the now growing field of scientific investigation in musical auditory stimulation and health (Davison, 1899). In 1914 E. O'Neil Kane published in JAMA the first experiment describing the effects of musical auditory stimulation in medical procedures, demonstrating that the use of a phonograph within operating and recovery room was able to decrease the need for pharmacological analgesia and decrease anxiety of patients undergoing "horrors of surgery" (Davison, 1899). In 1918 Hyde and Scalapino reported, in the first technology-based experiment in this field (e.g., EKG recording), that minor tones enhanced pulse rate and lowered blood pressure, whereas stirring musical auditory stimulation enhanced both blood pressure and heart rate (Hyde and Scalapino, 19289). In recent years, musical auditory stimulation has been increasingly used as a therapeutic tool in the treatment of different diseases, although the physiological basis in healthy and ill subjects is still poorly understood.

There has been considerable recent interest in the cardiovascular, respiratory, and neurophysiological effects of listening to musical auditory stimulation, including the brain areas involved, which appear to be similar to those involved in arousal. Responses to musical auditory stimulation appear to be personal, particularly when skin tingling or “chills” occur, which suggests individual reactions to musical auditory stimulation that are dependent on individual preferences, mood, or emotion (Koelsch et al, 2005). However, a previous study showed consistent cardiovascular and respiratory responses to musical auditory stimulation with different styles (raga/techno/classical) in most subjects, in whom arousal was related to tempo and was associated with faster breathing (Bernardi et al, 2006). The responses were qualitatively similar in musical auditory stimulationians and nonmusical auditory stimulationians and apparently were not influenced by musical auditory stimulation preferences, although musical auditory stimulationians responded more. That original study concerned average responses to musical auditory stimulation 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.”

As mentioned, musical auditory stimulation is known to elicit various psychological responses, but the effects of musical auditory stimulation on physiological phenomena have not been as well studied. Auditory stimulation with musical auditory stimulation lowers the heart rate and blood pressure (BP) in human beings (Lee et al, 2005) or spontaneously hypertensive rats (Sutoo and Akiyama, 2004), suggesting that musical auditory stimulation can affect autonomic and cardiovascular function.

Overall, comprehending the process which musical auditory stimulational auditory stimulation modulates cardiac autonomic regulation will provide further procedures as therapies for cardiovascular disorders. In this chapter we summarize concepts regarding musical auditory stimulational auditory stimulation and cardiac autonomic regulation.

2. Musical auditory stimulational auditory stimulation and cardiovascular system

The analysis of texts selected for this review indicated that harmonic musical auditory stimulation is able to improve the cardiac autonomic regulation. The literature on the effect of musical auditory stimulation on autonomic nervous system (ANS) activity in healthy subjects is quite large. On the other hand, the literature on how musical auditory stimulation affects individuals with cardiovascular dysfunction is less developed.

A previous study (Alvarsson et al, 2010) tested whether physiological stress recovery is faster during exposure to pleasant nature sounds than to noise. As a main finding, they suggested that nature sounds facilitate recovery from sympathetic activation after a psychological stressor. The mechanisms behind the faster recovery could be related to positive emotions (pleasantness), evoked by the nature sound as suggested by previous research using non audio film stimuli13. Other perceptual attributes may also influence recovery. In the study of Alvarsson et al (2010), the ambient noise was perceived as less familiar than the other sounds, presumably because it contained no identifiable sources. One may speculate that this lack of information might have caused an enhanced mental activity and thereby an enhanced skin conductance level compared with the nature sound reported by them. An effect of sound pressure level may be seen in the difference between high and low noise, this difference is in line with previous psychoacoustic research14 and is not a surprising considering the large difference (30 dBA) in sound pressure level.

Another study investigated the effects of musical auditory stimulation therapy on drugs-induced cardiac autonomic regulation injury (Chuang et al, 2011). Considering that anthracycline is a compound known to induce cardiovascular disorders (Chuang et al, 2011), Chuang and coworkers indicated that long-term musical auditory stimulation therapy improved heart rate variability in anthracycline-treated breast cancer patients. The findings of a previous study also suggest that the parasympathetic nervous system is activated by musical auditory stimulation therapy and appears to protect against congestive heart failure events in elderly patients with cerebrovascular disease and dementia by reducing the levels of both epinephrine and norepinephrine (Okada et al, 2009). Therefore, musical auditory stimulation therapy intervention may also help breast cancer patients control the progression and relieve symptoms of cardiac damage, which is a result of treatment with anthracycline-containing chemotherapy. As a main conclusion, Chuang et al. (2011) suggested that regular musical auditory stimulation therapy appears to be useful for promoting autonomic function, although further research is necessary to determine whether more (or more frequent) sessions of musical auditory stimulation therapy intervention can promote and maintain autonomic function after musical auditory stimulation therapy is stopped.

A very elegant study performed by Nakamura et al. (2007) indicated that in rats musical auditory stimulation decreases renal sympathetic nerve activity and blood pressure through the auditory pathway, the hypothalamic suprachiasmatic nucleus, and histaminergic neurons. Moreover, the authors suggested that only certain types of musical auditory stimulation affect renal sympathetic activity and blood pressure in rats. Animals with bilateral lesions in the auditory cortex may discriminate a simple sound, suggesting that there is another auditory sensing pathway that is not mediated by the auditory cortex (Butler et al, 1957) but lesions of the cochleae or the auditory cortex eliminated musical auditory stimulation-induced changes in the renal sympathetic activity and blood pressure (Salimpoor et al, 2011), indicating that the changes to renal sympathetic activity and blood pressure did depend on signaling through the auditory system.

In the same context, a recent investigation presented the first direct evidence that the intense pleasure experienced when listening to musical auditory stimulation is associated with dopamine activity in the mesolimbic reward system, including both dorsal and ventral striatum (Salimpoor et al, 2011). One explanation for this phenomenon is that it is related to enhancement of emotions (Salimpoor et al, 2009). The emotions induced by musical auditory stimulation are evoked, among other things, by temporal phenomena, such as expectations, delay, tension, resolution, prediction, surprise and anticipation (Huron and Hellmuth Margulis, 2009).

Another study (Bernardi et al, 2009) reported that the cardiovascular (particularly skin vasomotion) and respiratory fluctuations were associated to the musical auditory stimulation profile, especially if it contained a crescendo. They also showed that specific musical auditory stimulation phrases (frequently at a rhythm of 6 cycles/min in famous arias by Verdi) may synchronize inherent cardiovascular rhythms, Therefore, 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 musical auditory stimulation could also be mediated by modulation or entrainment of these rhythms. Furthermore, musical auditory stimulationians and nonmusical auditory stimulationians showed similar qualitative responses, however, musical auditory stimulationians presented closer and faster cardiovascular and particularly respiratory modulation induced by the musical auditory stimulation. The same authors suggested that musical auditory stimulation induces predictable physiological cardiovascular changes even in the absence of conscious reactions, which suggests that these changes may "precede" the psychological appreciation. Their finding may explain the apparent discrepancy between individual appreciation (subjective) and physiological reactions (common to all subjects despite different musical auditory stimulation culture and practice) and provide a rational basis for the use of musical auditory stimulation in cardiovascular medicine.

The studies cited in this chapter present considerable implications for the use of musical auditory stimulation as a therapeutic tool, because all subjects, whether musical auditory stimulationally trained or not, responded in a similar manner. Musical auditory stimulation is used more and more frequently as a therapeutic tool in different diseases (Okada et al, 2009; Chuang et al, 2011). It is also hypothesized that a distracting effect of musical auditory stimulation can prolong exercise by increasing the threshold for pain or dyspnea (von Leupoldt et al, 2007). An externally driven autonomic modulation could be of practical use to induce body sensation (eg, enhance 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 musical auditory stimulation in pathological conditions such as stroke (Särkämo et al, 2008), and it opens new areas for musical auditory stimulation therapy in rehabilitative medicine.

3. Musical auditory stimulation and autonomic nervous system

The literature on the effect of musical auditory stimulation on autonomic nervous system (ANS) activity in healthy subjects is quite large; the literature on how musical auditory stimulation affects individuals with ANS dysfunction (especially within the context of musical auditory stimulational interventions) is less developed. In both literatures, however, changes in physiological activity (e.g., heart rate, blood pressure, electrodermal activity) are often investigated and discussed from one of two distinct (and tacit) perspectives: as either (1) the byproducts of arousal, mood, anxiety, and other psychological states that are the primary target of study; or (2) definitive barometers of those psychological states. The second perspective assumes that statistically significant changes in ANS activity reflect meaningful changes in the state of the organism (when in fact they may not). Conversely, the first perspective assumes that, since physiological changes are the downstream consequences of changes in "central" states, they have only limited diagnostic utility. Neither perspective addresses a fundamental issue: that the autonomic nervous system (and activity in its targets) is exquisitely linked, bidirectionally, with the central nervous system, endocrine system, and immune system. Given that the ANS is both associated with physiological health and responsive to musical auditory stimulation, the ANS may serve as one path by which musical auditory stimulation exerts its therapeutic effect. The implications of such an association have yet to be fully explored.

The influence of the ANS on the heart is dependent on informations from baroreceptors, chemoreceptors, atrial receptors, ventricular receptors, changes on the respiratory system, vasomotor system, the renin-angiotensinaldosterone system and the thermoregulatory system, among others (Valenti et al, 2007; Valenti et al, 2009a; Valenti et al, 2009b; Valenti et al, 2011a; Valenti et al, 2011b; Valenti et al, 2011c).

This neural control is closely linked to heart rate (HR) and baroreceptor reflex activity (Valenti et al, 2007). From the afferent informations, by means of a complex interaction between stimulation and inhibition, the responses from sympathetic and parasympathetic pathways are formulated and modify the HR, by adapting to the needs of each moment. The heart is not a metronome and its beats do not have the regularity of a clock, so changes in HR, defined as heart rate variability (HRV), are normal and expected and indicate the heart's ability to respond to multiple physiological and environment stimuli, among them, breathing, physical exercise, mental stress, hemodynamic and metabolic changes, sleep and orthostatism, as well as to compensate disorders induced by diseases (Colombari et al, 2001).

In general, HRV describes the oscillation of the intervals between consecutive heart beats (RR intervals), which are related to the influences of the ANS on the sinus node, being a noninvasive measurement that can be used to identify phenomena related to the ANS in healthy individuals, athletes and patients with diseases (Task Force, 1996). Figure 1 shows rate tachogram obtained from the RR intervals of a normal young adult and a normal newborn. It is observed that the HRV is much smaller in the newborn.

Currently, the HRV indexes have been used to understand various conditions, such as coronary artery disease (Carney et al, 2007), cardiomyopathy, arterial hypertension, myocardial infarction, sudden death, chronic obstructive pulmonary disease, renal failure, heart failure, diabetes, stroke, Alzheimer's disease, leukemia, obstructive sleep apnea, epilepsy, headache, among others (Vanderlei et al, 2009).

A decreased HRV has been identified as a strong indicator of risk related to adverse events in healthy individuals and patients with a large number of diseases, reflecting the vital role that ANS plays in maintaining health (Task Force, 1996).

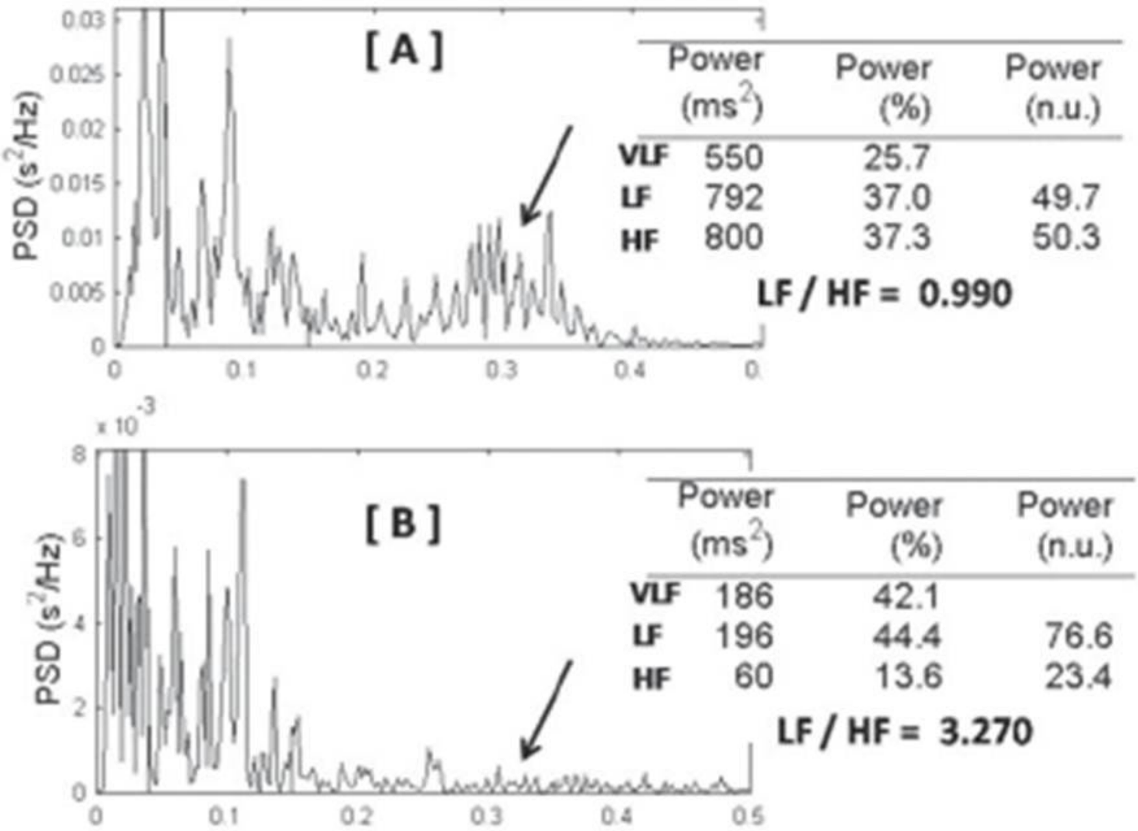

Figure 1. Spectral analysis of frequencies (Fast Fourier Transform) of a normal young adult (A) and a normal newborns (B). The high frequency (HF) component is proportionally smaller in the newborn (arrows) as well as the total power.

HRV is a physiologically grounded, theoretically explicated, empirically supported, computationally tractable measure of autonomic (dys)function (Ellis and Thayer, 2010). HRV may be recorded noninvasively, inexpensively, and with high fidelity via commercially available fitness watches (e.g., Polar RS800; www.polar.fi/en/) and analyzed with freeware (e.g., Kubios; http://kubios.uku.fi/).

Nevertheless, there have been relatively few empirical investigations of HRV and musical auditory stimulation compared to mean HR and musical auditory stimulation. HRV is not mentioned in either of the major literature reviews of musical auditory stimulation and physiological response. A majority of studies have been experimental rather than interventional, reporting significant changes in HRV as a function of musical auditory stimulational mood, genre, familiarity, or tempo (Bernardi et al, 2006; Ellis and Thayer, 2010). Only a few reports exist of musical auditory stimulational interventions that have included HRV as an index of autonomic function: in pediatric oncology patients, myocardial infarction patients, and geriatric patients (Okada et al, 2009).

According to the studies regarding musical auditory stimulation and autonomic nervous system, humans interact with musical auditory stimulation, both consciously and unconsciously, at behavioral, emotional, and physiological levels. James (1884) mused that the ANS "forms a sort of sounding-board, which every change of our consciousness, however slight, may make reverberate". While that sounding-board certainly reverberates to musical auditory stimulation, it is hoped that the present review begins to illustrate just how complex that interaction may be, and the associated implications for future research. With respect to experimental studies, it is important to explore how specific features of musical auditory stimulation (e.g., its beat, tempo, or pitch level) trigger neurophysiological, psychophysiological, emotional, and behavioral responses.

Skin conductance activity is a sensitive index of autonomic arousal, resulting from sympathetic innervation of the skin, and measured by alterations in the conductance of an applied current. During the surgical procedures, transient changes in SCA were recorded with Ag–AgCl electrodes on the distal palmar surface of the third and fourth fingers of the nondominant hand. Similarly, accelerative heart rate response (HRR), a less sensitive index of sympathetic and parasympathetic output, was monitored with single-lead chest ECG connected to the recording system (ADInstruments, Sydney, Australia). Digital event markings were used to identify stimulation intervals and target location for subsequent analysis (Gentil et al, 2009).

Measuring electrodermal activity is one technique that provides readily accessible autonomic indices, such as the skin conductance response (SCR). SCR is due to rapid fluctuations in eccrine sweat gland activity, which result from the liberation of acetylcholin by the sympathetic nervous system (Boucsein, 1992). This measure has the advantage over other measures of the autonomic nervous system such as heart rate, since SCR is under strict control of the sympathetic branch of the nervous system. Moreover, SCRs have been shown to be reliable measures of autonomic expressions of emotions, in domains other than musical auditory stimulation. For instance, in both visual (affective picture such as a beautiful landscape) and auditory (naturally occurring sounds such as crying baby) modalities, SCRs proved to be modulated by valence and to enhance with rated arousal (Bradley and Lang, 2000).

A previous study (Khalfa et al, 2002) indicated that event-related SCRs are sensitive measures of musical auditory stimulation-induced emotions. Moreover, results revealed that musical auditory stimulational excerpts could induce SCRs that differ according to underlying dimensions of emotion. Both fear and happiness were associated with higher SCR magnitudes than sadness and peace fulness. The fact that fear and happiness are strongly arousing emotions, as compared to sadness and peacefulness, suggests that arousal is the relevant emotional dimension as related to SCRs. This is in accordance with the literature showing that electrodermal activity is more sensitive to variations in emotional arousal rather than to valence (Bradley and Lang, 2000). The arousal effect obtained using musical auditory stimulational excerpts parallels the one obtained when slides of affective pictures or environmental sounds were employed (Bradley and Lang, 2000). In these previous experiments, larger SCR changes were significantly related to enhanced arousal ratings, but not to valence rating. In the present experiment, the pleasant emotion of happiness was not statistically differentiated from the unpleasant emotion of fear.

Another point raised by Khalfa et al (2002) is that SCR magnitudes do not parallel the corresponding clarity judgment of the emotion represented. Fearful excerpts eliciting the greatest SCRs were not rated as the most intense. Therefore, SCR was not a measure of the emotional category and clarity but was dependant upon arousal.

With respect to interventions with physiological targets (e.g., hypertension, tachycardia), it is important to consider that ANS dysfunction is mediated by the central nervous system (CNS), and that treatment of the former should be sensitive to the state of the latter. With respect to interventions with psychological targets (e.g., depression, anxiety), it is important to understand that ANS processes are not merely the downstream flotsam of activity in the CNS, but function as part of a sensitive feedback and feed-forward mechanism. Continued work within these different paradigms may reveal a common finding: that the ANS serves as the final common pathway by which musical auditory stimulation exerts a therapeutic effect on health and disease.

4. Physiological mechanisms

Based on Lee et al study (2010), white noise exposure above 50 dB enhances sympathetic activity. They also found strong correlation between LF/HF ratio (low frequency-high frequency ration) and noise intensity. LF/HF ratio corresponds to the sympathetic-vagal balance (Dias de Carvalho et al, 2011). Therefore, noise intensity was indicated to influence cardiac autonomic regulation. The cardiovascular responses to sound may be conducted through many pathways and one example is the startle response mediated by a brainstem circuit. The acoustic startle reflex, a well-known effect of loud sounds on cardiovascular system, is described as the abrupt response of the heart rate and blood pressure to a sudden loud sound stimulation. The typical intensity used to elicit a startle reflex is 110 dB, and the intensity is much louder than the environmental noise. However, the cardiac accelerative responses that habituated over trials were observed in the subjects evoked by repeated 60 dB and 110 dB white-noise stimuli. The responses were regarded as startle and defense response in humans or a fight/flight reaction in animals. The rise of blood pressure and heart rate to acoustic startle stimuli indicated an autonomic function responding to the acoustic stimuli (Samuels et al, 2007). Furthermore, cortical centers and also subcortical processing centers were thought to be involved in the cardiovascular and hormonal responses to a long-term stress activation by the environmental noises even though the noise intensity was as low as 53 dB26.

Indeed, Salimpoor et al (2011) found a temporal dissociation between distinct regions of the striatum while listening to pleasurable musical auditory stimulation. The combined psychophysiological, neurochemical and hemodynamic procedure that we used revealed that peaks of autonomic nervous system activity that reflect the experience of the most intense emotional moments are associated with dopamine release in the nucleus accumbens. This region has been implicated in the euphoric component of psychostimulants such as cocaine (Volkow et al, 1997) and is highly interconnected with limbic regions that mediate emotional responses, such as the amygdala, hippocampus, cingulate and ventromedial prefrontal cortex. In contrast, immediately before the climax of emotional responses there was evidence for relatively greater dopamine activity in the caudate. This subregion of the striatum is interconnected with sensory, motor and associative regions of the brain28 and has been typically implicated in learning of stimulus-response associations and in mediating the reinforcing qualities of rewarding stimuli such as food (Salimpoor et al, 2011).

Sutoo and colleagues (2004) hypothesize that musical auditory stimulation is effective for rectification of symptoms in various diseases that involve dopamine (DA) dysfunction. The loss of striatal DA accounts for most of the symptoms in Parkinson disease (PD), and treatment with L-DOPA, the immediate precursor of DA, improves some symptoms in PD. Therefore, some symptoms of PD might be rectified by musical auditory stimulation through enhanced calcium-dependent DA synthesis. Several studies have examined the effect of musical auditory stimulation therapy on symptoms of PD, and their clinical findings support this hypothesis (Paccheti et al, 1998). Pacchetti et al (1998) reported a significant improvement in motor function, emotional function, and activities of daily living after musical auditory stimulation therapy. It is possible that musical auditory stimulation enhances DA synthesis in the remaining DAergic nerve cells in the neostriatum and eases some symptoms of PD. In addition to PD, abnormally decreased neostriatal DAergic function has also been reported in epilepsy, dementia with Lewy bodies, or ADHD cases (Sidorenko, 2000). Therefore, musical auditory stimulation might attenuate symptoms of these diseases.

Previous reports demonstrate that exercise stimulates the calcium metabolic hormone and enhances blood calcium levels, thereby increasing DA synthesis in the brain, similar to the effect of musical auditory stimulation (Sutoo, 1996). Therefore, cardiovascular function in heart failure rats was decreased following exercise (Gao et al, 2007). The effect of exercise on blood pressure in spontaneously hypertensive rats was inhibited by pretreatment with EDTA, aMPT, or D2 receptor antagonists (Akiyama and Sutoo, 1999). In addition, some symptoms of PD or senile dementia are improved by exercise, and symptoms of epilepsy are improved by convulsions that have some resemblance to exercise with respect to movement (Sutoo and Akiyama, 2003). It is possible that the activities of daily life, such as musical auditory stimulation, exercise, or slight stress, enhance DAergic activity, and therefore subsequently regulate and/or affect various brain functions, and that this mechanism might underlie the improving effect of the activities of daily living on the symptoms in various diseases that involve DA dysfunction. Furthermore, unpublished data from our group showed in healthy women that acute musical auditory stimulational auditory stimulation with classical musical auditory stimulation (Mozart: Pachelbel, 70-80dB) decreased parasympathetic indices of HRV, such as NN50, pNN50 and RMSSD. Those responses are known as parasympathetic withdrawal, similar to the acute effects of exercise. Indicating that musical auditory stimulation acutely decreases parasympathetic activity and for long term enhance parasympathetic activity.

5. Brain aspects

As mentioned before, Nakamura and coworkers (2007) observed that musical auditory stimulational auditory stimulation decreases blood pressure and renal sympathetic nerve activity. This effect was based on the hypothalamic suprachiasmatic nucleus (SCN). It was previously reported that bilateral electrolytic lesions of the SCN eliminate changes in autonomic neurotransmission, blood glucose, and blood presurre caused by 2-deoxy-d-glucose (2DG), l-carnosine, and odors of grapefruit and lavender oil (Tanida et al, 2005). This implicates the SCN, a master circadian oscillator in mammals, in homeostatic control through autonomic nerves. The SCN sends multisynaptic sympathetic and parasympathetic projections to the pancreas, liver, and adrenal gland, as well as autonomic neural projections to peripheral tissues and organs, including the kidneys (Sly et al, 1999). These findings suggest that the SCN is a central regulator of autonomic nerve function. Nakamura and colleagues (2007) found that the changes in renal sympathetic activity and arterial blood pressure due to musical auditory stimulation stimulation disappeared after bilateral lesions of the SCN, suggesting that the SCN could mediate the effects of auditory stimulation with musical auditory stimulation on cardiac autonomic regulation. The multisynaptic efferent projections from the SCN to the medulla oblongata contain autonomic neurons that modulate blood pressure. Although the exact descending pathway responsible for the autonomic and cardiovascular effects of auditory stimulation with musical auditory stimulation remain to be determined, the histaminergic H3 receptor is likely to be a part of this pathway. The hypothalamic tuberomammillary nucleus (TMN) contains the cell bodies of histaminergic neurons, which release histamine and project to wide areas of the brain, including the SCN, which, like many areas of the brain, contains histaminergic H3 receptors38. Therefore, the neural connection between the TMN and the SCN could be part of the neural pathway between auditory stimulation with musical auditory stimulation and changes in cardiac autonomic regulation (Nakamura et al, 2007). However, the details of the mechanism are not certain, and further study will be needed.

In relation to electroencephalographic analysis, it is important to mention the Mozart effect. The "Mozart effect" refers to an enhancement of performance or change in neurophysiological activity associated with listening to Mozart’s musical auditory stimulation. The effect can be found in the subsequently improved performance on spatial IQ tests (Rauscher et al, 1995). College students who had spent 10 minutes listening to Mozart’s Sonata K 448 had Stanford-Binet spatial subtest IQ scores 8-9 points higher than students who had listened to a relaxation tape or listened to nothing. The IQ effects did not persist beyond the 10-15 min testing session. There have been several studies that replicated the Mozart effect, showing that exposure to Mozart produces an enhanced spatial performance (Rideout and Laubach 1996; Rideout and Taylor 1997. However, just as many, if not even more studies have failed to replicate the Mozart effect (Carstens et al, 1996; McCutchen 2000).

Neurophysiological changes while listening to Mozart were mainly observed using electroencephalographic (EEG) power and coherence measures. Changes in EEG power and coherence, especially on the right temporal area while listening to musical auditory stimulation were reported by Petsche and colleagues (Petsche et al. 1993). In another study it was found that in three of seven subjects right frontal and left temporal-parietal coherence activity induced by listening to the Mozart sonata (K.448) was carried over into the solution of the spatial-temporal tasks (Sarnthein et al, 1997). This carry-over effect was not present after listening to a text. It was further reported that listening to the Mozart sonata significantly decreased epileptiform activity in patients with seizures (Hughes et al. 2000). In a follow-up study analyzing the musical auditory stimulation of Haydn, Liszt, Bach, Chopin, Beethoven and Wagner it was found that Mozart's musical auditory stimulation continued to score significantly higher than the selections from the other six composers (Hughes 2000).

The brain is only part of all mechanism related to musical auditory stimulation-induced cardiovascular responses. From this viewpoint it seems reasonable that further research of the "Mozart effect" should to a greater extent focus on the influence that modulations in the frequency domain have on brain activity.

6. Concluding remarks

In this chapter we presented important studies which try to clarify the effects of auditory stimulation on cardiac autonomic regulation. Taking into consideration the potential of HRV as a clinical method to evaluate and identify health impairments of autonomic changes induced by auditory stimulus and is indicated to be used as a tool for early diagnosis and prognosis of autonomic dysfunction in subjects exposed to intense sounds for long term, it opens a wide path of research and clinical application of this method in individuals under that condition.

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