

## RELATIONSHIP BETWEEN CARDIAC AUTONOMIC REGULATION AND AUDITORY MECHANISMS: IMPORTANCE FOR GROWTH AND DEVELOPMENT

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### Abstract

The literature has already demonstrated that auditory stimulation with music influences the cardiovascular system. In this study, we performed a literature review in order to investigate the relationship between auditory mechanisms and cardiac autonomic regulation. The selected studies indicated that there is a strong correlation between noise intensity and vagal-sympathetic balance. Also, it was reported that music therapy improved heart rate variability in anthracycline-treated breast cancer patients. It was hypothesized that dopamine release in the striatal system induced by pleasure songs are involved in the cardiac autonomic regulation. Further studies are necessary to add new elements in the literature to improve new therapies to treat cardiovascular disorders.

**Key words:** auditory stimulation; autonomic nervous system.

### INTRODUCTION

Music has always been part of the diverse cultures of humanity, establishing a link between human sensations and pleasures and senses through melody and rhythm. However, with abuse in duration, intensity and/or frequency of music, the noise may become a problem for hearing<sup>1</sup>. The noise-induced hearing loss is well known in studies related to the workplace. On the other hand, there is growing concern about the damage caused by non-occupational exposure to noise, as in the cases of the use of headphones (stereo portable systems)<sup>2</sup>.

Recently a study regarding the knowledge of children and their parents about the risk of hearing loss, reported that 17.3% of the children interviewed in intensive listening music through earphones<sup>3</sup>. This habit in this young population is increasing the risk for the acquisition of music-induced hearing loss, the author of this study noted that 14% of youth surveyed reported risk behavior for acquiring auditory loss<sup>4</sup>.

Another study related to the knowledge of students about attitudes and practices for the

hearing health and use of iPods and/or personal listening devices, demonstrated that a portion of the students surveyed use their equipment at high sound pressure levels for extended periods of time. Therefore, there are at risk for auditory damage<sup>5</sup>. Within this theme 1687 adolescents (12-19 years of age) were surveyed, of which 90% reported listening to music through headphones on MP3 players and 28.6% were classified as listeners at risk for hearing loss according to the Scientific Committee on Emerging and Newly Identified Health Risks<sup>6</sup> - listen for a period e" 1 hour per day in loudness > 89 dBA<sup>7</sup>.

The inner ear contains the vestibulocochlear system, which is related to the reception of sound and maintaining balance. It lies within the petrous portion of the temporal bone and consists of bags and ducts of the membranous labyrinth. The labyrinth is irrigated by internal labyrinthine artery, in most cases branch of the anterior inferior cerebellar artery and in some cases branch of basilar artery. The labyrinthine artery divides into: cochlear artery, for irrigation of the cochlea and vestibular arteries anterior and posterior semicircular canals to irrigate, utricle, saccule and part of the cochlea<sup>8</sup>.

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Nerve cells and sensory organs are very sensitive to changes in blood flow. Some studies have shown a significant association between hearing loss and hypertension<sup>9,10</sup>. And an important meta-analysis presented data demonstrating statistically that in a group of workers with high exposure to noise, increased: blood pressure systolic and diastolic, the prevalence of hypertension, and electrocardiographic changes in relation to groups and intermediate exposure low noise exposure. In addition, there was an increase in heart rate with high exposure group compared to the group with low exposure<sup>11</sup>.

In view of the above considerations, this review was undertaken to investigate the relationship between cardiac autonomic regulation and auditory mechanisms and its relevance for human growth and development.

## **MUSICAL AUDITORY STIMULATION AND CARDIOVASCULAR SYSTEM**

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

A previous study<sup>12</sup> test 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 stimuli<sup>13</sup>. Other perceptual attributes may also influence recovery. In the study of Alvarsson et al<sup>12</sup>, 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 increased mental activity and thereby an increased 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 research<sup>14</sup> and is not a surprising considering the large difference (30 dBA) in sound pressure level.

Considering that anthracycline is a compound known to induce cardiovascular disorders<sup>15</sup>, Chuang and coworkers indicated that long-term music therapy improved heart rate variability in anthracycline-treated breast cancer patients<sup>15</sup>. The findings of a previous study also suggest that the

parasympathetic nervous system is activated by music 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<sup>16</sup>. Therefore, music 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.<sup>15</sup> suggested that regular music therapy appears to be useful for promoting autonomic function, although further research is necessary to determine whether more (or more frequent) sessions of music therapy intervention can promote and maintain autonomic function after music therapy is stopped.

A very elegant study performed by Nakamura et al.<sup>17</sup> and coworkers indicated that in rats music reduces renal sympathetic nerve activity and blood pressure through the auditory pathway, the hypothalamic supraoptic nucleus, and histaminergic neurons. Moreover, the authors suggested that only certain types of music 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<sup>18</sup> but lesions of the cochleae or the auditory cortex eliminated music-induced changes in the renal sympathetic activity and blood pressure<sup>17</sup>, 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 music is associated with dopamine activity in the mesolimbic reward system, including both dorsal and ventral striatum<sup>19</sup>. One explanation for this phenomenon is that it is related to enhancement of emotions<sup>20</sup>. The emotions induced by music are evoked, among other things, by temporal phenomena, such as expectations, delay, tension, resolution, prediction, surprise and anticipation<sup>21</sup>.

## **PHYSIOLOGICAL MECHANISMS AND GROWTH**

Based on Lee et al study<sup>22</sup>, 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<sup>23</sup>. Thus, 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<sup>24</sup>. 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<sup>25</sup>. 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 dB<sup>26</sup>.

Indeed, Salimpoor et al<sup>19</sup> found a temporal dissociation between distinct regions of the striatum while listening to pleasurable music. 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<sup>27</sup> and is highly interconnected with limbic regions that mediate emotional responses, such as the amygdala, hippocampus, cingulate and ventromedial prefrontal cortex<sup>28</sup>. 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 brain<sup>28</sup> and has been typically implicated in learning of stimulus-response associations<sup>28</sup> and in mediating the reinforcing qualities of rewarding stimuli such as food<sup>29</sup>.

A recent study investigated whether children with and without autism spectrum disorder differ in autonomic activity at rest and in response to auditory stimuli and whether behavioral problems related to sounds in everyday life are associated with autonomic responses to auditory stimuli<sup>30</sup>. They measured skin conductance at rest and in response to auditory stimuli as well as behavioral responses using the Sensory Processing Measure Home Form. The autism spectrum disorder group presented significantly higher resting skin conductance and stronger skin conductance reactivity to tones than the control group. Correlations between skin conductance and sensory processing measure indicated that more severe auditory behavioral difficulties were associated with higher sympathetic activation at rest and stronger sympathetic reactivity to sound. The authors concluded that high sympathetic reactivity to sound may underlie the difficult behavioral responses to sound that children with autism spectrum disorder often demonstrate.

## BRAIN ASPECTS

As mentioned before, Nakamura and coworkers observed that musical 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 BP caused by 2-deoxy-d-glucose (2DG)<sup>31</sup>, l-carnosine<sup>32</sup>, and odors of grapefruit and lavender oil<sup>33</sup>. This implicates the SCN, a master circadian oscillator in mammals, in homeostatic control through autonomic nerves<sup>34</sup>. The SCN sends multisynaptic sympathetic and parasympathetic projections to the pancreas, liver, and adrenal gland<sup>35</sup>, as well as autonomic neural projections to peripheral tissues and organs, including the kidneys<sup>36</sup>. These findings suggest that the SCN is a central regulator of autonomic nerve function. Nakamura and colleagues found that the changes in renal sympathetic activity and arterial blood pressure due to music stimulation disappeared after bilateral lesions of the SCN, suggesting that the SCN could mediate the effects of auditory stimulation with music on cardiac autonomic regulation. The multisynaptic efferent projections from the SCN to the medulla oblongata contain autonomic neurons that modulate blood pressure<sup>37</sup>. Although the exact descending pathway responsible for the autonomic and cardiovascular effects of auditory stimulation with music 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<sup>38</sup>, which, like many areas of the brain, contains histaminergic H3 receptors<sup>39</sup>. Therefore, the neural connection between the TMN and the SCN could be part of the neural pathway between auditory stimulation with music and changes in cardiac autonomic regulation. However, the details of the mechanism are not certain, and further study will be needed.

A very interesting study performed by Skoe and Kraus<sup>40</sup> indicated that playing a musical instrument changes the anatomy and function of the brain. The authors addressed this issue by measuring auditory brainstem responses in a cohort of healthy young human adults with varying amounts of past musical training. It was observed that adults who received formal music instruction as children have more robust brainstem responses to sound than peers who never participated in music lessons and that the magnitude of the response correlates with how recently training ceased. The results suggested that neural changes accompanying musical training during childhood are retained in adulthood. These findings advance the comprehension of long-term neuroplasticity and

have general implications for the development of effective auditory training programs.

In the same context, motor timing tasks have been employed in studies of neurodevelopmental disorders such as developmental dyslexia and attention deficit hyperactive disorder, where it is provided an index of temporal processing ability. Investigations of these disorders have used different stimulus parameters within the motor timing tasks that are likely to affect performance measures. Birkett and Talcott<sup>41</sup> assessed the effect of auditory and visual pacing stimuli on synchronised motor timing performance and its relationship with cognitive and behavioural predictors that are commonly used in the diagnosis of these highly prevalent developmental disorders. Twenty-one children (mean age 9.6 years) completed a finger tapping task in two stimulus conditions, together with additional psychometric measures. As anticipated, synchronization to the beat (ISI 329 ms) was less accurate in the visually paced condition. Decomposition of timing variance indicated that this effect resulted from differences in the way that visual and auditory paced tasks are

processed by central timekeeping and associated peripheral implementation systems. The ability to utilize an efficient processing strategy on the visual task correlated with both reading and sustained attention skills. Dissociations between these patterns of relationship across task modality suggest that not all timing tasks are equivalent.

## CONCLUDING REMARKS

In this review we presented important studies which try to clarify the effects of auditory stimulation on cardiac autonomic regulation and its relationship with human growth and development. 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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