

Mozart, Music and Medicine

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Key Words

Music · Mozart effect · Neurobiology · Positron emission tomography · Functional magnetic resonance imaging · Emotion · Well-being

Abstract

According to the first publication in 1993 by Rauscher et al. [Nature 1993;365:611], the Mozart effect implies the enhancement of reasoning skills solving spatial problems in normal subjects after listening to Mozart's piano sonata K 448. A further evaluation of this effect has raised the question whether there is a link between music-generated emotions and a higher level of cognitive abilities by mere listening. Positron emission tomography and functional magnetic resonance imaging have revealed that listening to pleasurable music activates cortical and subcortical cerebral areas where emotions are processed. These neurobiological effects of music suggest that auditory stimulation evokes emotions linked to heightened arousal and result in temporarily enhanced performance in many cognitive domains. Music therapy applies this arousal in a clinical setting as it may offer benefits to patients by diverting their attention from unpleasant experiences and future interventions. It has been applied in the context of various important clinical conditions such as cardiovascular disorders, cancer pain, epilepsy, depression and dementia. Furthermore, music may modu-

late the immune response, among other things, evidenced by increasing the activity of natural killer cells, lymphocytes and interferon- γ , which is an interesting feature as many diseases are related to a misbalanced immune system. Many of these clinical studies, however, suffer from methodological inadequacies. Nevertheless, at present, there is moderate but not altogether convincing evidence that listening to known and liked music helps to decrease the burden of a disease and enhances the immune system by modifying stress.

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All colours in music come from emotional states.
Murray Perahia in 'Play It Again' by Alan Rusbridger

Introduction

Throughout the centuries, music has been used to raise the spirit of people. The power of music in eliciting mental and physical well-being was already recognized by the ancient Greeks. Pythagoras was intrigued by the fact that people appreciated consonant sounds. He discovered that

Prof. Pauwels dedicates this paper to Maestra Sonia Rubinsky, who helped him tremendously with her musical and pianistic interpretation of the sonatas of Mozart and Scarlatti.

harmonic music is able to soothe people and cure ailments of the spirit, body and soul. He believed that the mathematical nature of music influenced the mind and the body and termed it 'musical medicine'. In addition, he believed that the principles of harmony had the power to incite various emotions [1]. In *The Republic*, book III, Plato declared musical training a more potent instrument than any other because 'rhythm and harmony find their way into the inward places of the soul' [2]. In book 8 of Aristotle's *Politics*, it is argued that music has cathartic effects and that catharsis should be understood as a harmless release of emotions [3]. In modern times, a definite link was made between music and emotion, intuitively felt – and experimentally assessed by Goldstein [4] – as when one experiences chills and shivers while listening to preferred music. Recent papers confirm that listening to music for pleasure is related to a change in emotional arousal [5, 6]. In this way, music has a positive effect on psychological well-being, giving rise to a higher level of performance. It is likely that the so-called Mozart effect, first described in an article published in 1993 by Rauscher et al. [7] as comprising better spatial reasoning skills in normal subjects after listening to Mozart's piano sonata K 448, comes into this category. Subsequent multidisciplinary research in the music domain has attested that musical stimuli can activate physiological pathways that can modulate body responses [8]. Growing evidence shows that listening to preferred music shows beneficial effects in the areas of cardiac and neurological function [9, 10]. On this basis, it is plausible that listening to pleasurable music is suitable as an adjunctive therapeutic tool in the treatment of various heart- and brain-related diseases, a field known as 'music therapy' [11].

Examining recent studies, mostly not older than 5 years, this review will elucidate relevant neurobiological effects of music listening in adults, followed by some remarks on the above-mentioned Mozart effect. After this, the use of music for medical ailments will be illustrated, highlighting various beneficial aspects in adults. We like to emphasize that the effect of music on domains such as speech, language abilities and verbal intelligence is beyond the scope of this paper.

Neurobiological Studies and Music

Positron Emission Tomography and Functional Magnetic Resonance Imaging Studies

Modern imaging techniques [positron emission tomography (PET) and functional magnetic resonance im-

aging (fMRI)] suggest that a large bilateral cerebral area, known as the limbic (e.g. amygdala and hippocampus) and paralimbic structures (e.g. the orbitofrontal cortex, parahippocampal gyrus and temporal poles), is engaged when listening to music. Koelsch [12] has mapped the music-evoked areas that are repeatedly reported by various researchers. It appears that the amygdala, the nucleus accumbens and the hippocampus are frequently mentioned as activated structures, and this suggests that music is able to modulate activity in the core areas of emotion, among other regions. fMRI studies have also demonstrated that unpleasant irregular chords may elicit brain activity related to emotional processes, as evidenced by increased bilateral blood oxygen levels in the amygdala [13].

A number of studies have attempted to map the effects of tonality on neural activation. It has been observed that the minor keys activate larger areas of the brain than do major keys, which suggests that the two musical modes are processed differently [14]. When minor consonant chords are perceived as beautiful, the right striatum is strongly activated. This structure is known to be strongly involved in the processing of rewards and emotional processing. By contrast, major consonant chords induce activity in the left middle temporal gyrus, which is related to coherent information processing [15]. A recent study by Trost et al. [16] using fMRI confirmed that high-arousal joyful musical activity takes place in the left striatum and insula, whereas low-arousal nostalgic sad music activates the right striatum and orbitofrontal cortex. Other researchers have also demonstrated that distinct parts of the brain are activated by music as a function of tonality. For example, Pallesen et al. [17] demonstrated that the minor tonality, compared with the major one, showed a selective engagement of the amygdala, retrosplenial cortex, brain stem and cerebellum. On the other hand, Brattico et al. [18] found that sad music, often associated with the minor key, induced activity in the right caudal head and the left thalamus. Green et al. [19] revealed that minor tonalities cause an increased activity in the left parahippocampal gyrus, the left medial prefrontal cortex and the bilateral ventral anterior cingulate. From these imaging experiments, it is clear that various cerebral structures may be activated, which is ascribed to different factors in the classification of emotion and dissimilar neural activation [20, 21].

Neurobiochemical Features of Music Listening

The biological mechanisms involved in music appreciation are far from understood, but some hypotheses based on experimental results are worth considering. Fukui and Toyoshima [22] mention that listening to music

lowers the secretion of cortisol and improves mood disturbances. This is a rewarding effect of listening to music. Furthermore, they hypothesize that these biological changes may facilitate neurogenesis as well as the regeneration and repair of cerebral nerves, possibly mediated by brain-derived neurotrophic factor [23]. The production of this factor as well as its receptor is increased by listening to music, as demonstrated by Angelucci et al. [24] in an experimental setting.

Another biochemical feature of listening to music is the increased secretion of the neurotransmitter dopamine. Using PET imaging with ^{11}C -radiolabeled raclopride, Salimpoor et al. [25] were able to demonstrate endogenous dopamine release in the striatum at peak emotional arousal while listening to music. It is known that increased levels of dopamine in healthy subjects improve executive functions, cognition and attention [26, 27]. Thus, improved performance may well be mediated by the dopaminergic system. Regarding the role of neurotransmitters, Evers and Suhr [28] found that during the perception of pleasant music, the platelet content of serotonin is higher than during the perception of unpleasant music. Recent genetic research has demonstrated that the serotonergic system is associated with music aptitude and creativity [29]. However, there have only been few studies in this area, and other mechanisms may be involved as well. One suggestion is that pleasurable music brings about enhanced glutamatergic neurotransmission and N-methyl-D-aspartic acid-mediated neural plasticity [30]. Another hypothesis is the effect of music-induced changes on attentional networks in the context of the noradrenaline system [31, 32], but little is known about a direct link between music and increased brain noradrenaline turnover in humans [33, 34].

The Mozart Effect: 'Jubilate' or 'Lacrimosa'?

Soon after the publication by Rauscher et al. [7] on the so-called Mozart effect, a flurry of research activity focused on the notion that 'music makes you smarter'. The effect on cognition has been replicated by Smith et al. [35], who showed a better spatial reasoning performance in young adults. Previous studies by Rideout and Laubach [36], Rideout et al. [37], Jausovec and Habe [38] and Jausovec et al. [39] confirmed that the first movement of Mozart sonata K 448 enhanced the learning of three-dimensional mental rotation tasks. Suda et al. [40] reported that this music enhanced cognitive performance in intelligence tests, compared with music by Beethoven or silence. These findings confirmed pioneering work by

Schellenberg [41], who studied 144 children and noticed intelligence enhancement in those taking music lessons compared with those in randomly assigned control groups receiving drama lessons or no lessons.

These intriguing findings inspired several other research groups to study the subject with different approaches. An interesting report by Chabris [42] deals with a meta-analysis to estimate the effect size. This author combined the results reported in 20 publications on Mozart-silence comparisons involving a total of 714 participants. The analysis yielded an average cognitive enhancement of 1.4 IQ points. The enhancement related to a single task of spatial-temporal processing amounted to 2.1 IQ points. In general, a single person's IQ test comes with a 50% confidence interval of 4.5 IQ points. This made the author conclude that any cognitive enhancement is not translated into any significant change in IQ. If there were any, it would be restricted to the performance of one specific type of cognitive task in the field of spatial reasoning. This explicit finding is in line with results obtained by other researchers at later stages. McCutcheon [43] found no significant differences in the spatial reasoning performance of his study participants after listening to Mozart, jazz or silence. In an attempt to generalize the Mozart effect, Lints and Gadbois [44] demonstrated that enhanced spatial reasoning occurred following a variety of conditions and not just after listening to Mozart. Other investigators [45] replicated the Mozart effect but observed a Schubert effect as well. Moreover, participants who preferred listening to a narrated story rather than Mozart performed better on a spatial task after listening to the story. It is meaningful that the authors named their article 'The Mozart effect: an artifact of preference'. Roth and Smith [46] investigated the effect of music or nonmusical auditory stimuli immediately prior to an examination in 72 undergraduate students. The obtained results did not support a Mozart-specific effect: individual elements of music (rhythm and melody) and traffic sounds provided similar effects. The authors explained their results in terms of physiological reactions evoked by heightened arousal. This may result in temporarily enhanced performance in many cognitive domains [47–51]. This arousal framework associated with music listening has paved the way for applications in music therapy.

Music and Medicine

Music may offer benefits to patients as it may divert their attention from unpleasant experiences and future interventions. The effect of listening to music can dimin-

ish or take away unpleasant thoughts in patients. In this sense, music therapy has been recognized as an allied medical intervention with evidence-based clinical benefits [52]. In the following, we will discuss the clinical application of music therapy in adults, but in view of the fact that many ailments find their origin in a misbalanced immune system, we will first dwell on the effect of music on the immune system.

Music and the Immune System

Many studies have documented that stress-induced immune dysregulation may produce changes in the humoral and cellular immune response, increasing health risks [53]. A meta-analysis by Segerstrom and Miller [53] based on effect sizes derived from 293 independent studies including 18,941 subjects showed that psychological stress affects the immune system. In their article, the authors described that time-limited stressors such as public speaking and mental arithmetic in healthy subjects were associated with the adaptive upregulation of natural immunity, evidenced by measurements of natural killer (NK) cells ($r = 0.43$), large granular lymphocytes ($r = 0.53$), neutrophil members ($r = 0.30$), IL-6 (r values not provided) and interferon (IFN)- γ (r values not provided) in peripheral blood. In healthy adults, brief naturalistic stressors such as examination changed the profile of cytokine production: decreased Th1 cytokine production resulted in a decrease in T cell proliferative response ($r = -0.19$ to -0.32) as well as NK cell cytotoxicity ($r = -0.11$). These changes were accompanied by increased antibody production, which is consistent with decreased cellular immunity and an enhancement of humoral immunity. With older age, decreases in NK cell cytotoxicity, T lymphocyte proliferation and the production of IFN- γ were more pronounced.

One of the early indications of the relationship between the immune system and music has been found in a single trial experiment by Bittman et al. [54], who provided evidence that group drumming increased NK cell activity, lymphokine-activated killer cell activity and the dehydroepiandrosterone-to-cortisol ratio in normal subjects. Likewise, Koyama et al. [55] found that recreational music making modulates immunological responses in adults demarcated at the age of 65 years. Significant increases in the number of lymphocytes, T cells, CD4+ T cells and memory T cells as well as in the production of IFN- γ and IL-6 were observed. Contrary to what is expected with stress, increases in Th1 cytokine IFN- γ and unchanged Th2 cytokine IL-4 and IL-10 levels were noted. Similar results were obtained by Wachi et al. [56], who

studied the effects of recreational music making on the modulation of the immune response in healthy corporate employees. These investigators documented significant changes in NK cell activity and in the level of gene expression for IFN- γ and IL-10. A recent study by Bittman et al. [57] has confirmed the above-mentioned findings on a genetic level: their results support the hypothesis that different sets of genes play important roles in both stress and the relaxation response in humans. If these findings can be confirmed by other research groups, the implications may be of particular importance: they could provide a means for tailored music therapy by identifying the patients who would benefit the most from the clinical effect of music.

Cardiovascular Disorders

A direct physiological effect of classical music on the cardiac autonomic balance has been demonstrated by White [58, 59]. In patients recovering from acute myocardial infarction, a reduction in heart rate, respiratory rate and anxiety level was noticed when they were listening to classical music under restful circumstances as compared with a control group undergoing treatment as usual. The author's findings confirmed previous findings by Guzzetta [60], who studied 80 cases suspected of having acute myocardial infarction who were randomly assigned to relaxing music in a coronary care unit. The results demonstrated that apical heart rates were lower and peripheral temperatures were higher in the relaxation group than in a control group. Regarding the effect of music intervention on psychological and physiological responses in persons with coronary heart disease, a Cochrane Database (www.cochrane.org) analysis was published by Bradt and Dileo [61]. These two reviewers analyzed the data from 23 trials comprising 1,461 participants in whom music listening was the main intervention. It was concluded that music listening may have a beneficial effect on blood pressure, heart rate, respiratory rate, anxiety and pain, although the quality of the evidence was not strong.

Various studies have analyzed the effect of music listening on patients in intensive care units after cardiac surgery. A randomized controlled trial by Nilsson [62] comprising 58 patients who had undergone bypass grafting or aortic valve replacement revealed that listening to soft relaxing music (New Age style) was associated with significantly lower levels of serum cortisol, a measure of stress response. Other parameters including heart rate, respiratory rate, mean arterial pressure, arterial oxygen tension, arterial oxygen saturation, and subjective pain and anxiety levels were not significantly different between the

groups. The same author has reported on another randomized controlled study in 40 patients who had undergone similar surgery, in whom listening to music during bed rest had some effect on the relaxation system as regards oxytocin and subjective relaxation levels [63]. A recent review of 16 studies by Fredericks et al. [64] provided evidence that anxiety and depression in patients following heart surgery can be soothed by listening to music. A study published after this review aimed to investigate the effect on postoperative oxygen saturation and pain by listening to music of personal choice in 87 patients (including 43 patients in a control group) who had undergone open heart surgery. The authors reported a statistically significant increase in oxygen saturation and a lower pain score (both $p = 0.001$), which provides further evidence of the effectiveness of music listening for patients after open heart surgery [1, 65]. The highest benefit for health comes from classical (Bach, Mozart or Italian composers) and New Age music [66].

Music and Cancer Pain

In 2002, Evans [67] reviewed the effectiveness of music in the reduction of anxiety in hospital patients undergoing normal care. This meta-analysis was based on 19 studies and showed that music improves the mood and pain tolerance of patients. This knowledge has been applied to oncology patients, especially for cancer pain management. Igawa-Silva et al. [68] performed a comprehensive systematic evaluation of data-based literature and concluded that music reduces anxiety and, consequently, lessens the intensity of pain in chronic cancer patients. The authors of a Cochrane review came to a similar conclusion and stated that listening to music reduces pain intensity and opioid requirements [69]. This analysis, dating from 2006, was updated in 2011, comprising 30 trials with a total of 1,891 cancer patients. A moderate pain-reducing effect was found ($p = 0.0003$), together with small reductions in heart rate, respiration rate and blood pressure [70]. A compelling example of a beneficial effect of music in relieving pain in cancer patients has been published by Huang et al. [71]. These researchers carried out a randomized controlled trial in 126 hospitalized persons with cancer pain divided almost equally into an experimental group and a control group. The patients were allowed to listen to their preferred music for 30 min. Using an advanced pain assessment technique and appropriate statistical analysis, it turned out that the music listeners had significantly less posttest pain ($p < 0.001$). The fact that the patients were offered familiar, culturally appropriate music appeared to be a key element in the

intervention. Also, other authors showed that music has a more analgesic effect on pain if it is self-chosen and familiar [72, 73]. A recent paper by Villarreal et al. [74] provides evidence that familiarity with the music drives the emotional mechanisms to modulate pain. In case of unfamiliar music, the main analgesic mechanism may be of a cognitive nature rather than emotional.

Music and Depression

Depression is a widespread and disabling disease, and although psychotherapy and/or pharmacotherapy can be effective, it has been emphasized that conventional pharmacologic methods might result in dependence and an impairment of psychomotor and cognitive functioning [75]. Against this background, various reviews and meta-analyses have mentioned a positive clinical response in patients listening to music either combined with standard therapy or not [9, 76–78]. Recently, various randomized controlled trials have studied the effect of music as a monotherapy (including that by Chan et al. [79]) and as an addition to standard therapy (including those by Erkkila et al. [80] and Fachner et al. [81]) in depressed individuals. Without exception, these studies show that music listening or music making reduces depression. The importance of music making as a social and pleasurable event has been stressed by Maratos et al. [82], who mentioned that music therapy may result in high levels of engagement in patient groups who are difficult to engage. Moreover, in patients with mild-to-moderate dementia and associated depression, group music making may have a beneficial effect. Chu et al. [83] performed a prospective randomized controlled study and showed that music therapy reduced depression, the effect occurring immediately after the onset of music making and lasting throughout the course of the therapy. Interestingly, cortisol levels, a measure of global mood state, are not significantly decreased after the therapy. To sum up, the results show that music therapy is an effective method for decreasing the burden of depression.

Music and Epilepsy

Epilepsy is clinically characterized by recurrent seizures. The patients are at an increased risk of comorbidities such as cardiovascular, respiratory and inflammatory diseases. Medication remains the best treatment, but drug resistance is an important clinical problem [84]. Non-pharmacological treatment may therefore be of benefit, and music therapy has been suggested as complementary treatment based on a pioneering case study by Hughes et al. [85], who found a significant decrease in epileptic ac-

tivity as demonstrated by EEG in 23 of 29 patients (even when in coma) listening to Mozart's sonata K 448. Hughes and Fino [86] investigated whether the effect was specific to this music and found a similarity between the music of Mozart and that of Bach but not between the music of Mozart and the minimalist music of Philip Glass, which 'may not resonate within the cerebral cortex'. A reduction in seizures has also been reported in case studies by Lahiri and Duncan [87] and by Lin et al. [88]. Recently, a randomized controlled clinical study on the antiepileptiform effect of specific music has been carried out by Bodner et al. [89]. The reduction in, or even prevention of, seizures was investigated through auditory cortical stimulation by Mozart's sonata K 448 from sustained passive nightly exposure. This CONSORT study consisted of 73 randomized patients assessed for eligibility, of whom 48 were allocated to receive the musical stimulation. The remaining 25 subjects served as a control group and received only regular antiepileptic drug treatment. After 3 years, 25 patients in the treatment group and 11 patients in the control group could be included in the final analysis. This investigation revealed that a significant ($p = 0.024$) treatment effect was present: exposure to the music was likely to result in a remarkable reduction in seizure rate of 24%. Furthermore, it was noted that 24% (6 patients) of the treatment group exhibited a complete absence of seizures during treatment. Moreover, during the posttreatment follow-up year, a reduced average seizure rate of 33% was maintained after cessation of the therapy, indicating a long treatment effect in these 6 patients. Such a long-term effect had previously been observed by Lin et al. [90] in a case study on children in which epileptiform discharges decreased ($71.6 \pm 45.8\%$) 6 months after listening to Mozart's sonata K 448. A recent publication by the same research group provided evidence that Mozart music stimuli induce a parasympathetic activation which leads to a reduction in seizure rate [91].

Music and Dementia

With the aging of the world population, the growing incidence and prevalence of dementia have become more and more apparent [92]. Apart from cognitive enhancers for mild cognitive impairment such as Alzheimer's dementia, no treatment has been established for patients with vascular and frontotemporal dementia [93]. Of particular risk is antipsychotic medication, as cerebrovascular events and cases of death have been reported following this therapy [94]. These and other safety concerns regarding psychopharmacological medication [95] have been the impetus to search for nonpharmacological methods

for improving the quality of life. A recent meta-analysis of the effect of music interventions on patients with various degrees of dementia revealed that many studies indicate large positive effects on behavioral, cognitive and physiological main outcome measures and medium effects on affective measures, assessed in both subjective (e.g. well-being and/or reasoning abilities) and objective ways (decreased blood pressure and/or increased oxygen uptake), the overall effect size ranging from 0.04 to 4.56 (mean: 1.04). The fact that studies with undefined measuring methods and patients with various degrees of dementia were included in this meta-analysis may explain the large range of measured overall effects [96]. Other systematic reviews and meta-analyses [97–101] have confirmed these beneficial effects but have also indicated that the study designs were diverse and that randomized controlled trials need to confirm the outcome. One prospective randomized controlled study in 104 elderly persons with dementia by Chu et al. [83] made clear that music therapy delayed the deterioration in cognitive functions. A randomized controlled crossover trial in 42 participants with dementia by Ridder et al. [102] showed that agitation disruptiveness increased during standard care and decreased during music therapy. This is not in agreement with a previous randomized controlled crossover study by Cooke et al. [103], who found no effect of music therapy on the degree of agitation in 24 patients who attended more than 50% of the music sessions, although improvements in self-esteem and depressive symptoms were registered. The contrasting findings between these two studies may be due to the geographical difference between the two study groups, which makes a racial and socioeconomic background very likely. An additional difference between the Danish [102] and the Australian study [103] is that the former is a crossover study, whereas the latter uses a control group.

A Critical Note

It is remarkable that many studies regarding music therapy have been published in specialized journals, the contents of which are not easily retrievable. It should be stressed that it is not always clear whether, for these articles, an independent peer review process had been carried out and in how far only papers with beneficial results were published. Another remark concerns methodological inadequacies which are present in various studies mentioned throughout the section Music and Medicine, as only 11 of the 21 included studies are randomized con-

trolled trials. Of these, only 8 [62, 63, 71, 75, 80, 81, 102, 103] describe the methods of measuring effects, randomization and statistical analysis and report details on patient selection, dropouts and exclusion. Thus, a risk of bias is present not only in the remaining case and case-control studies but also in the randomized trials, which may limit the strength of the evidence. A further examination of the patient studies reveals limitations regarding their sample size: only 2 randomized controlled trials [71, 83] and 1 case study [54] based their statistical analysis on data assessed in more than 50 patients and 50 controls. Also Cochrane Database systematic reviews noticed the low methodological quality of some of the studies, including the poor categorization of diseases and inhomogeneity of the study groups, which diminishes the evidence and the generalizability of their conclusions [62, 69, 77, 104, 105].

Implications

Auditory stimulation with music evokes emotions which are often accompanied by physiological reactions such as changes in heart rate, respiration, skin properties and hormone secretion [106–109]. These reactions are linked to heightened arousal [47], resulting in temporarily enhanced performance in many cognitive domains including spatial reasoning [44], attention [24, 28], information processing [110] and recognition memory [111] in healthy subjects. Thus, the overall positive effect of listening to pleasurable music can serve as a stimulant that enhances cognitive performance. This strongly suggests that the Mozart effect is explained by a complex interplay between music, arousal and intellectual performance. It is hardly conceivable that it is an isolated phenomenon typically associated with specific Mozart music. Rather, it is an example of a wide range of stimulating circumstances.

In this context, it is plausible that music therapy can affect the autonomous nervous system and diminish stress and stress-related health issues [112], rebalancing the immune system, especially when the music is known and liked [31, 35]. It is the aim of the music therapist to optimize the effect of music therapy by registering the degree of enjoyment and the hedonic response. This is important, since preferences are based on numerous individual factors [113].

Apart from the effect of pleasurable music on cognition, the esthetic value as experienced by the patient adds to the management of pain and anxiety, e.g. in cardiovas-

cular and surgical patients. Indeed, a growing body of evidence suggests that making music and listening to preferred music is a valuable adjunct to medical practice.

It should be noted, however, that little is known about the neural substrates and psychological mechanisms that are the basis of the esthetic emotion evoked by music [114, 115], nor do we know enough about the duration of each single effect and the total of effects as follow-up studies in adult patients are missing. These follow-ups and other factors, including cognitive mastering of the musical experience and the perception of musical emotions as suggested by Brattico and Pearce [116], are important issues for further research in music therapy, a noble endeavor to promote the health of patients.

Conclusions

From neurobiological investigations, it is apparent that preferred music may evoke emotions that are associated with heightened arousal, which results in temporarily enhanced performance in many cognitive domains. This positive effect is not necessarily confined to Mozart's piano sonata K 448, as was suggested by some studies performed in the 1990s.

The arousal phenomenon is successfully being applied in various clinical settings. However, many clinical studies in this area suffer from methodological inadequacies limiting their scientific quality. This urges the need for well-designed prospective randomized studies, if possible in a blinded mode, to establish the efficacy under clinical circumstances. Nevertheless, present knowledge suggests that there is moderate but not altogether convincing evidence that listening to known and liked music, a regular feature in music therapy, leads to a decreased disease burden and increased well-being as well as less tension in patients suffering from cardiovascular disease, cancer pain, epilepsy, depression and dementia. It would be worthwhile to investigate a genetically, individually increased predisposition to respond emotionally to music as this would open pathways to tailored music therapy.

Disclosure Statement

The authors declare no conflict of interest whatsoever with regard to this article.

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