Chapter 5

# Music and Brain Plasticity: How Sounds Trigger Neurogenerative Adaptations

Mark Reybrouck, Peter Vuust and Elvira Brattico

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.74318

**Abstract**

This contribution describes how music can trigger plastic changes in the brain. We elaborate on the concept of neuroplasticity by focussing on three major topics: the ontogenetic scale of musical development, the phenomenon of neuroplasticity as the outcome of interactions with the sounds and a short survey of clinical and therapeutic applications. First, a distinction is made between two scales of description: the larger evolutionary scale (phylogeny) and the scale of individual development (ontogeny). In this sense, listeners are not constrained by a static dispositional machinery, but they can be considered as dynamical systems that are able to adapt themselves in answer to the solicitations of a challenging environment. Second, the neuroplastic changes are considered both from a structural and functional level of adaptation, with a special focus on the recent findings from network science. The neural activity of the medial regions of the brain seems to become more synchronised when listening to music as compared to rest, and these changes become permanent in individuals such as musicians with year-long musical practice. As such, the question is raised as to the clinical and therapeutic applications of music as a trigger for enhancing the functionality of the brain, both in normal and impaired people.

**Keywords:** music, neuroplasticity, ontogenetic development, adaptation, connectivity, neurorehabilitation

## 1. Introduction

Going to concerts, listening to music in your living room, singing together or even playing an instrument is part of most people's everyday life. Recent research indicates that apart from just changing the current mood this may have long-lasting influences on the brain. This contribution, therefore, describes how music shapes the brain as the outcome of interactions with the sounds. These interactions can be multifarious, as in the case of performing, listening or mentally imaging music, but they all show complex and widespread activity in many areas of the brain. This activity, moreover, is related to training, previous exposure, personal preference, emotional involvement and many other modulating factors related to the cultural background and biological repertoire of each individual [1–7]. Musical training, moreover, is related to structural changes within auditory and motor areas of the brain and reinforces functional coupling of these regions during musical tasks as evidenced by many neuroimaging studies [8–10]. These changes have been observed also in white-matter tracts, such as the corpus callosum, the corticospinal tract and the arcuate fasciculus [11–13]. Studies (particularly those with a longitudinal design) showing the causal relation between the brain changes and the duration of musical training have convinced some researchers to consider musical training as a model for investigating practice-related brain plasticity in humans [14].

Music is a powerful stimulator of the brain. Acoustically, it consists of time-varying sound events that are characterised by a large number of features—more than hundred features can be computationally extracted that are tracked by several regions of the brain [15]. Many low-level features, such as timbre and pitch, are partly processed in Heschl's gyrus and the right anterior part of the superior temporal gyrus, in which the primary and non-primary auditory cortices are located [16, 17]. Besides auditory cortices, also motor regions, such as the supplementary motor area and the cerebellum, are involved during musical activities, including both playing and listening. Due to audio-motor coupling that is necessary for playing an instrument, listening is influenced by the motor demands intrinsic to musical practice, even to the extent that this would become manifest also in the brain responses to music listening alone [18, 19]. Moreover, practising and performing music is a complex, multimodal behaviour that requires extensive motor and cognitive abilities. It relies on immediate and accurate associations between motor sequences and auditory events leading to multimodal predictions [10, 20, 21], which engage broad networks of the brain [16, 22, 23]. Music training has thus been associated with changes in the brain, and some of these changes have been causally linked to the duration of the training, which makes the musician's brain a most interesting model for the study of neuroplasticity [9, 24]. This holds in particular for performing musicians, who provide a unique pool of subjects for investigating both the features of the expert brain and, when considering the length of the training, also the neural correlates of skill acquisition. Musicians' training and practice require the simultaneous integration of multimodal sensory and motor information in sensory and cognitive domains, combining skills in auditory perception, kinaesthetic control, visual perception and pattern recognition [25, 26]. In addition, musicians have the ability to memorise long and complex bimanual finger sequences and to translate musical symbols into motor sequences (see **Figure 1**). Some musicians are even able to perceive and identify tones in the absence of a reference tone, a rare ability termed absolute pitch [27, 28].

The brain changes that musical training entails are numerous and well-documented [2, 3, 5, 9, 24, 26–34]: they involve brain regions important for auditory processing, coordination of fast movements and cognitive control, as well as sensory-to-motor coupling mechanisms (see [35],

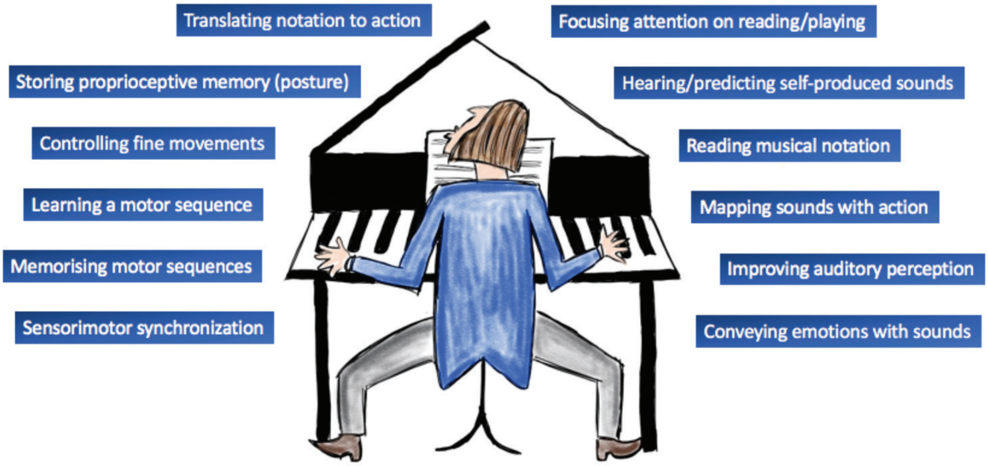

**Figure 1.** Illustration of several perceptual, motor, interoceptive and emotional skills that are acquired during musical training.

for an overview). While some of these changes might be what characterise individuals that decide to undertake a musical profession, and hence might exist at birth, others could be a direct result of training, as suggested by the significant relations between years of training and brain measures (e.g., [36]), as well as by longitudinal designs recording brain responses before and after music training (e.g., [29, 37]).

Here, we propose that the differences observed between the brains of musicians and non-musicians can be attributed to neuroplastic adaptations responding to the challenging demands of musical practice. Alternative explanations are also possible, such as that the differences exist even before training in those individuals that choose music as their profession, but accumulating evidence points at a causal relation between music training and brain changes. The behavioural correlates of these differences are multiple and can be seen especially in childhood (e.g., [38]). Besides, it has been shown that music may be beneficial in relation to a number of symptoms in several kinds of impairment, such as epilepsy, Alzheimer's disease, Parkinson's disease and senile dementia (see [39] for an overview). Hence, it is possible to conceive of dealing with music in educational, clinical and therapeutic terms.

In this contribution, we first expose the concept of adaptation, both from the phylogenetic and ontogenetic points of view. We then narrow down this concept by putting forward the hypothesis of music-induced neuroplasticity, with a first distinction between macrostructural and microstructural adaptations. Thereafter, we consider the reorganisation of the brain as the outcome of learning and skill acquisition, both at a structural and functional level of description with a major focus on the adult musician or listener as a model for the interaction between ontogeny and phylogeny. This latter, further, is considered from the point of view of network science with a major focus on the role of resting-state networks. Clinical and therapeutic applications, finally, are envisioned also.

## 2. Phylogenetic and ontogenetic claims: the role of adaptation

Brain plasticity is an adaptation to the environment with an evolutionary advantage. It allows an organism to be changed in order to survive in its environment by providing better tools for coping with the world [40]. This biological concept of adaptation can be approached from two different scales of description: the larger evolutionary scale of the human as a species (phylogeny) and the more limited scale of the human from newborn to old age (ontogeny). This phylogenetic/ontogenetic distinction is related to the "nature/nurture" and "culture/biology" dichotomy, which refers to the neurobiological claims of wired-in circuitry for perceptual information pickup as against the learned mechanisms for information processing and sense-making and immersion in a culture [41, 42].

These approaches may seem to be diverging at first glance, but they are complementary to some extent. This holds, in particular, for the here-hypothesised music-induced plasticity, which espouses a biocultural view that aims at a balance between genetic or biological constraints and historical/cultural contingencies. This places all human beings on equal ground (unity) by stating that diversity in culture is only an epiphenomenon of an underlying biological disposition that is shared by people all over the world [43]. The assumed unity is attributed to the neural constraints that underlie musical processing in general, but these constraints should not be considered as a static dispositional machinery. The picture that emerges from recent research is arguing, on the contrary, for a definition of the neural machinery as a dynamic system that is able to adapt in answer to the solicitations of a challenging environment [6]. The neurobiological approach to music, therefore, deals not only with the nature and evolution of the innate and wired-in neural mechanisms that are the hallmark of the hominid phylogenetic evolution but also with the ontogenetic development of these mechanisms [43]. As such, it makes sense to conflate neurobiological and developmental claims by taking the concept of adaptation as a working hypothesis.

The relation between adaptation and development, however, is asymmetrical in the sense that it is possible to conceive of development without adaptation, but no adaptation is conceivable without development. This development, further, can be natural, when it is the outcome of maturation, but it is possible also to intervene in its trajectory by combining development and learning. This is the case when an organism faces continued and long-term exposure to challenging environments, which triggers plastic changes in the structure and the functions of the brain. This brings us to the concept of brain plasticity, which refers to the fact that neuronal circuits are tuned in close interaction with the environment. It was introduced by William James, who defined plasticity as "the possession of a structure weak enough to yield to an influence, but strong enough not to yield all at once" [44] (p. 106). The idea was further developed by Ramón y Cajal, who claimed that to fully understand the phenomenon it is necessary to admit the formation of new pathways in the brain through ramification and progressive growth of the dendritic arborisation and the nervous terminals in addition to the reinforcement of pre-established organic pathways. The same idea was elaborated further by Donald Hebb, who proposed that neuronal cortical connections are strengthened and remodelled by experience. There is, however, another aspect of plasticity that goes beyond the level of synapses and that incorporates the level of cortical representation areas or cortical maps, which can be modified by sensory input and training [45]. It is suggested, in this regard, that additional neurons are recruited when they are needed and that rapid and transient alterations of cortical representations can be seen during learning tasks. Such short-term modulations are important in the acquisition of new skills, but they can lead also to structural changes in the intra-cortical and sub-cortical network once the skill has been established.

## 3. Neuroplasticity and music: macrostructural and microstructural adaptations

The evolutionary claims of adaptation—both at the phylogenetic and ontogenetic level—have received empirical evidence from neuroimaging and morphometric studies. In order to elucidate its underlying mechanisms, there is currently a whole body of research related to the psychobiological approach to the study of action, cognition and perception. A major claim in this research field is that the nervous system provides the immediate, necessary and sufficient mechanisms that underlie all mental processes, and that mental processes are reducible to the function, arrangement and interaction of neurons as the constituent building blocks of the nervous system [46]. This is the axiom of psychobiological equivalence, which claims an equivalence of maintained information from the neural to the psychological state [47]. The related research revolves around three major themes: (i) the localisation of functions in the brain, (ii) the representation or coding and (iii) the dynamic change or learning [46]. The first investigates which brain structures are responsive for particular processes. The second investigates how neural networks represent, encode or instantiate cognitive processes, both at macrostructural and microstructural level of description (see [48]). The third, finally, investigates how our brain adapts to experience and learning, what changes occur in its neural networks and how these changes correspond to externally observed behaviour.

The third theme—dynamic change or learning—concerns the neural correlates of skill acquisition and has been studied mainly at the level of perceptual processing and motor output. Yet, there is also the whole domain of creativity [49], musical aesthetics [6, 50–53] and human interaction [54, 55], which have been poorly investigated in relation to long-term music training. However, the topic is exemplary of a paradigm shift in current neuromusicological research, with a transition from a static conception of brain modules to a conception of reorganisational plasticity of the developing and adult brain [6]. Plasticity, in fact, is a fundamental organisational feature of the human brain, which can be modified throughout the life span in response to changes in environmental stimulation. This has been observed not only during a critical period in the developing brain but also even throughout the whole life span.

Skill learning, such as learning to play a musical instrument, can thus be used for the study of neuroplasticity. It typically starts early in life, while the brain is most sensitive to plastic changes, and continues often throughout life. It involves multiple sensory modalities and motor planning, preparation and execution systems [27, 56]. The role of environmental enrichment—being defined as a combination of complex inanimate and social stimulation [57]—on the other hand, should be stressed also as an emerging area of research. Music, in this view, can be considered as "sounding environment" [42], which is likely to drive brain plasticity. Even in the foetal phase of development, sounds can trigger ways of implicit learning [58]. Neonates and infants also learn to talk and sing quasi-effortless as the result of mere exposure, thus demonstrating implicit learning and developmental plasticity, which is even cross-modal to a large extent, in the sense that loss of one sensory modality may lead to neural organisation of the remaining modalities [2].

Neuroplasticity is also related to the field of sensory-motor learning, with a major role attributed to the challenges of a rich environment. It favours multiple interactions with the world—both at the sensory and at the motor level—stressing the interdependency of an organism and its environment through which it "enriches its repertory of genetic adaptations with acquired dispositions that are immediately at hand and mobilizable when confronted with a situation that can be foreseen or recognized as a familiar one" [59] (p. 925).

Musical training, accordingly, may be related to sensory and motor changes in the human brain of professional musicians. As a rule, music training involves years of sensory-motor training, often beginning in early childhood, with the aim to develop an expertise in a chosen instrument or mastery over the own voice, together with an improvement of the ability to attend to the fine-grained acoustics of musical sounds, including pitch, timing and timbre [3]. The brains of musicians might adapt to the demands of their instrumental practice at two levels: the gross anatomical differences between professional musicians and amateurs or laymen, and the subtle functional differences after enhanced musical practice and/or experience, which have to be sought in ever finer modifications of synaptic strength in distributed cortical networks. As such, it is possible to distinguish between macrostructural and microstructural adaptations. The macrostructural differences related to volume, morphology, density and connectivity of brain structures are measured with magnetic resonance imaging (MRI), whereas the microstructural differences in the functional activity of brain regions are measured with functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and neurophysiology (electroencephalography, EEG and magnetoencephalography [MEG]) (see [5] for an overview). It is further hypothesised that functional reorganisation may cause structural adaptation. For instance, bimanual instrument training, such as for the piano, may cause an increase in cortical functionality for symmetric areas involved in motor, auditory and visuospatial processing, as well as in the white matter tracts of the corpus callosum [20] as compared with less bimanual training (such that for the violin) and especially as opposed to laypersons.

At the macrostructural level, studies show differences in the size of the primary motor cortex size, the cerebellum, the planum temporale, the corpus callosum, Heschl's gyrus and the arcuate fasciculus, all of which seem to correlate with the ability of musicians to identify and process acoustic variations [60]. The microstructural adaptations, on the other hand, happen at the level of individual neurons and synapses, with the aim to change the efficacy of neural connectivity. In general, the brain shows adaptation to extraordinary challenges by giving birth to new neurons (neurogenesis) and glial cells and by the formation and remodelling of new connections by the outgrowth of dendrites, axonal sprouting and increasing or strengthening of synaptic connections [61] (see **Box 1** for an overview). Such adaptations have been studied in the context of deafferentation studies—in the case of brain lesion—and in the case of motor skill learning [62]. In the former, some cortical remodelling has been found, including microstructural changes, such as the strengthening of existing synapses, the formation of new synapses (synaptogenesis), axonal sprouting and dendrite growth. In the latter, similar changes have been found, including an increased number of synapses per neuron and changes in the number of microglia and capillaries [63], which all lead to volumetric changes that are detectable also at the macrostructural level [27, 64].

The bulk of studies on neuroplasticity has been performed in the context of within-modality plasticity, particularly in the domain of sensory and motor modalities. They aim at demonstrating the adaptive capabilities of the human brain to shape the processing of sensory stimuli or to perform motor acts after repeated sensory exposure or action [9]. With regard to the sensory modality, animal studies have shown that environmental change critically affects brain development. Experience-driven neural activity, in fact, regulates the refinement of the neural circuitry by influencing various neural processes, such as synapse formation, pruning and synaptic plasticity (see **Box 1**) with modifications in synaptic connectivity as a result [65]. This enhanced connectivity, further, acts as a basis for learning and memory through alterations at the level of neural circuits [66], such as strengthening or weakening of the synaptic links or altering their number, changes in the number or properties of postsynaptic receptors in transmitter release and the formation of new synapses. The result is an increase in synaptic strength, which may be persistent and facilitate learning and memory so that experience-dependent plasticity could involve selective changes in pre-existing brain circuits [65].

As to the enhanced auditory skills, it has been argued that they may prime the brain for the processing of musical sounds and that these skills may percolate to other domains, such as speech, emotion and auditory processing in general [67, 68]. This has been observed already in the early stages of the auditory pathway, which are located mainly in the brainstem. Musicians have enhanced temporal and frequency coding in the auditory brainstem with

**Myelinisation**: the acquisition, development or formation of a myelin sheath around a nerve fibre. This fatty coating serves as insulation of individual fibres to enhance specificity of connections and increases markedly the quick and accurate transmission of electrical current from one nerve cell to another.

**Pruning**: a process that helps sculpt the adult brain and by which neurons and synaptic connections that are no longer used or useful are eliminated in order to increase the efficiency of neuronal transmissions.

**Sprouting**: a process by which a neuron generates additional branches or outgrowths to establish new links between existing neurons, as seen frequently in the case of growth of axons or dendrites from a damaged or intact neuron that projects to an area that is denervated.

**Synaptic plasticity**: strengthening or weakening of the synaptic links either by modulating the strength of synapses or by altering their numbers.

**Synaptic efficacy**: changes in the number or properties of postsynaptic receptors in transmitter release and the formation of new synapses (synaptogenesis).

**Adult neurogenesis**: birth of neurons from neural stem cells in the adult brain. In humans, adult neurogenesis has been shown to occur only in the hippocampus (particularly in the sub-granular zone of the dentate gyrus) and in the striatum. It differs from developmental neurogenesis.

**Box 1.** Overview of some basic mechanisms for refinement of the neural circuitry earlier (as early as 10 ms after acoustic onset) and larger responses than non-musicians to both speech and music stimuli. This has been shown for the onset response and the frequency-following response (FFR), i.e., a neuronal ensemble response that phase-locks to the incoming stimulus and that underlies perception of pitch as it relates to the sustained portion of a periodic sound with less or more stable frequencies [68, 69].

The role of auditory brainstem processing of behaviourally relevant sounds such as speech and music is important here. It can be measured by using the onset response and the FFR to see how the brainstem represents pitch, timing and timbre [68]. It has been shown that both temporal and spectral characteristics of sounds are preserved in this subcortical response (see [70] for an overview), reflecting the physical properties of sound with an unrivalled fidelity. As a rule, it occurs automatically at pre-attentive levels of auditory processing but is shaped by both long-term and short-term experience [71–73]. Subcortical function, moreover, is neither passive nor hardwired but interacts dynamically with higher-level cognitive processes refining the transcription of sounds into neural code. Hence, the responses do not originate merely in the brainstem but receive feedback from top-down cortical influences even at the earliest stages of auditory processing [3] via corticofugal feedback pathways [74, 75]. As such, it can be demonstrated that musical practice changes the early sensory encoding of auditory stimuli [68] relying on a top-down feedback system—consisting of efferent effects on cochlear biomechanics—that is continuously and automatically engaged to extract and represent regularities in the auditory system [3]. Musical training is thus not limited to the modification of cortical organisation but the modifications extend to subcortical sensory structures and generalise to early processing of speech and sounds in general.

Moreover, early auditory evoked responses and particularly the negative–positive complex (N19-P30) in the auditory evoked potential [76] localised in the primary auditory cortex (the anteromedial portion of Heschl’s gyrus) have been found to be larger in musicians compared to amateurs and non-musicians. Moreover, it has been found that the generating neural tissue, namely the grey matter volume of the primary auditory cortex, was broader in volume for professional musicians [77] as compared to laypersons. It thus seems that music can trigger both macrostructural and microstructural or functional changes, not as separate and distinct levels of adaptations, but as phenomena that are dynamically and tightly interconnected.

## 4. Music facilitates neural connectivity

Music can trigger plastic changes in the brain, as evidenced by the rich history of structural and functional neuroimaging studies of the past decades. Recent advances in functional neuroimaging have furthermore provided new tools for measuring the functional interactions and communication between distinct regions in the brain and for examining their functional connectivity [78]. In an attempt to study the brain as a complex network of functionally and structurally interconnected regions, a fuller understanding of its organisation and function is proposed by relying on the contributions of network science [79], which investigates complex systems in terms of their elements and the relationships and interactions between these elements.

Functional connectivity can be defined as the temporal dependence of neuronal activity patterns of anatomically separated and removed regions in the brain, reflecting the level of communication between them [80]. It makes it possible to examine the brain as an integrative network of functionally interacting regions and to gain new insights into large-scale neuronal communication in the human brain. Such whole-brain connectivity patterns can be studied by measuring the synchronisation of spontaneous fMRI or MEEG time-series reflecting neural activity of anatomically separated brain regions, which are recorded during rest. These resting–state networks are believed to reflect the functional communication between brain regions [78, 81] and suggest an ongoing information processing and functional connectivity between them even at rest, which is related to neuronal firing. The pattern of correlations between distinct brain areas, moreover, points at the existence of organisational networks in the brain [81], which seems to be analogous to the networks that are engaged during the performance of sensory-motor and cognitive tasks, and which are dependent upon the brain's anatomical connectivity [10]. Such spontaneous neuronal interaction has been first investigated in motor cortices but were later extended to other cortical systems, such as the visual and auditory networks, the default mode network (DMN) and attention and memory related regions. It has been suggested that at least 10–12 resting-state networks (RSNs) can be detected in the cerebral cortex in resting state, which implicates that they represent some intrinsic form of brain connectivity with temporal correlations between spatially discrete regions [82].

DMN has been related to specific brain functions, such as self-referential thoughts, emotional perspectives and levels of self-awareness. DMN is believed to be a neural circuit that constantly monitors the sensory environment and displays high activity during lack of focused attention on external events [83]. It seems to function as a toggle switch between outwardly focused mind states and the internal or subjective sense of self [84] and can be used to explore the functional connections of the complex integrative network of functionally linked brain regions, which continuously share information with each other. As such, there are interconnected resting-state neuronal communities or functional brain networks with functional communication between them. Being organised according to an efficient topology, they combine efficient local information processing with efficient global information integration with the most pronounced functional connections found between those regions that share common functions.

Overall, resting-state fMRI oscillations reflect ongoing functional communication between distinct brain regions [78], which makes them indicative of the level of cognitive functioning in general. There seems to be, in fact, a link between an efficient organisation of the brain network and intellectual performance—this is the neural efficiency hypothesis—so that functional connectivity patterns may be used as a powerful predictor for cognitive performance [85]. This resting-state connectivity, further, is not to be considered as an established and fixed property, but as a state that can be modulated by recent experiences and learning episodes, both within and between the networks they recruit. Such modulation points in the direction of a learning consolidation function of resting-state brain activity, as evidenced by the findings that high learners manifest stronger pre-task resting-state functional connectivity between the involved regions than low learners [10]. It thus seems that, even in the absence of external stimuli or demands, the brain is constantly sharing information. It thus consolidates recent learning and maintains the association of activity of brain areas that are likely to be used together in future [86].

Initial research suggests that musical training might enhance this pattern of increased resting-state connectivity by triggering heightened connections at a functional level between those brain regions that are structurally and functionally altered as the result of training. This is manifested even during a task-free condition, pointing to the "silent" imprint of musical training on the human brain [35]. Research on the differences between musicians and non-musicians in their functional connectivity during rest, however, is still in its infancy [10, 82]. By selecting predefined seed regions for computing connectivity analysis, increased connectivity between contralateral homologue regions has been found in musicians between prefrontal, temporal, inferior-parietal and premotor areas [35]. It is to be questioned, however, whether the study of predefined regions or seed regions does not neglect residual whole-brain dynamics. However, for the seed regions for which plastic changes in musicians have been found already—as evidenced by increased grey matter volume—connectivity analyses have revealed brain areas whose resting-state time series activity was more closely synchronised with one of them. Four networks were found to supply integrative interpretations for the cognitive functions during musical practice: (i) autobiographical memory-related regions belonging to the default mode network, recruited by the encoding, storage and recall of melodies with an emotional and biographical quality; (ii) areas that belong to the salience network with access to semantic memory that is related to the storage of music in terms of verbal labels and auditory structure; (iii) regions that are implied in language processing and the resting-state auditory network and (iv) structures that belong to the executive control network, and which could subserve the motor modulation required for an emotionally expressive interpretation of music. The question whether this practice-related plasticity is triggered by local grey matter volume, however, is not yet satisfactorily resolved, in the sense that other variables may be implicated in the expertise-related resting-state functional reorganisation of musician's plastic brain [10].

## 5. Clinical and therapeutic applications

To stretch further our hypothesis about music-induced neuroplastic adaptation, music, as a cognitive-demanding activity stimulating neuroplasticity, may be able to slow down, arrest or even reverse the detrimental effects of ageing on learning and memory capacity of the elderly [33]. Recent studies have provided evidence that music-induced plasticity may help also to overcome neurological impairments, such as neurodevelopmental disorders and acquired brain injuries [56]. For instance, attentive music listening recruits multiple forms of working memory, attention, semantic processing, target detection and motor function, relying mainly on bilateral brain areas—superior temporal gyrus, intraparietal sulcus, precentral sulcus, inferior sulcus and gyrus, and frontal operculum—which all serve general functions rather than music-specific cortical regions [87, 88]. Complex musical tasks, moreover, engage the co-activation of many processes involving widely distributed and partly interchangeable substrates of the brain [89]. This may explain, to some extent, the sparing of some musical functions in cases of progressive destruction of some areas in degenerative diseases of the brain. This has been shown most typically in the case of Alzheimer's disease (AD), which is characterised by a general and progressive decline in cognitive function, with the first symptom as an impaired episodic memory. Music, in this case, has been reported as one of the domains in which general skill and memory are preserved in spite of otherwise severe impairment [90]. This preserved musical processing, moreover, is not limited to procedural memory but often includes also stories of music, which can be used as an effective mnemonic device [91].

Hence, music may shape the development of normal and healthy human beings over the lifespan, but its potential as a non-pharmacological interventional aid for caregivers to help the cognitive and emotional capacity of patients with neurological and psychiatric brain disorders is receiving growing interest [15]. The use of resting-state fMRI techniques, e.g., with a main focus on the default mode network, seems to be well-suited to examine possible functional disconnectivity effects in disorders such as Alzheimer's disease, depression, dementia and schizophrenia. Also, other neurogenerative diseases like multiple sclerosis and amyotrophic lateral sclerosis seem to show changed connectivity in the default network as well as in other resting-state networks [78]. This may suggest that neurodegenerative diseases would attack interconnected cortical networks rather than single regions in the brain [92] and can thus be targets of a music intervention aimed at stabilising abnormal patterns of functional connectivity between compromised brain areas.

Music has been used already as a treatment for some psychiatric and neurological pathologies, such as schizophrenic disorders, Alzheimer's disease, Parkinson's disease, cerebral ischemia, pain, autism, anxiety and depression [15]. Music, furthermore, has been reported to improve also the well-being and cognitive functions in healthy adults, such as autobiographical memory, semantic memory, language ability and cognitive functions, and to alleviate neuropsychiatric symptoms, such as agitation, apathy, depression and anxiety (see [39] for an overview). Effects of music on AD are exemplary of the mechanisms that might mediate the impact of music on human well-being. Latent benefits of musical mnemonics as an aid to standard mnemonic methods, which may seem to be insufficient for AD patients, have been reported (for a review, see [15]). The mechanisms behind these memory-enhancing effects, however, are still not fully understood, but there is strong evidence for a benefit of music as a mnemonic device in a variety of clinical settings [91]. A possible explanation is that the areas of the brain associated with music cognition are preferentially spared in the case of AD. It has been suggested that procedural memory and priming effects for musical stimuli remain intact, whereas short-term and long-term episodic memory for melodic excerpts is impaired [93].

This dissociation between memory and general performance in AD patients holds in particular for listening to their favourite songs, which seems to recruit previously encoded memories. These memories seem to support and sustain brain introspection via connectivity within the default mode network and also to effectively reprocess autobiographic and episodic memories [84]. An additional explanation for this dissociation is that in patients with general cortical and hippocampal atrophy, which impairs standard episodic learning, musically-associated stimuli allow for a more diversified encoding. Music processing, in that case, encompasses a neural network that is recruiting from multiple areas of the brain, including cortical as well as subcortical areas. Musical stimuli and stimuli accompanied by music seem to create a more robust association at the stage of encoding and support a more composite encoding and retrieval process by inducing oscillatory synchrony in those neural networks that are associated with learning and memory [91, 94].

## 6. Conclusion and perspectives

Neuroplasticity is now an established topic in music and brain studies. Revolving around the concept of adaptation, it has been found that the brain is able to adapt its structure and function to cope with the solicitations of a challenging environment. This concept can be studied in the context of music performance studies and long-term and continued musical practice. It has been shown that some short-term plastic changes can even occur in the case of merely listening to music—without actually performing—(e.g., [95]) and in the short-time perspective of both listening and performing (e.g., [96]). Attentive listening to music in a real-time situation, in fact, is very demanding: it recruits multiple forms of memory, attention, semantic processing, target detection and motor function [18, 97]. As such, we propose here that music represents a sort of enriched environment that invites the brain to raise its general level of conscious functioning.

Traditional research on musical listening and training, however, has focussed mainly on structural changes, both at the level of macro- and microstructural adaptations. This has been well-documented with morphometric studies, which aimed at showing volumetric changes of target areas in the brain as the outcome of intensive musical practice. Recent contributions, however, have shown that the brain can be studied also from the viewpoint of network science. The brain, in this view, is not to be considered as an aggregate of isolated regions, but as a dynamic system that is characterised by multiple functional interactions and communication between distinct regions of the brain. Whole-brain connectivity patterns can be studied by measuring the co-activation of separate regions. Much is to be expected from the study of resting-state networks with a special focus on the default mode network. These networks seem to be indicative of the level of cognitive functioning in general and are subject to the possibility of modulation by experience and learning, both in the developing and in the mature brain. We propose that music has the potential to alter the organisation of these brain networks and enhance the connectivity of the brain, both in normal people and in those with an impaired brain.

A major emerging topic, therefore, is the tension between neurogenerative and neurodegenerative forces with the critical question as to the possible role of music as an intervening force to develop, maintain or even restore the connectivity in brain tissue. The idea that age-related cognitive decline may be slowed, arrested or even reversed through appropriately designed training or activities, such as musical practice, is supported already by some research. Moreover, the finding that the adult brain can undergo continual modifications highlights the potential of music intervention for inducing the plastic changes that can ultimately attenuate the impairments due to brain injury. Much more research, however, is still needed towards an integration of findings from neuroscience, education, music therapy and development.

## Author details

Mark Reybrouck[1,2]*, Peter Vuust[3] and Elvira Brattico[3]

*Address all correspondence to: mark.reybrouck@kuleuven.be

1 Musicology Research Group, KU Leuven – University of Leuven, Belgium

2 IPEM Institute for Systematic Musicology, Ghent University, Belgium

3 Department of Clinical Medicine, Center for Music in the Brain, Aarhus University and The Royal Academy of Music, Aarhus/Aalborg, Denmark

## References

[1] Altenmüller E. Apollo's gift and curse: Brain plasticity in musicians. Karger's Gazette. 2009;**70**:8-10. DOI: http://www.karger.com/gazette/70/altenmueller/art_4.htm

[2] Johansson B. Music and brain plasticity. European Review. 2006;**14**:49-64. DOI: 10.1017/s1062798706000056

[3] Kraus N, Chandrasekaran B. Music training for the development of auditory skills. Nature Reviews Neuroscience. 2010;**11**:599-605. DOI: 10.1038/nrn2882

[4] Miendlarzewska EA, Trost WJ. How musical training affects cognitive development: Rhythm, reward and other modulating variables. Frontiers in Neuroscience. 2013;**7**:279. DOI: 10.3389/fnins.2013.00279

[5] Merrett DL, Peretz I, Wilson SJ. Moderating variables of music training-induced neuroplasticity: A review and discussion. Frontiers in Psychology. 2013;**4**:606. DOI: 10.3389/fpsyg.2013.00606

[6] Reybrouck M, Brattico E. Neuroplasticity beyond sounds: Neural adaptations following long-term musical aesthetic experiences. Brain Sciences. 2015;**5**:69-91. DOI: 10.3390/brainsci5010069

[7] Vuust P, Liikala L, Näätänen R, Brattico P, Brattico E. Comprehensive auditory discrimination profiles recorded with a fast parametric musical multi-feature mismatch negativity paradigm. Clinical Neurophysiology. 2016;**127**:2065-2077. DOI: http://dx.doi.org/10.1016/j.clinph.2015.11.009

[8] Bangert M, Peschel T, Schlaug G, Rotte M, Drescher D, Hinrichs H, Heinze H-J, Altenmüller E. Shared networks for auditory and motor processing in professional pianists: Evidence from fMRI conjunction. NeuroImage. 2006;**30**:917-926. DOI: 10.1016/j.neuroimage.2005.10.044

[9] Münte TF, Altenmüller E, Jancke L. The musician's brain as a model of neuroplasticity. Nature Reviews Neuroscience. 2002;**3**:473-477. DOI: 10.1038/nrn843

[10] Fauvel B, Groussard M, Chételat G, Fouquet M, Landeau B, Eustache F, Desgranges B, Platel H. Morphological brain plasticity induced by musical expertise is accompanied by modulation of functional connectivity at rest. NeuroImage. 2014;**90**:179-188. DOI: 10.1016/j.neuroimage.2013.12.065

[11] Bengtsson SL, Nagy Z, Skare S, Forsman L, Forssberg H, Ullén F. Extensive piano practicing has regionally specific effects on white matter development. Nature Neuroscience. 2005;**8**:1148-1150. DOI: 10.1038/nn1516

[12] Imfeld A, Oechslin M, Meyer M, Loenneker T, Jancke L. White matter plasticity in the corticospinal tract of musicians: A diffusion tensor imaging study. NeuroImage. 2009; **46**:600-607. DOI: 10.1016/j.neuroimage.2009.02.025

[13] Öztürk HA, Tascioglu B, Aktekin M, Kurtoglu Z, Erden I. Morphometric comparison of the human corpus callosum in professional musicians and nonmusicians by using in vivo magnetic resonance imaging. Journal of Neuroradiology. 2002;**29**:29-34

[14] Fauvel B, Groussard M, Eustache F, Desgranges B, Platel H. Neural implementation of musical expertise and cognitive transfers: Could they be promising in the framework of normal cognitive aging? Frontiers in Human Neuroscience. 2013;**7**:693. DOI: http://dx.doi.org/10.3389/ fnhum.2013.00693

[15] Matrone C, Brattico E. The power of music on Alzheimer's disease and the need to understand the underlying molecular mechanisms. Journal of Alzheimer's Disease & Parkinsonism. 2015;**5**:1-7. DOI: 10.4172/2161-0460.1000196

[16] Alluri V, Toivianen P, Jääskeläinen I, Glerean E, Sams M, Brattico E. Large-scale brain networks emerge from dynamic processing of musical timbre, key and rhythm. NeuroImage. 2012;**59**:3677-3689. DOI: S1053-8119(11)01300-0 [pii]

[17] Brattico E. Cortical Processing of Musical Pitch as Reflected by Behavioural and Electrophysiological Evidence. Yliopistopaino: Helsinki; 2006

[18] Alluri V, Toiviainen P, Burunat I, Kliuchko M, Vuust P, Brattico E. Connectivity patterns during music listening: Evidence for action-based processing in musicians. Human Brain Mapping. 2017;**38**:2955-2970. DOI: 10.1002/hbm.23565

[19] Burunat I, Tsatsishvili V, Brattico E, Toiviainen P. Coupling of action-perception brain networks during musical pulse processing: Evidence from region-of-interest-based independent component analysis. Frontiers in Human Neuroscience. 2017;**11**:230. DOI: 10.3389/fnhum.2017.00230

[20] Burunat I, Brattico E, Puoliväli T, Ristaniemi T, Sams M, Toiviainen P. Action in perception: Prominent Visuo-motor functional symmetry in musicians during music listening. PLoS One. 2015;**30**:1-18. DOI: https://doi.org/10.1371/journal.pone.0138238

[21] Pantev C, Herholz SC. Plasticity of the human auditory cortex related to musical training. Neuroscience & Biobehavioral Reviews. 2011;**35**:2140-2154. DOI: 10.1016/j.neubiorev.2011.06.010

[22] Pallesen KJ, Brattico E, Bailey CJ, Korvenoja A, Koivisto J, Gjedde A, Carlson S. Cognitive control in auditory working memory is enhanced in musicians. PLoS One. 2010;**5**:e11120. DOI: https://doi.org/10.1371/journal.pone.0011120

[23] Abrams DA, Ryali S, Chen T, Chordia P, Khouzam A, Levitin D, Menon V. Inter-subject synchronization of brain responses during natural music listening. European Journal of Neuroscience. 2013;**37**:1458-1469. DOI: 10.1111/ejn.12173

[24] Habib M, Besson M. What do music training and musical experience teach us about brain plasticity? Music Perception. 2009;**26**:279-285. DOI: 10.1525/mp.2009.26.3.279

[25] Barrett K, Ashley R, Strait D, Kraus N. Art and science: How musical training shapes the brain. Frontiers in Psychology. 2013;**4**(713). DOI: https://doi.org/10.3389/fpsyg.2013.00713

[26] Gaser C, Schlaug G. Brain Structures differ between musicians and non-musicians. The Journal of Neuroscience. 2003;**23**:9240-9245

[27] Schlaug G. The brain of musicians. A model for functional and structural adaptation. Annals of the New York Academy of Sciences. 2001;**930**:281-299

[28] Schlaug G, Marchina S, Norton A. Evidence for plasticity in white-matter tracts of patients with chronic Broca's aphasia undergoing intense intonation-based speech therapy. Annals of the New York Academy of Sciences. 2009;**1169**:385-394. DOI: 10.1111/j.1749-6632.2009.04587.x

[29] Hyde K, Lerch J, Norton A, Forgeard M, Winner E, Evans A, Schlaug G. Musical training shapes structural brain development. Journal of Neuroscience. 2009;**29**:3019-3025. DOI: https://doi.org/10.1523/JNEUROSCI.5118-08.2009

[30] Gärtner H, Minnerop M, Pieperhoff P, Zilles K, Altenmüller E, Amunts K. Brain morphometry shows effects of long-term musical practice in middle-aged keyboard players. Frontiers in Psychology. 2013;**4**. DOI: 10.3389/fpsyg.2013.00636

[31] Jäncke L. Music drives brain plasticity. F1000Reports Biology. 2009;**1**. DOI: 10.3410/B1-78

[32] Stewart L. Do musicians have different brains? Clinical Medicine. 2008;**8**:304-308

[33] Wan C, Schlaug G. Music making as a tool for promoting brain plasticity across the life span. The Neuroscientist. 2010;**16**:566-577. DOI: 10.1177/1073858410377805

[34] Pascual-Leone A. The brain that makes music and is changed by it. In: Peretz I, Zatorre R, editors. The Cognitive Neuroscience of Music. Oxford – New York: Oxford University Press; 2003. pp. 396-409

[35] Klein C, Liem F, Hänggi J, Elmer S, Jäncke L. The "silent" imprint of musical training. Human Brain Mapping. 2016;**37**:536-546. DOI: 10.1002/hbm.23045

[36] Brattico E, Pallesen KJ, Varyagina O, Bailey C, Anourova I, Jarvenpaa M, Eerola T, Tervaniemi M. Neural discrimination of nonprototypical chords in music experts and laymen: An MEG study. Journal of Cognitive Neuroscience. 2009;**21**:2230-2244. DOI: 10.1162/jocn.2008.21144

[37] Lahav A, Saltzman E, Schlaug G. Action representation of sound: Audiomotor recognition network while listening to newly acquired actions. Journal of Neuroscience. 2007; **27**:308-314. DOI: 10.1523/JNEUROSCI.4822-06.2007

[38] Schellenberg EG, Peretz I. Music, language and cognition: Unresolved issues. Trends in Cognitive Sciences. 2008;**12**:45-46

[39] Ueda T, Suzukamo Y, Sato M, Izumi S. Effects of music therapy on behavioral and psychological symptoms of dementia: A systematic review and meta-analysis. Aging Research Reviews. 2013;**12**:628-641. DOI: 10.1016/j.arr.2013.02.003

[40] Fleagle J. Primate Adaptation and Evolution. San Diego: Academic Press; 1999

[41] Reybrouck M. From sound to music: An evolutionary approach to musical semantics. Biosemiotics. 2013;**6**:585-606. DOI: https://doi.org/10.1007/s12304-013-9192-6

[42] Reybrouck M. Music as environment: An ecological and biosemiotic approach. Behavioral Sciences. 2015;**5**:1-26. DOI: 10.3390/bs5010001

[43] Brown S, Merker B, Wallin N. An introduction to evolutionary musicology. In: Wallin N, Merker B, Brown S, editors. The Origins of Music. Cambridge, MA – London: The MIT Press; 2000. pp. 3-24

[44] James W. The Principles of Psychology. Vol. 1. New York: Holt; 1890

[45] Kaas J. Plasticity of sensory and motor maps in adult mammals. Annuals Reviews of Neurosciences. 1991;**114**:137-167. DOI: 10.1146/annurev.ne.14.030191.001033

[46] Uttal W. The Psychobiology of Mind. Hillsdale, NJ: Lawrence Erlbaum; 1978

[47] Reybrouck M. Musical universals and the axiom of psychobiological equivalence. In: Leroy J-J, editor. Topicality of Musical Universals/Actualité des Universaux musicaux Paris. France: Editions des Archives Contemporaines; 2013. pp. 31-44

[48] Deco G, Kringelbach M. Great expectations: Using whole-brain computational connectomics for understanding neuropsychiatric disorders. Neuron. 2014;**84**:892-905. DOI: 10.1016/j.neuron.2014.08.034

[49] Sachs ME, Ellis RE, Schlaug G, Loui P. Brain connectivity reflects human aesthetic responses. Social Cognitive and Affective Neuroscience. 2016;**11**:1-8. DOI: 10.1093/scan/nsw009

[50] Brattico E. From pleasure to liking and back: Bottom-up and top-down neural routes to the aesthetic enjoyment of music. In: Nadal M, Houston JP, Agnati L, Mora F, Cela Conde CJ, editors. Art, Aesthetics, and the Brain. Oxford – New York: Oxford University Press; 2015. pp. 303-318

[51] Brattico E, Bogert B, Jacobsen T. Toward a neural chronometry for the aesthetic experience of music. Frontiers in Psychology. 2013;**4**:1-21. DOI: doi.org/10.3389/fpsyg.2013.00206

[52] Brattico P, Brattico E, Vuust P. Global sensory qualities and aesthetic experience in music. Frontiers in Neuroscience. 2017;**11**:59. DOI: 10.3389/fnins.2017.00159

[53] Brattico E, Pearce M. The neuroaesthetics of music. Psychology of Aesthetics, Creativity, and the Arts. 2013;**7**:48-61 http://dx.doi.org/10.1037/a0031624

[54] Brattico E, Vuust P. Brain-to-brain coupling and culture as prerequisites for musical interaction. In: Lesaffre M, Leman M, Maes P-J, editors. The Routledge Companion to Embodied Music Interaction. Abingdon-on-Thames, UK: Routledge; 2016

[55] Konvalinka I, Roepstorff A. The two-brain approach: How can mutually interacting brains teach us something about social interaction? Frontiers in Neuroscience. 2012;**6**:215. DOI: 10.3389/fnhum.2012.00215

[56] Schlaug G. Musicians and music making as a model for the study of the brain. Progress in Brain Research. 2015;**217**:37-54. DOI: 10.1016/bs.pbr.2014.11.020

[57] van Praag H, Kempermann G, Gage F. Neural consequences of environmental enrichment. Nature Reviews Neuroscience. 2000;**1**:191-198. DOI: 10.1038/35044558

[58] Gerhardt K, Abrams R. Fetal exposures to sound and vibroacoustic stimulation. Journal of Perinatology. 2000;**20**:20-S29

[59] Paillard J. La conscience. In: Richelle M. Requin J, Robert M, editors. Traité de psychologie expérimentale. Vol. 2. Paris: Presses Universitaires de France; 1994. pp. 639-684

[60] Schneider P, Sluming V, Roberts N, Bleeck S, Rupp A. Structural, functional, and perceptual differences in Heschl's gyrus and musical instrument preference. Annals of the New York Academy of Sciences. 2005;**1060**:387-394. DOI: 10.1196/annals.1360.033

[61] Chen JL, Nedivi E. Neuronal structural remodeling; is it all about access? Current Opinion in Neurobioly. 2010;**20**:557-562. DOI: 10.1016/j.conb.2010.06.002

[62] Ziemann U, Hallet M, Cohen LG. Mechanisms of deafferentation-induced plasticity in human motor cortex. Journal of Neuroscience. 1998;**18**:7000-7007

[63] Segal M. Dendritic spines: Morphological building blocks of memory. Neurobiology of Learning and Memory. 2017;**138**:3-9. DOI: 10.1016/j.nlm.2016.06.007

[64] Hutchinson S, Hui-Lin Lee L, Gaab N, Schlaug G. Cerebellar volume in musicians. Cerebral Cortex. 2003;**13**:943-949. DOI: https://doi.org/10.1093/cercor/13.9.943

[65] Chaudhury S, Chandra Nag T, Wadhwa S. Effect of prenatal auditory stimulation on numerical synaptic density and mean synaptic height in the posthatch day 1 chick hippocampus. Synapse. 2008;**63**:152-159. DOI: 10.1002/syn.20585

[66] Martin SJ, Morris RG. New life in an old idea: The synaptic plasticity and memory hypothesis revisited. Hippocampus. 2002;**12**:609-636. DOI: 10.1002/hipo.10107

[67] Hannon EE, Trainor LJ. Music acquisition: Effects of enculturation and formal training on development. Trends in Cognitive Science. 2007;**11**:466-472. DOI: 10.1016/j.tics.2007.08.008

[68] Musacchia G, Sams M, Skoe E, Kraus N. Musicians have enhanced subcortical auditory and audiovisual processing of speech and music. Proceedings of the National Academy of Sciences of the USA. 2007;**104**:15894-15898. DOI: 10.1073/pnas.0701498104

[69] Chandrasekaran B, Kraus N. The scalp-recorded brainstem response to speech: Neural origins and plasticity. Psychophysiology. 2010;**47**:236-246. DOI: 10.1111/j.1469-8986.2009.00928.x

[70] Skoe E, Kraus N. Auditory brain stem response to complex sounds: A tutorial. Ear and Hearing. 2007;**31**:302-324. DOI: 10.1097/AUD.0b013e3181cdb272

[71] Song JH, Skoe E, Wong PC, Kraus N. Plasticity in the adult human auditory brainstem following short-term linguistic training. Journal of Cognitive Neuroscience. 2008;**20**:1892-1902. DOI: 10.1162/jocn.2008.20131

[72] Strait DL, Kraus N, Skoe E, Ashley R. Musical experience and neural efficiency: Effects of training on subcortical processing of vocal expressions of emotion. European Journal of Neuroscience. 2009;**29**:661-668. [PubMed: 19222564] DOI: 10.1111/j.1460-9568.2009.06617.x

[73] Tzounopoulos T, Kraus N. Learning to encode timing: Mechanisms of plasticity in the auditory brainstem. Neuron. 2009;**62**:463-469. DOI: 10.1016/j.neuron.2009.05.002

[74] Suga N. Role of corticofugal feedback in hearing. Journal of Comparative Physiology. 2008;**194**:169-183. DOI: 10.1007/s00359-007-0274-2

[75] Suga N, Ma X. Multiparametric corticofugal modulation and plasticity in the auditory system. Nature Reviews Neuroscience. 2003;**4**:783-794. DOI: 10.1038/nrn1222

[76] Rupp A, Hack S, Gutschalk A, Schneider P, Picton T, Stippic C, Scherg M. Fast temporal interactions in human auditory cortex. Neuroreport. 2000;**11**:3731-3736

[77] Schneider P, Scherg M, Dosch HG, Specht HJ, Gutschalk A, Rupp A. Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians. Nature Neuroscience. 2002;**5**:688-694

[78] van den Heuvel M, Hulshoff Pol H. Exploring the brain network: A review on resting-state fMRI functional connectivity. European Neuropsychopharmacology. 2010;**20**:519-534. DOI: 10.1016/j.euroneuro.2010.03.008

[79] Bassett DS, Gazzaniga MS. Understanding complexity in the human brain. Trends in Cognitive Science. 2011;**15**:200-209. DOI: http://dx.doi.org/10.1016/j.tics.2011.03.006

[80] Friston KJ, Frith CD, Liddle PF, Frackowiak RS. Functional connectivity: The principal-component analysis ofl arge (PET) data sets. Journal of Cerebral Blood Flow & Metabolism. 1993;**13**:5-14. DOI: 10.1038/jcbfm.1993.4

[81] Damoiseaux JS, Rombouts SA, Barkhof F, Scheltens P, Stam CJ, Smith SM, Beckmann CF. Consistent resting-state networks across healthy subjects. Proceedings of the National Academy of Science of USA. 2006;**103**13:848-853

[82] Luo C, Qiu C, Guo Z, Fang J, Li Q, Lei X, Xia Y, Lai Y, Gong Q, Zhou D, Yao D. Disrupted functional brain connectivity in partial epilepsy: A resting-state fMRI study. PLoS One. 2012;**7**:e28196. DOI: 10.1371/journal.pone.0028196

[83] Raichle M. The brain's default network. Annual Review of Neuroscience. 2015;**8**:433-447. DOI: 10.1196/annals.1440.011

[84] Wilkins RW, Hodges DA, Laurienti PJ, Steen M, Burdette JH. Network science and the effects of music preference on functional brain connectivity: From beethoven to eminem. Scientific Reports. 2014;**4**. Article number: 6130. DOI: 10.1038/srep0613

[85] van den Heuvel MP, Stam CJ, Kahn RS, Hulshoff Pol HE. Efficiency of functional brain networks and intellectual performance. Journal of Neuroscience. 2009;**29**:7619-7624

[86] Fox MD, Raichle ME. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nature Reviews Neuroscience. 2007;**8**:700-711. DOI: 10.1038/nrn2201

[87] Janata PB, Tillmann B, Bharucha JJ. Listening to polyphonic music recruits domain-general attention and working memory circuits. Cognitive, Affective and Behavioral Neuroscience. 2002;**2**:121-140

[88] Karmonik C, Brandt A, Anderson J, Brooks F, Lytle J, Silverman E. Music listening modulates functional connectivity and information flow in the human brain. Brain Connectivity. 2016;**6**:632-641. DOI: 10.1089/brain.2016.0428

[89] Cuddy L, Duffin J. Music, memory, and Alzheimer's disease: Is music recognition spared in dementia, and how can it be assessed? Medical Hypotheses. 2005;**64**:229-235. DOI: 10.1016/j.mehy.2004.09.005

[90] Jacobsen JH, Stelzer J, Fritz TH, Chetelat G, La Joie R, Turner R. Why musical memory can be preserved in advanced Alzheimer's disease. Brain. 2015;**138**(Pt 8):2438-2450. DOI: 10.1093/brain/awv135

[91] Simmons-Stern N, Budson A, Ally B. Music as a memory enhancer in patients with Alzheimer's disease. Neuropsychologia. 2010;**48**:3164-3167. DOI: 10.1016/j.neuropsy chologia.2010.04.033

[92] Seeley W, Crawford RK, Zhou J, Miller BL, Greicius MD. Neurodegenerative diseases target large-scale human brain networks. Neuron. 2009;**62**:42-52. DOI: 10.1016/j.neuron. 2009.03.024

[93] Baird A, Samson S. Memory for music in Alzheimer's disease: Unforgettable? Neuropsycholigal Review. 2009;**19**:85-101. [PubMed: 19214750]

[94] Thaut MH, Peterson DA, McIntosh GC. Temporal entrainment of cognitive functions: Musical mnemonics induce brain plasticity and oscillatory synchrony in neural networks underlying memory. Annals of the New York Academy of Sciences. 2005;**1060**:243-254. [PubMed: 16597771] DOI: 10.1196/annals.1360.017

[95] Brattico E, Tervaniemi M, Picton TW. Effects of brief discrimination-training on the auditory N1 wave. Neuroreport. 2003;**14**:2489-2492. DOI: 10.1097/01.wnr.0000098748.87269.a1

[96] Lappe C, Herholz SC, Trainor L, Pantev C. Cortical plasticity induced by short-term unimodal and multimodal musical training. Journal of Neuroscience. 2008;**28**:9632-9639. DOI: 0.1523/JNEUROSCI.2254-08.2008

[97] Burunat I, Alluri V, Toiviainen P, Numminen J, Brattico E. Dynamics of brain activity underlying working memory for music in a naturalistic condition. Cortex. 2014;**57**: 254-269. DOI: 10.1016/j.cortex.2014.04.012