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Neurobiological Aspects of Neurologic Music Therapy

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Abstract

Making music is a powerful way of engaging multisensory and motor networks, inducing changes within these networks and linking together distant brain regions. These multimodal effects of music making together with music's ability to tap into the emotion and reward system in the brain can be used to facilitate therapy and rehabilitation of neurological disorders. In this article, we review short- and long-term effects of listening to music and making music on functional networks and structural components of the brain. The specific influence of music on the developing brain is emphasized and possible transfer effects on emotional and cognitive processes are discussed. Furthermore, we present data on the potential of music making to support and facilitate neurorehabilitation. We focus on interventions such as melodic intonation therapy and music-supported motor rehabilitation to showcase the effects of neurologic music therapies and discuss their underlying neural mechanisms.

Keywords

brain plasticity, melodic intonation therapy, music-supported training, neurologic music therapy, neurorehabilitation

Music as a Driver of Brain Plasticity

Musical experience is one of the richest human emotional, sensorimotor, and cognitive experiences. It involves listening, watching, feeling, moving and coordinating, remembering, and expecting. It is frequently accompanied by strong emotions resulting in joy, happiness, bittersweet sadness, or even in overwhelming bodily reactions like tears in the eyes or shivers down the spine. A large number of cortical and subcortical brain structures contribute to processing and production of music (for reviews, see Tramo[1] and Altenmüller and McPherson[2]).

For example, primary and secondary regions in the cerebral cortex are critical for any conscious perception of sensory information, be it auditory, visual, or somatosensory. However, music also changes activity in multisensory and motor integration regions in the frontal and parietal lobes. The frontal lobe is involved in guidance of attention, in planning and motor preparation, in integrating auditory and motor information, and in specific human skills such as imitation and empathy. The latter 2 play an important role in the acquisition of musical skills and emotional expressiveness. Multisensory integration regions in the parietal lobe and temporo-occipital areas integrate different sensory inputs from the auditory, visual, and somatosensory systems into a combined sensory impression; it is this multisensory brain representation that constitutes the typical musical experience. The cerebellum is another important part of the brain that plays a critical role in musical experience. It not only is important for motor coordination, but also plays an important role in various cognitive tasks, especially when they include demands on timing. Typically, the cerebellum is activated in rhythm processing or by tapping in synchrony with an external pacemaker such as a metronome. Finally, the emotional network (comprising the basis and the inner surfaces of the 2 frontal lobes, the cingulate gyrus, and brain structures in the evolutionarily old parts of the brain such as the amygdala, the hippocampus, and the midbrain) is crucial for the emotional perception of music and hitherto for an individual's motivation to listen to or to engage in any musical activity.

The brain as a highly dynamically organized structure can change and adapt as a result of activities and demands imposed by the environment. Musical activity has proved to be a powerful stimulus for this kind of brain adaptation, or brain plasticity, as pointed out by Wan and Schlaug.[3] Effects of plasticity are not restricted to musical prodigies, but they occur in children learning to play a musical instrument[4] and in adult musical amateurs,[5] albeit to a lesser extent. Thus, with the main topic of our article in mind, we suggest that brain plasticity induced through music making may produce manifold benefits. This holds not only for changing and/or restoring compromised

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sensorimotor brain networks but also for influencing neurohormonal status as well as cognitive and emotional processes in healthy and neurologically diseased/disordered individuals. Thus, various sensorimotor, coordinative, or emotional disabilities can be improved with music-supported therapy (MST).

In the following, we first briefly review the mechanisms of how music may induce brain plasticity. We then clarify the impact of music on emotion and neurohormones. Subsequently, we demonstrate the transfer effects of music exposure and music making to other cognitive and emotional domains and finally show examples of the potential of music making to support and facilitate neurorehabilitation. Here we will not give an exhaustive review, but focus on improving rehabilitation in aphasia and motor impairments following brain injury.

Some Mechanisms of Music-Induced Brain Plasticity

During the past decade, brain imaging has provided important insights into the enormous capacity of the human brain to adapt to complex demands. These adaptations are referred to as brain plasticity and include not only the quality and extent of functional connections of brain networks, but also the fine structure of nervous tissue and even the macroscopic gross structure of brain anatomy.[6] Brain plasticity is best observed in complex tasks, including for example temporospatially precise movements with high behavioral relevance. These behaviors are usually accompanied by emotional arousal and motivational activation of the reward system. Furthermore, plastic changes are more pronounced when the specific activities started before puberty and require intense training. Obviously, continued musical activities provide in an ideal manner these prerequisites of brain plasticity. It is therefore not astonishing that the most dramatic effects of brain plasticity have been demonstrated in professional musicians (for a classic review, see Münte et al[7]; for more recent reviews, see Wan and Schlaug[3] and Altenmüller and Schlaug[8]).

Our understanding of the molecular and cellular mechanisms underlying these adaptations is far from complete. Brain plasticity may occur at different time axes. For example, the efficiency and size of synapses may be modified in a time window of seconds to minutes, and the growth of new synapses and dendrites may require hours to days. An increase in gray matter density, reflecting an enlargement of neurons, a change in synaptic density, more support structures such as capillaries and glial cells, or a reduced rate of physiological cell death (termed apoptosis), needs several weeks. White matter density also changes as a consequence of musical training. This effect seems to be primarily due to an enlargement of myelin cells; the myelin cells, wrapped around the nerve fibers (axons), are contributing essentially to the velocity of the electrical impulses traveling along the nerve fiber tracts. Under these conditions, requiring rapid information transfer and high temporal precision, these myelin cells grow, and, as a consequence, the nerve conduction velocity increases. Finally, brain regions involved in specific tasks may also be enlarged after long-term training due to the growth of structures supporting the nerve function, for example, blood vessels that are necessary for the transportation of oxygen and glucose, sustaining nerve function.

Comparison of the brain anatomy of skilled musicians with that of nonmusicians shows that prolonged instrumental practice leads to an enlargement of the hand area in the motor cortex[9] and to an increase in gray matter density corresponding to more and/or larger neurons in the respective area.[10] These adaptations appear to be particularly prominent in all instrumentalists who have started to play prior to the age of 10 and correlate positively with cumulative practice time. Furthermore, in professional musicians, the normal anatomical difference between the larger, dominant (mostly right) hand area and the smaller, nondominant (left) hand area is less pronounced when compared to nonmusicians. These results suggest that functional adaptation of the gross structure of the brain occurs during training at an early age.

Similar effects of specialization have been found with respect to the size of the corpus callosum. Professional pianists and violinists tend to have a larger anterior (front) portion of this structure, especially those who have started playing the instrument prior to the age of 7.[11] Since this part of the corpus callosum contains fibers from the motor and supplementary motor areas, it seems plausible to assume that the high demands for coordination between the 2 hands and the rapid exchange of information may either stimulate the nerve fiber growth—the myelination of nerve fibers that determines the velocity of nerve conduction—or prevent the physiological loss of nerve tissue during the typical pruning processes of adolescence or during aging. These between-group differences in the midsagittal size of the corpus callosum were confirmed in a longitudinal study comparing a group of children learning to play musical instruments versus a group of children without instrumental music experience.[4]

Another impressive adaptation of white matter structures has recently been shown by Halwani and colleagues.[12] They reported differences in macrostructure and microstructure of the arcuate fasciculus (AF), a prominent white matter tract connecting temporal and frontal brain regions, between singers, instrumentalists, and nonmusicians. Both groups of musicians had higher tract volumes in the right dorsal and ventral tracts than that of nonmusicians but did not show a significant difference between each other. Singers had higher tract volume and different microstructures of the tract on the left side when compared to instrumental musicians and nonmusicians. This suggests that the right-hemisphere AF might show a more general effect of music making, while the left-hemisphere AF has a stronger response to the specific aspects of vocal–motor training and control. The microstructure of the left dorsal branch of the arcuate fascicle was correlated with the number of years of participants' vocal training, suggesting that long-term vocal–motor training might lead to an increase in volume and microstructural complexity of specific white matter tracts constituting the so-called aural–oral loop and connecting regions that are fundamental to sound perception, production, and its feedforward and feedback control. Similarly, Bengtsson and her colleagues[13] have found structural differences in the corticospinal tract, particularly in the posterior limb of the internal capsule, between musicians and nonmusicians. This difference was related to measures of training intensity. It is worth mentioning that subcortical structures also seem to be affected. In professional musicians, the cerebellum, which contributes significantly to the precise timing and accuracy of motor commands, is also enlarged.[10,13]

In summary, when training starts at an early age (before puberty), these plastic adaptations of the nervous system affect brain anatomy by enlarging the brain structures that are involved in different types of musical skills. When training starts at a later age, it modifies brain organization by re-wiring neuronal networks and involving adjacent nerve cells to contribute to the required tasks. These changes result in enlarged cortical representations of, for example, specific fingers or sounds within existing brain structures. In the following, we more closely examine the emotional prerequisites for brain plasticity and the impact of music on emotions and neurohormones.

The Role of Music-Induced Emotions for Brain Plasticity

An intriguing question is why music is such a powerful driver of beneficial brain plasticity. This brings us to the specific motivational and emotional role of musical experience. Emotional responses to music are often cited when people describe why they value music and why they ascribe certain effects of music on health. Music is known to have a wide range of physiological effects on the human body including for example changes in heart rate, respiration, blood pressure, skin conductivity, skin temperature, muscle tension, and biochemical responses (for a review, see Hutchinson et al[14] and Hodges[15]).

Joyful musical behaviors, for example, learning to play a musical instrument or to sing is characterized by curiosity, stamina, and the ability to strive for rewarding experiences in future. This results in incentive goal-directed activities over prolonged time periods, which are mainly mediated by the transmitter substance dopamine. Most nerve cells sensitive to this neurotransmitter are found in a small part of the brain, which is localized behind the basis of the frontal cortex, the so-called mesolimbic system, an important part of the “emotional” brain. Dopamine plays a dominant role in the neurobiology of reward, learning, and addiction. Virtually all drugs of abuse, including heroin, alcohol, cocaine, and nicotine, activate dopaminergic systems. The so-called natural rewards such as musical experiences and other positive social interactions likewise activate dopaminergic neurons and are powerful aids to attention and learning.[16] There is ample evidence that the sensitivity to dopamine in the mesolimbic brain regions is largely genetically determined, resulting in the enormous variability in reward-dependent behavior. The genetic “polymorphism” of dopaminergic response explains the different motivational drives we observe in children with a similar social and educational background. It is intriguing that there is a strong link of dopaminergic activity to learning and memory, which in turn promote plastic adaptations in brain areas involved in the tasks to be learned.

Serotonin is another neurotransmitter important for music-induced brain plasticity. It is commonly associated with feelings of satisfaction from expected outcomes, whereas dopamine is associated with feelings of pleasure based on novelty or newness. In a study of neurochemical responses to pleasant and unpleasant music, serotonin levels were significantly higher when participants were exposed to music they found pleasing.[17] In another study with participants exposed to pleasing music, functional and effective connectivity analyses showed that listening to music strongly modulated activity in a network of mesolimbic structures involved in reward processing including the dopaminergic nucleus accumbens and the ventral tegmental area as well as the hypothalamus and insula. This network is believed to be involved in regulating autonomic and physiological responses to rewarding and emotional stimuli.[18]

Using positron-emission tomography (PET) technology, Blood and Zatorre[19] determined changes in regional cerebral blood flow (rCBF) during intense emotional experiences involving sensations such as goose bumps or shivers down the spine while listening to music. Each participant listened to a piece of their own favorite music to which they usually had an emotional reaction. Increasing emotional intensity correlated with rCBF decrease in the amygdala as well as the anterior hippocampal formation. An increase in rCBF correlating with increasing emotional intensity was observed in the ventral striatum, the midbrain, the anterior insula, the anterior cingulate cortex, and the orbitofrontal cortex. Again, these latter brain regions are related to reward and positive emotional valence.

In a newer study by the same group, the neurochemical specificity of [(11)C]raclopride PET scanning was used to assess dopamine release on the basis of the competition between endogenous dopamine and [11C]raclopride for binding to dopamine D2 receptors.[20] They combined dopamine-release measurements with psychophysiological measures of autonomic nervous system activity during listening to intensely pleasurable music and found endogenous dopamine release in the striatum at peak emotional arousal during music listening. To examine the time course of dopamine release, the authors used functional magnetic resonance imaging (fMRI) with the same stimuli and listeners and found a functional dissociation: The caudate was more involved during the anticipation and the nucleus accumbens was more involved during the experience of peak emotional responses to music. These results indicate that intense pleasure in response to music can lead to dopamine release in the striatal system. Notably, the anticipation of an abstract reward can result in dopamine release in an anatomical pathway distinct from that associated with the peak pleasure itself. Such results may well help to explain why music is of such high value across all human societies. As stated above, dopaminergic activation regulates and heightens arousal and motivation and supports memory formation in the episodic and the procedural memory,[21] thereby contributing to memorization of auditory stimuli producing such strong emotional responses. In a very recent study, the authors could even demonstrate that the degree of activation and connectivity in a network comprising the accumbens nucleus, auditory cortices, amygdala, and ventromedial frontal cortex predicted the amount of money participants were willing to spend in an auction paradigm.[22]

Taken together, these powerful music-induced modulations of neurohormonal status may not only account for pleasurable experiences but may also play a role in neurologic music therapy.

Facilitating Recovery From Nonfluent Aphasia Through a Form of Singing

The ability to sing in humans is evident from infancy and does not depend on formal vocal training but can be enhanced by training. Given the behavioral similarities between singing and speaking, as well as the shared and distinct neural correlates of both, researchers have begun to examine whether forms of singing can be used to treat some of the speech–motor abnormalities associated with various neurological conditions.[23]

Aphasia is a common and devastating complication of stroke or other brain injuries, which results in the loss of ability to produce and/or comprehend language. It has been estimated that between 24% and 52% of patients with acute stroke show some form of aphasia if tested within 7 days of their stroke; 12% of survivors still have significant aphasia at 6 months after stroke.[24] The nature and severity of language dysfunction depends on the location and extent of the brain lesion. Accordingly, aphasia can be classified broadly into fluent or nonfluent. Fluent aphasia often results from a lesion involving the posterior superior temporal lobe known as Wernicke area. Patients who are fluent exhibit articulated speech with relatively normal utterance length. However, their speech may be completely meaningless to the listener and littered with jargon. Furthermore, it may contain violations of syntactic and grammatical rules. These patients also have severe speech comprehension deficits. In contrast, nonfluent aphasia results most commonly from a lesion in the left frontal lobe, involving the left posterior inferior frontal region known as Broca area. Patients who are nonfluent tend to have a relatively intact comprehension for conversational speech but have marked impairments in articulation and speech production.

The general consensus is that there are 2 routes to recovery from aphasia. In patients with small lesions in the left hemisphere, there tends to be recruitment of both left-hemispheric, perilesional cortex with variable involvement of right-hemispheric homologous regions during the recovery process.[25-28] In patients with large left-hemispheric lesions involving language-related regions of the frontotemporal lobes, the only path to recovery may be through recruitment of homologous language and speech–motor regions in the right hemisphere.[29,30] It has been suggested that recovery via the right hemisphere may be less efficient than recovery via the left hemisphere,[28,31] possibly because patients with relatively large left-hemispheric lesions are generally more impaired and recover to a lesser degree than patients with smaller left-hemisphere lesions. Nevertheless, activation of right-hemispheric regions during speech/language fMRI tasks has been reported in patients with aphasia, irrespective of their lesion size.[26] For patients with large lesions that cover the language-relevant regions on the left, therapies that specifically engage or stimulate the homologous right-hemispheric regions have the potential to facilitate the language recovery process beyond the limitations of natural recovery.[30,32,33] Based on clinical observations of patients with severe nonfluent aphasia and their ability to sing lyrics better than they can speak the same words,[34-36] an intonation-based therapy called melodic intonation therapy (MIT) was developed, which would emphasize melody and contour and engage a sensorimotor network of articulation on the unaffected hemisphere through rhythmic tapping.[34-36] The 2 unique components of MIT are (1) the intonation of words and simple phrases using a melodic contour that follows the prosody of speech and (2) the rhythmic tapping of the left hand, which accompanies the production of each syllable and serves as a catalyst for fluency.

To date, studies using MIT have produced positive outcomes in patients with nonfluent aphasia. These outcomes range from improvements in the Boston Diagnostic Aphasia Examination (BDAE[37]) to improvements in articulation and phrase production[38,39] after treatment. The effectiveness of this intervention is further demonstrated in a recent study that examined transfer of language skills to untrained contexts. Schlaug et al[31] compared the effects of MIT with a control intervention (speech repetition) on picture naming performance and measures of propositional speech. After 40 daily sessions, both therapy techniques resulted in significant improvement in all outcome measures, but the extent of this improvement was far greater for the patients who underwent MIT than for those who underwent the control therapy.

The therapeutic effect of MIT is also evident in neuroimaging studies that show reorganization of brain functions. Melodic intonation therapy resulted in increased activation in a right-hemispheric network involving the premotor, inferior frontal, and temporal lobes[29] as well as increased fiber number and volume of the AF in the right hemisphere.[30] These findings demonstrate that intensive experimental therapies such as MIT—when applied over a longer period in patients with chronic stroke—can induce functional and structural brain changes in a right-hemispheric vocal–motor network, and these changes are related to improvements in speech output.

Music-Supported Motor Therapy in Patients With Stroke

Music-supported therapy (MST) in the rehabilitation of fine motor hand skills was first systematically investigated by Schneider et al.[40] Patients were encouraged to play melodies with the paretic hand on a piano or to tap with the paretic arm on 8 electronic drum pads that emitted piano tones. It was demonstrated that these patients regained their motor abilities more quickly and showed improvement in timing, precision, and smoothness of fine motor skills. Along with fine motor recovery, an increase in neuronal connectivity between sensorimotor and auditory regions was demonstrated by means of

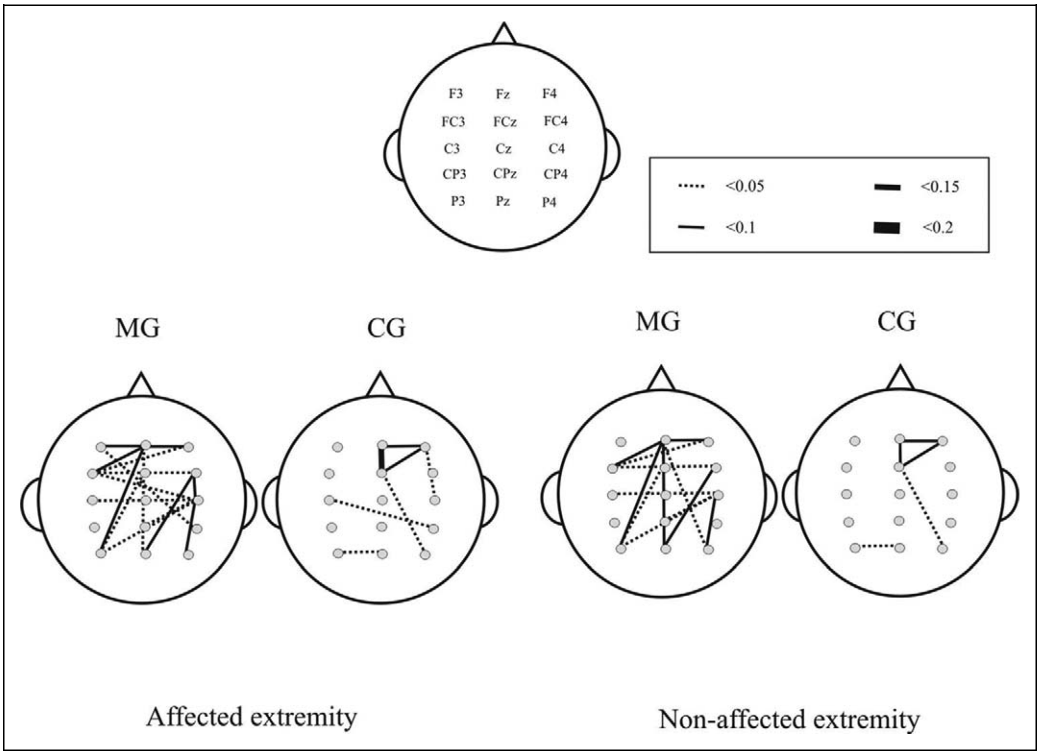

Figure 1. Music-supported therapy (MST). Topographic task-related coherence maps for the music group (MG) compared to the control group (CG) during self-paced arm movements for the drum pad condition in the β band (18-22 Hz). Statistically significant increases in task-related coherence during the motor performance after 3 weeks and 15 sessions of music-supported therapy on sonified drum pads are displayed. Adapted with permission from Altenmüller and Schlaug.[8]

electroencephalograph-coherence measures.[41-43] Therefore, establishing an audio-sensorimotor co-representation may support the rehabilitation process (see Figure 1). This notion is corroborated by findings in a patient who underwent music-supported training 20 months after a stroke. Along with clinical improvement, fMRI follow-up provided evidence for the establishment of an auditory–sensorimotor network due to the training procedure.[44]

Undoubtedly, music-supported training is efficient and seems to be even more helpful than functional motor training using no auditory feedback but otherwise similar fine motor training. A randomized prospective study comprising all 3 groups is presently under the way and will clarify the differential effects of functional motor training and music-supported training. With respect to the underlying mechanisms, a number of open questions still remain. First, the role of motivational factors must be clarified. From the patients' informal descriptions of their experience with the music-supported training, it appears that this was highly enjoyable and a highlight of their rehabilitation process. Thus, motivational and emotional factors might have contributed to the success of the training program. Furthermore, according to a study by Särkämö and colleagues,[45] music listening activates a widespread bilateral network of brain regions related to attention, semantic processing, memory, motor functions, and emotional processing. Särkämö and colleagues showed that music exposure significantly enhances cognitive functioning in the domains of verbal memory and focused attention in patients with stroke. The music group also experienced less depressed mood than did the control groups. These mechanisms may also hold true for the music-supported training we applied.

Another issue is related to the auditory feedback mechanisms. Up to now, it has not been clear whether any auditory feedback (eg, simple beep tones) would have a similar effect on fine motor rehabilitation or whether explicit musical parameters such as a sophisticated pitch and time structure are prerequisites for the success of the training. This will be addressed in a planned study comparing the effects of musical feedback compared to simple acoustic feedback. With respect to the latter, according to a study by Thaut and colleagues,[46] simple rhythmic cueing with a metronome significantly improves the spatiotemporal precision of reaching movements in patients with stroke.

Furthermore, it is not clear whether timing regularity and predictability are crucial for the beneficial effect of MST using keyboard playing or tapping on drum pads. Although it has been argued that the effectiveness of this therapy relies on the fact that the patient's brain receives a time-locked auditory feedback with each movement, new results challenge this viewpoint. In a recent study, 15 patients in early stroke rehabilitation with no previous musical background learned to play simple finger exercises and familiar children's songs on the piano. The participants were assigned to 1 of 2 groups: In the *normal* group, the keyboard emitted a tone immediately at keystroke, and in the *delay* group, the tone was delayed by a random time interval between 100 and 600 ms. To assess recovery, we performed standard clinical tests such as the 9-hole pegboard test and index finger tapping speed and regularity. Surprisingly, patients in the delay group improved strikingly in the 9-hole pegboard test, whereas patients in the normal group did not. In finger tapping rate and regularity both groups showed similar marked improvements. The normal group showed reduced depression, whereas the delay group did not.[47] Here we conclude that music therapy on a randomly delayed keyboard can significantly boost motor recovery after stroke. We hypothesize that the patients in the delayed feedback group implicitly learn to be independent of the auditory feedback and therefore outperform those in the normal condition.

Finally, the stability of improvements needs to be assessed in further studies, and the length and number of training sessions might be manipulated in future research. Additionally, the effect of training in chronic patients with motor impairments following a stroke for more than a year will be assessed.

Conclusion

Emerging research over the last decade has shown that long-term music training and the associated sensorimotor skill learning can be a strong stimulant for neuroplastic changes in the developing as well as in the adult brain, affecting both white and gray matter as well as cortical and subcortical structures. Making music including singing and dancing leads to a strong coupling of perception and action mediated by sensory, motor, and multimodal brain regions and affects either in a top-down or bottom-up fashion important relay stations in the brain stem and thalamus. Furthermore, listening to music and making music provokes motions and emotions, increases between-participant communications and interactions, and—mediated via neurohormones such as serotonin and dopamine—is experienced as joyous and rewarding through activity changes in amygdala, ventral striatum, and other components of the limbic system. Making music makes rehabilitation more enjoyable and can remediate impaired neural processes or neural connections by engaging and linking brain regions with each other that might otherwise not be linked together.

As other experimental interventions, music-based experimental interventions need to be grounded on a neurobiological understanding of how and why particular brain systems could be affected. The efficacy of these experimental interventions should be assessed quantitatively and in an unbiased way. A neuroscientific basis for music-based interventions and data derived from randomized clinical trials are important steps in establishing neurologically based music therapies that might have the power to enhance brain recovery processes, ameliorate the effects of developmental brain disorders, and neuroplasticity in general.

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References

1. Tramo MJ. Biology and music. Music of the hemispheres. *Science*. 2001;291(5501):54-56.
2. Altenmüller E, McPherson G. Motor learning and instrumental training. In: Gruhn W, Rauscher F, eds. *Neurosciences in Music Pedagogy*. New York, NY: Nova Science Publisher; 2007:145-155.
3. Wan CY, Schlaug G. Music making as a tool for promoting brain plasticity across the life-span. *Neuroscientist*. 2010;16(5): 566-577.
4. Hyde KL, Lerch J, Norton A, et al. Musical training shapes structural brain development. *J Neurosci*. 2009;29(10):3019-3025.
5. Bangert M, Altenmüller E. Mapping perception to action in piano practice: a longitudinal DC-EEG-study. *BMC Neurosci*. 2003;4:26.
6. Bangert M, Schlaug G. Specialization of the spezialized in features of external brain morphology. *Eur J Neurosci*. 2006;24(6): 1832-1834.
7. Münte TF, Altenmüller E, Jäncke L. The musician's brain as a model of neuroplasticity. *Nat Rev Neurosci*. 2002;3(6):473-478.
8. Altenmüller E, Schlaug G. Music, brain, and health: exploring biological foundations of music's health effects. In: MacDonald R, Kreutz G, Mitchell L, eds. *Music, Health, and Wellbeing*. Oxford, England: Oxford University Press; 2012:12-24.
9. Amunts K, Schlaug G, Jäncke L, et al. Motor cortex and hand motor skills: structural compliance in the human brain. *Human Brain Mapp*. 1997;5(3):206-215.
10. Gaser C, Schlaug G. Brain structures differ between musicians and non-musicians. *J Neurosci*. 2003;23(27):9240-9245.
11. Schlaug G, Jäncke L, Huang Y, Steinmetz H. Increased corpus callosum size in musicians. *Neuropsychologia*. 1995;33(8): 1047-1055.
12. Halwani GF, Loui P, Rüber T, Schlaug G. Effects of practice and experience on the arcuate fasciculus: comparing singers, instrumentalists, and non-musicians. *Front Psychol*. 2011;2:156. doi: 10.3389/fpsyg.2011.001561.
13. Bengtsson SL, Nagy Z, Skare S, Forsman L, Forssberg H, Ullen F. Extensive piano practicing has regionally specific effects on white matter development. *Nat Neurosci*. 2005;8(9):1148-1150.
14. Hutchinson S, Lee LH, Gaab N, Schlaug G. Cerebellar volume: gender and musicianship effects. *Cereb Cortex*. 2003;13(9): 943-949.
15. Hodges DA. Psychophysiological measures. In: Juslin PN, Sloboda JA, eds. *Handbook of Music and Emotion*. Oxford, England: Oxford University Press; 2010:279-311.
16. Kreutz G, Murcia CQ, Bongard S. Psychoneuroendocrine research on music and health. An overview. In: MacDonald R,

Kreutz G, Mitchell L, eds. *Music, Health and Wellbeing*. Oxford, England: Oxford University Press; 2012:457-476.

17. Keitz M, Martin-Soelch C, Leenders KL. Reward processing in the brain: a prerequisite for movement preparation? *Neural Plast*. 2003;1(1-2):121-128.
18. Evers S, Suhr B. Changes of the neurotransmitter serotonin but not of hormones during short time music perception. *Eur Arch Psychiatry Clin Neurosci*. 2000;250(3):144-147.
19. Blood AJ, Zatorre RJ. Intensely pleasurable responses to music correlate with activity in brain regions implicated in reward and emotion. *Proc Natl Acad Sci U S A*. 2001;198(20):11818-11823.
20. Menon V, Levitin DJ. The rewards of music listening: response and physiological connectivity of the mesolimbic system. *Neuroimage*. 2005;28(1):175-184.
21. Salimpoor VN, Benovoy M, Larcher K, Dagher A, Zatorre RJ. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. *Nat Neurosci*. 2011;14(2): 257-262.
22. Karabanov A, Cervenka S, de Manzano O, Forssberg H, Farde L, Ullén F. Dopamine D2 receptor density in the limbic striatum is related to implicit but not explicit movement sequence learning. *Proc Natl Acad Sci*. 2010;107(16):7574-7579.
23. Salimpoor VN, van den Bosch I, Kovacevic N, McIntosh AR, Dagher A, Zatorre RJ. Interactions between the nucleus accumbens and auditory cortices predict music reward value. *Science*. 2013;340(6129):216-219.
24. Wan CY, Rüber T, Hohmann A, Schlaug G. The therapeutic effects of singing in neurological disorders. *Music Percept*. 2010;27(4):287-295.
25. Wade DT, Hewer RL, David RM, Enderby PM. Aphasia after stroke: natural history and associated deficits. *J Neurol Neurosurg Psychiatry*. 1976;49(1):11-16.
26. Heiss WD, Kessler J, Thiel A, Ghaemi M, Karbe H. Differential capacity of left and right hemispheric areas for compensation of poststroke aphasia. *Ann Neurol*. 1999;45(4):430-438.
27. Rosen HJ, Petersen SE, Linenweber MR, et al. Neural correlates of recovery from aphasia after damage to left inferior frontal cortex. *Neurology*. 2000;55(12):1883-1894.
28. Heiss WD, Thiel A. A proposed regional hierarchy in recovery of post-stroke aphasia. *Brain Lang*. 2006;98(1):118-123.
29. Hillis AE. Aphasia: progress in the last quarter of a century. *Neurology*. 2007;69(2):200-123.
30. Gerstman HL. A case of aphasia. *J Speech Hear Disord*. 1964;29: 89-91.
31. Schlaug G, Marchina S, Norton A. From singing to speaking: why patients with Broca's aphasia can sing and how that may lead to recovery of expressive language functions. *Music Percept*. 2008; 25(4):315-323.
32. 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. *Ann N Y Acad Sci*. 2009;1169:385-394.
33. Geschwind N. Current concepts: aphasia. *N Engl J Med*. 1971; 284(12):654-656.
34. Keith RL, Aronson AE. Singing as therapy for apraxia of speech and aphasia: report of a case. *Brain Lang*. 1975;2(4):483-488.
35. Albert ML, Sparks RW, Helm NA. Melodic intonation therapy for aphasia. *Arch Neurol*. 1973;29(2):130-131.
36. Sparks RW, Holland AL. Method: melodic intonation therapy for aphasia. *J Speech Hear Disord*. 1976;41(3):287-297.
37. Schlaug G, Norton A, Marchina S, Zipse L, Wan CY. From singing to speaking: facilitating recovery from nonfluent aphasia. *Future Neurol*. 2010;5(5):657-665.
38. Goodglass H, Kaplan E. *Boston Diagnostic Aphasia Examination*. 2nd ed. Philadelphia, PA: Lea & Febiger; 1983.
39. Bonakdarpour B, Eftekharzadeh A, Ashayeri H. Preliminary report on the effects of melodic intonation therapy in the rehabilitation of Persian aphasic patients. *Iran J Med Sci*. 2000;25(3-4): 156-160.
40. Schneider S, Schönle PW, Altenmüller E, Münte TF. Using musical instruments to improve motor skill recovery following a stroke. *J Neurolol*. 2007;254(10):1339-1346.
41. Wilson SJ, Parsons K, Reutens DC. Preserved singing in aphasia: a case study of the efficacy of the Melodic Intonation Therapy. *Music Percept*. 2006;24(1):23-36.
42. Altenmüller E, Schneider S, Marco-Pallares PW, Münte TF. Neural reorganization underlies improvement in stroke induced motor dysfunction by music supported therapy. *Ann N Y Acad Sci*. 2009;1169:395-405.
43. Schneider S, Münte TF, Rodriguez-Fornells A, Sailer M, Altenmüller E. Music supported training is more efficient than functional motor training for recovery of fine motor skills in stroke patients. *Music Percept*. 2010;27(4):271-280.
44. Rojo N, Amengual J, Juncadella M, et al. Music-supported therapy induces plasticity in the sensorimotor cortex in chronic stroke: a single-case study using multimodal imaging (fMRI-TMS). *Brain Inj*. 2012;25(7-8):787-793.
45. Särkämö T, Tervaniemi M, Laitinen S, et al. Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. *Brain*. 2008;131(pt 3):866-876.
46. Thaut MH, Kenyon GP, Hurt CP, McIntosh GC, Hoemberg V. Kinematic optimization of spatiotemporal patterns in paretic arm training with stroke patients. *Neuropsychologia*. 2002;40(7): 1073-1081.
47. Van Vugt FT, Kuhn W, Rollnik JD, Altenmüller E. Random delay boosts musical fine recovery after stroke. Proceedings of ICMPC, August 2012, Thessaloniki, Greece.

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