

Music and the brain: neuromusicology

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ABSTRACT

Music may be considered a special type of language. In addition to performing a communicative function –particularly that of transmitting emotions– it includes artistic and cultural facets. Musical aptitudes have a substantial genetic component, and formal practice results in noticeable changes in the functional structure of specific regions of the brain (cerebellum, corpus callosum, motor cortex, planum temporale). The right hemisphere is associated with innate phenomena in music, especially the components of melody and timbre; the left hemisphere is associated with rhythm and other formal or analytical aspects. Conditions affecting musical ability are classified by the type of dysfunction they cause: deficits of perception and/or production, and total or partial dysfunction (melody, tone, timbre, rhythm, and notation). The emotional component may also be affected selectively. Musicogenic epilepsy, defined as reflex seizures triggered by the subject's listening to or playing a specific passage of music, is caused by a dysfunction of the superior temporal gyrus of the non-dominant hemisphere. It must be distinguished from paroxysmal songs or auditory seizures, phenomena in which the patient reports hearing a specific melody. Musician's dystonia is a specific type of motor control disorder which, given the presence of genetic predisposition and excessive and incorrect training, will result in distortion of the precise motor patterns that govern playing an instrument. Meanwhile, music therapy as a treatment alternative has delivered encouraging results.

KEYWORDS

Neuromusicology, amusia, task-specific dystonia, epilepsy, absolute pitch, music therapy

Introduction

According to Greek mythology, the Muses were the deities that provided the inspiration for artistic activities. In addition to inspiring mortals, they also entertained the gods and therefore provided a sort of umbilical cord between the human and the divine. This link to the divine, that which distinguishes mankind from the animals and, in a sense, immortalises us, is none other than art. The word 'music' refers to an activity involving or related to the Muses.

According to its traditional definition, music is the art of arranging sound and silence in time. Sound and silence are omnipresent in nature, but in music, these elements imply or convey a purpose: music is a language used to evoke, express, and even intensify emotions.¹⁻⁴ In mentioning such concepts as language, emotions, inten-

tionality, and art, we recognise that the function of music has a social dimension.

Acoustics is the science that studies sound, and sounds are composed of one or more tones. Sound is the result of the vibration of an elastic body, and it is transmitted by air at a velocity of 340 m/s. When the periodic curve produced by a vibrating elastic body is irregular, the sound in question is known as noise.² The number of vibrations per second, measured in Hertz (Hz), is what makes a tone lower or higher-pitched (on a scale from low to high frequency). The human ear can perceive pitches ranging from 16 Hz (the C beginning the lowest octave on a piano) to 16 000 Hz (the C note of the 10th octave, or C10). A modern 'A' tuning fork produces a tone of 445 Hz. A triangle can produce a pitch of 16 000 Hz; a trumpet, 9000 Hz; a violin, 8000 Hz, and a flute, 4000 Hz.² Sound intensity (from *piano* to *forte*) depends on the

mass of the vibrating body and on the amplitude of the vibration. Timbre is the 'tone colour' peculiar to the instrument emitting the sound. It depends on a fundamental pitch and an array of pitches of different frequencies that are all multiples of the fundamental. The combination and procession of pitches rising, falling, and repeating produces a sense of tension that intensifies as pitches rise and relaxes as they descend. This procession, known as melody, is perceived as a contour that oscillates and advances. Subtle loss in discrimination between tones may not affect an individual's perception of melody. Rhythm refers to the succession of tones expressed in units of time and subdivided into strong (accented) beats and weak beats. Rhythm and melody are the fundamental pillars of music.

Music remains closely related to other artistic manifestations including dance, literature, painting, architecture, cinema, and even philosophy and cosmology.² The brain is what allows us to generate, perceive, and enjoy music, and the act of experiencing music is beneficial to cerebral development.⁵ Neuromusicology provides a window into the study of the brain and its plasticity.

This study reviews current knowledge in the field of neuromusicology. To this end, we performed a literature search of the databases Medline and Science Direct (keywords: brain and music, amusia, musicogenic epilepsy, task-related dystonia, music therapy).

Development

Neurology's traditional method for locating lesions, based on the deficits in a specific brain function that have been detected and mapped out using the patient's medical history and clinical findings, yields only scarce results when it comes to musical impairment. Until quite recently, only a few cases in professional musicians had been studied in detail. However, the field of neuromusicology is currently developing at an uncommon rate thanks to such functional neuroimaging techniques as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), plus neurophysiological techniques including evoked potentials and magnetoencephalography (MEG). This research is yielding data that is highly relevant for understanding such important topics as brain plasticity and connectivity. A new and productive avenue is opening up in the field of the neurosciences.⁶

By establishing parallels between music and prototypical language, we can classify disorders affecting musical

function as congenital or acquired; as interpretation and production disorders; or as alterations in reading and writing music.

Cerebral processing of musical language

A love of consonant sounds and regular tempos, combined with the interaction of multiple sensory stimuli, is a common element in the development of music by people around the world.^{7,8} Each culture would later develop scales, metre, and elements of pitch. Lastly, study and practice would facilitate playing, reading, and gathering an explicit knowledge of music. Musicality as a higher cognitive ability is highly dependent on a genetic factor complemented by learning, especially the study of its complex abstract rules. Studies have shown that 6-month-old babies like consonant intervals more than dissonant ones, and they tend to vocalise in scales with tones and semitones.^{9,10}

It has also been shown that experience produces substantial modifications in the cerebral systems related to music. The right hemisphere is responsible for the innate approach to the phenomenon of music,¹¹ especially its melodic component. In trained musicians, however, the left hemisphere also comes into play to integrate an additional analytical component.¹²⁻¹⁸ The above has been demonstrated by fMRI studies that have also found that trained musicians display certain particularities. As stated, they exhibit more use of the left hemisphere, without any decrease in right hemisphere involvement, such that their left temporal dominance is less marked than in the general population. Secondly, they display activation of a smaller area of the cortical surface when performing a specific task; and thirdly, the anterior regions of the corpus callosum and cerebellum are larger in trained musicians.^{19,20} These findings are coherent with other results from animal models showing microstructural changes (increase in the numbers of synapses and glial cells, and in capillary density) in both the cerebellum and the primary motor cortex after repeated exercises of a specific motor paradigm. MEG studies have shown that professional musicians experience a peculiar phenomenon by which cerebral response to notes played by their instruments is 25% higher than in neutral subjects.²¹

It is currently believed that musical perception involves both hemispheres, although we have observed cases of aphasia caused by lesion to the dominant hemisphere without any accompanying amusia. There are docu-

mented cases of musicians with total aphasia who were yet able to continue playing and composing music, and of other patients with pure forms of impaired perception of melody.²²⁻²⁴ One of the most striking examples of the dissociation between musical and language abilities is provided by patients with Broca's aphasia, who are able to sing fluently. Such cases are not rare. Transcortical magnetic stimulation of the left temporal lobe temporarily impedes speaking, but not singing.²⁵ Maurice Ravel presented symptoms of progressive aphasia with alexia, agraphia, and ideomotor apraxia; his musical ideation, however, remained intact, despite his inability to dictate or write music.²⁶ In cases of frontal lobe dementia in which the non-dominant hemisphere is initially affected, doctors have described amusia and dysprosody. This constitutes a type of musical reflection of primary progressive aphasia that depends on impairment of the dominant hemisphere.²⁷ In turn, writing music seems to depend on the dominant parietal lobe,²⁸ although an fMRI study showed that the right temporal-occipital region could play a decisive role in translating pitch notation to a keyboard.²⁹ Ian McDonald, well known for his studies of multiple sclerosis and also an excellent pianist, described his own particular case of musical alexia which arose due to an ischaemic injury in the non-dominant angular gyrus.³⁰ Another case study reported selective loss of the ability to perceive the timbre of keyed and percussion instruments following an ischaemic lesion to the right temporal lobe that affected the superior and medial temporal gyri and part of the insula.³¹

In some cases in which brain lesions have caused profound changes in the perception of rhythm, pitch, and melody, the patient is still able to perceive the emotional element of music, whereas the opposite occurs in other cases.³²⁻³⁴ One study examined two patients who had been professional musicians, one with Alzheimer disease and the other with semantic dementia. It clearly showed that the first patient had lost the ability to recognise compositions and musical notation, but was still able to recognise instruments by their timbre and experience emotion through music. Abilities were reversed in the second patient.³⁵ This example provides proof that the emotional element of music is processed independently from other elements. PET studies have shown that unpleasant music lowers activity in the orbitofrontal cortex and anterior cingulate gyrus and increases activity in the precuneus and right parahippocampal gyrus.³⁶ Circuits related to the reward

system are involved in the pleasure we experience when listening to some types of music.^{37,38} Functional MRI studies indicate that dissonant (unpleasant) music activates the amygdala, hippocampus, parahippocampus, and temporal poles. These structures are involved in processing stimuli with a negative emotional valence. In turn, pleasant music activates the inferior frontal gyrus, superior insula, ventral striatum, and Rolandic operculum.³⁹ In some cases of dementia, generally frontotemporal dementia, patients may experience addictions to different types of music or changes in their taste in music.^{40,41}

Pitch, timbre, rhythm, melody, and the emotional response triggered by music all seem to have different cerebral localisations. Timbre is fundamentally processed and perceived in the right hemisphere, whereas melody is processed in both hemispheres and rhythm and sequential elements are received by the left hemisphere, according to PET studies.¹⁵ The right auditory cortex plays a major role in pitch perception.⁴² Regarding melodic processing, it seems that the right hemisphere focuses more on contour, whereas the left hemisphere detects pitch intervals.^{43,44}

The sensation of swing may be defined as an urge, in response to music, to sway and move (anything from tapping a foot, swaying at the waist, or waving an arm to dancing). This is a specific type of emotion awakened by the rhythmic element in music. Another phenomenon related to the emotional component of sublimely enjoyable music is called 'goosebumps' or 'shivers down the spine', and some people experience these sensations when they listen to certain types of music. Both phenomena are derived from a pleasurable experience with music in which the reward system is activated. As such, their onset and significance differ from those of other emotions. This situates musical pleasure in the same category as pleasure arising from sexual activity, food, and social interaction.⁴⁵

Neurological illnesses may affect the musical function and produce positive symptoms (epilepsy, hallucinations, synaesthesia), or negative symptoms. The latter can be classified as receptive amusia, expressive amusia, or impairment affecting specific components of musical language (pitch, timbre, rhythm, melody, harmony, notation, emotional response).⁴⁶ Examinations for patients presumed to have musical processing impairment due to a brain injury cannot be standardised. Knowledge of music and musical ability vary enor-

mously between mere music lovers and professional musicians, and even between singers, instrumentalists, and conductors. On the other hand, not all neurologists have sufficient musical knowledge to tackle this problem. The Montreal Battery of Evaluation of Amusia is a useful tool for investigating amusia, but it is used only infrequently in clinical practice.⁴⁷

Congenital amusia and absolute pitch

Individuals with congenital amusia are unable to recognise and distinguish between very familiar melodies; similarly, they cannot tell which of two successive pitches is higher. Famous confirmed cases of amusia include Sigmund Freud and Ernesto 'Che' Guevara. Studies by I. Peretz et al.⁴⁸⁻⁵⁰ show that subjects with congenital amusia, regardless of exposure to formal studies in music, present severe deficits not only in processing pitch variations, but also in melodic recognition, singing ability, and the ability to copy simple rhythmic patterns. These individuals have no difficulty recognising environmental sounds and they display normal speech production, including prosody, which clearly distinguishes them from patients with congenital aphasia. The authors mentioned above believe that the underlying deficiency in congenital amusia is in processing of pitch variations. As in the case of dyslexia, this deficiency has a hereditary basis. Neurophysiological studies have demonstrated an abnormal brain response in N2-P3; following a change in the pitch of a sound, this response presented with a latency of 200 ms, and it was more right-lateralised.⁵⁰ Authors from the same Canadian team recently attributed amusia to a specific and localised neuronal migration disorder of the non-dominant hemisphere (increased thickness of the auditory cortex and inferior frontal gyrus).^{51,52}

One definition of absolute pitch (or perfect pitch) is the ability to identify one pitch without using a second as a reference. This definition applies to passive absolute pitch, whereas individuals with active absolute pitch are able to sing on any pitch without using another reference tone. The frequency of absolute pitch in the general population is one case in 1500 to 10 000 subjects. We know that this ability is more common among women and tends to run in families. Furthermore, it can be detected among young children and it is often associated with learning disabilities, as J. Profita concluded based on his research.⁵³ Profita studied violin and piano at Juilliard in New York before attending medical school, and he exhibited this trait. We

have already mentioned that pitch perception occurs in the right hemisphere, but evidence from subjects with absolute pitch also indicates involvement of the left hemisphere. A professional violinist with absolute pitch lost that ability after a left middle cerebral artery stroke, but was able to retain relative pitch. PET studies performed by Zatorre et al.⁵⁴ have demonstrated activation of a posterior dorsolateral area of the left frontal lobe in subjects with absolute pitch. Studying and playing music at a young age favour the development of absolute pitch, but this alone is not sufficient, nor is it even strictly necessary.⁵⁵ Absolute pitch is more prevalent among patients with Williams syndrome, who have special musical abilities (they often begin playing at a young age), in addition to good face recognition and language skills. In contrast, they exhibit difficulty with visuospatial tasks, mathematics, and abstract thought; they typically have overall learning disability and a lower IQ.^{56,57}

Music and epilepsy

When a patient's seizures are triggered exclusively by a specific type of music, a single instrument, a voice, or even by the patient himself singing a particular song, these seizures are known as musicogenic epilepsy. This entity can be considered a special type of reflex epilepsy that may be either idiopathic or else the result of a precise structural brain lesion. In musicogenic epilepsy, music will often induce a state of emotional tension before triggering the seizure. The epileptogenic focus is typically located in the right temporal lobe.⁵⁸ In addition to the seizures occurring in musicogenic epilepsy, we also find partial seizures characterised by musical hallucinations (songs, orchestral melodies, voices) and seizures during which the patient will sing automatically. The focus is usually located on the upper temporal gyrus, especially on the right side. One case study described a temporary loss in pitch perception caused by transitory ischaemic attacks that might be mistaken for seizures.⁵⁹

People with hearing loss may experience musical hallucinations due to cortical sensory deprivation.⁶⁰ The causes of musical hallucinations are diverse, however, and they include a long list of drugs (quinine, imipramine, phenytoin, propranolol).⁶¹

Task-specific dystonia in musicians

The brain of a professional musician will exhibit structural and functional peculiarities. Melatonin and corti-

cortropin (ACTH) are directly associated with musical talent, whereas testosterone levels display an inverse association. Listening to music stimulates the secretion of oxytocin, a hormone that strengthens mother-child and adult pair bonds, and even social and group relationships.^{5,62}

Focal dystonias related to specific motor paradigms used in playing music (task-specific dystonia) are significantly frequent and they are extremely disabling for the musicians who suffer from them. Numerous types of dystonia have been described in musicians who play very different instruments (strings, keyboard, percussion, woodwinds, brass, etc.). The problem may be restricted to a limb, or it may even affect the facial musculature. While the pathogenic mechanism is not precisely known, it is thought that an underlying genetic predisposition, coupled with excessive and perhaps improper practising that compromises the peripheral nervous system, could result in altered function of the central circuits that control these specific motor actions. The cortical activation patterns in such cases display regression and are almost comparable to those of an amateur musician in that they show involvement of a larger part of the cortex.⁶³⁻⁶⁵

Music therapy

The Mozart effect (enhancement of certain cerebral functions, including visuospatial abilities, as a result of listening to that composer's works) is short-lived, with any benefits lasting no more than a few minutes.⁶⁶⁻⁶⁸ Music as treatment is an elitist therapy that is not widely used, even though experimental data point to biochemical changes in the brain, including increased dopaminergic transmission.⁶⁹ This therapy may be useful in such entities as attention deficit hyperactivity disorder, dementia, Parkinson's disease, epilepsy, and numerous emotional disorders. It may also lessen the episodic anxiety many patients experience before or during such procedures as catheterisations and endoscopies.⁶⁹⁻⁷² One study, carried out in stroke patients, showed that subjects who listened to their favourite music at least one hour daily displayed improvements in attention and mood.⁷³ Music therapy programmes have a similarly beneficial impact on anxiety and depression in patients hospitalised due to brain lesions caused by trauma.⁷⁴ In the elderly population, listening to music may mitigate hearing loss, facilitate comprehension, and delay cognitive decline.⁷⁵

Conclusions

Music as a language is specific to the human species. It allows us to convey our emotions, as well as being an expression of art and culture. Musical aptitudes have a substantial genetic component, and the formal practice undertaken by professional musicians results in noticeable changes in the functional structure of specific regions of the brain. The right hemisphere is associated with innate phenomena in music, and especially the components of melody and timbre; the left hemisphere is associated with rhythm and other formal or analytical aspects. The emotional component of music may be affected exclusively. Musicogenic epilepsy is a type of reflex epilepsy characterised by seizures precipitated by listening to or playing a specific piece of music. Task-specific dystonia is a particular of motor control disorder which, in the presence of genetic predisposition and excessive and incorrect training, will distort the precision motor patterns that govern playing an instrument. Lastly, music therapy seems to yield promising results.

References

1. Valls M. *Aproximación a la música*. Madrid: Salvat Editores; 1970.
2. Hamel F, Hürlimann M. *Enciclopedia de la música*. Barcelona: Grijalbo; 1970.
3. Marco T. *Historia cultural de la música*. Madrid: Ediciones Autor; 2008.
4. Arias M. *Música y neurología*. *Neurología*. 2007;22:39-45.
5. Lewis PA. Musical minds. *Trends Cogn Sci*. 2002;6:364-6.
6. Zatorre R, McGill J. Music, the food of neuroscience? *Nature*. 2005;434:312-5.
7. Wong K. Neanderthal notes: did ancient humans play modern scales? *Sci Am*. 1997;277:28-30.
8. Hannon EE, Trainor LJ. Music acquisition: effects of enculturation and formal training on development. *Trend Cogn Sci*. 2007;11:466-72.
9. Peretz I, Hyde KL. What is specific to music processing? Insights from congenital amusia. *Trends Cogn Sci*. 2003;7:362-7.
10. Schellenberg EG, Trehub SE. Natural musical intervals: evidence from infant listeners. *Psychol Sci*. 1996;7:272-7.
11. Kimura D. Left-right differences in the perception of melodies. *Q J Exp Psychol*. 1964;16:355-8.
12. Bever TG, Chiarello RJ. Cerebral dominance in musicians and nonmusicians. *Science*. 1974;185:537-9.
13. Mazziotta JC, Phelps ME, Carson RE, Kuhl DE. Tomographic mapping of human cerebral metabolism: auditory stimulation. *Neurology*. 1982;32:921-37.
14. Zatorre RJ, Evans AC, Meyer E. Neural mechanisms underlying melodic perception and memory for pitch. *J Neurosci*. 1994;14:1908-19.

15. Platel H, Price C, Baron JC, Wise R, Lambert J, Frackowiak RSJ, et al. The structural components of music perception. A functional anatomical study. *Brain*. 1997;120:229-43.
16. Tramo MJ. Biology and music. Music of the hemispheres. *Science*. 2001;291:54-6.
17. Brown S, Martínez MJ, Hodges DA, Fox PT, Parsons LM. The song system of the human brain. *Brain Res Cogn Brain Res*. 2004;20:363-75.
18. Koelsch S. Neural substrates of processing syntax and semantics in music. *Curr Opin Neurobiol*. 2005;15:207-12.
19. Schlaug G, Jaencke L, Huang Y, Steinmetz H. In vivo evidence of structural brain asymmetry in musicians. *Science*. 1995;267:699-701.
20. Schlaug G, Jaencke L, Huang Y, Steinmetz H. Increased corpus callosum size in musicians. *Neuropsychologia*. 1995;33:1047-55.
21. Peretz I, Zatorre RJ. Brain organization for music processing. *Annu Rev Psychol*. 2005;56:89-114.
22. Yamadori A, Osumi S, Masuhara S, Okubo M. Preservation of singing in Broca's aphasia. *J Neurol Neurosurg Psychiatry*. 1977;40:221-4.
23. Tzortzis C, Goldblum MC, Dang M, Forette F, Boller F. Absence of amusia and preserved naming of musical instruments in an aphasic composer. *Cortex*. 2000;36:227-42.
24. Sparr SA. Receptive amnesia in a trained musician. *Neurology*. 2002;59:1659-60.
25. Stewart L, Walsh V, Frith U, Rothwell J. Transcranial magnetic stimulation produces speech arrest but not song arrest. *Ann N Y Acad Sci*. 2001;930:433-5.
26. Alajouanine T. Aphasia and artistic realization. *Brain*. 1948;71:229-41.
27. Confavreux C, Croisile B, Garassus P, Aimard G, Trillet M. Progressive amusia and aprosody. *Arch Neurol*. 1992;49:971-6.
28. Midorikawa A, Kawamura M. A case of musical agraphia. *Neuroreport*. 2000;11:3053-7.
29. Schön D, Anton JL, Roth M, Besson M. An fMRI study of music sight-reading. *Neuroreport*. 2002;13:2285-9.
30. McDonald I. Musical alexia with recovery: a personal account. *Brain*. 2006;129:2554-61.
31. Kohlmetz C, Müller SV, Nager W, Munte TF, Altenmüller E. Selective loss of timbre perception for keyboard and percussion instruments following a right temporal lesion. *Neurocase*. 2003;9:86-93.
32. Peretz I, Brattico E, Tervaniemi M. Abnormal electrical brain responses to pitch in congenital amusia. *Ann Neurol*. 2005;58:478-82.
33. Peretz I, Gagnon L, Bouchard B. Music and emotion: perceptual determinants, immediacy and isolation after brain damage. *Cognition*. 1998;68:111-41.
34. Mazzoni M, Moretti P, Pardossi L, Vista M, Muratorio A, Puglioli M. A case of music imperception. *J Neurol Neurosurg Psychiatry*. 1993;56:322.
35. Omar R, Hailstone JC, Warren JE, Crutch SJ, Warren JD. The cognitive organization of music knowledge: a clinical analysis. *Brain*. 2010;133:1200-13.
36. Griffiths TD, Warren JD, Dean JL, Howard D. "When the feeling's gone": a selective loss of musical emotion. *J Neurol Neurosurg Psychiatry*. 2004;75:344-5.
37. Blood AJ, Zatorre RJ, Bermudez P, Evans AC. Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. *Nat Neurosci*. 1999;2:382-7.
38. Menon V, Levitin DJ. The rewards of music listening: response and physiological connectivity of the mesolimbic system. *Neuroimage*. 2005;28:175-84.
39. Koelsch S, Fritz T, Cramon DY, Müller K, Friederici AD. Investigating emotion with music: an fMRI study. *Hum Brain Mapp*. 2006;27:239-50.
40. Boeve BF, Geda YE. Polka music and semantic dementia. *Neurology*. 2001;57:1485.
41. Geroldi C, Metitieri T, Binetti G, Zanetti O, Trabucchi M, Frisoni GB. Pop music and frontotemporal dementia. *Neurology*. 2000;55:1935-6.
42. Tramo M, Shah GD, Braida LD. Functional role of auditory cortex in frequency processing and pitch perception. *J Neurophysiol*. 2002;87:122-39.
43. Peretz I. Processing of local and global information by unilateral brain-damaged patients. *Brain*. 1990;113:1185-202.
44. Peretz I, Kolinsky R. Boundaries of separability between melody and rhythm in music discrimination: a neuropsychological perspective. *Q J Exp Psychol A*. 1993;46:301-25.
45. Morten P, Krigenbalch ML. The pleasure of music. In: Krigenbalch ML, Berridge KC, editors. *Pleasures of the brain*. New York: Oxford University Press; 2010. p. 255-69.
46. Brust JC. Music and the neurologist. A historical perspective. *Ann N Y Acad Sci*. 2001;930:143-52.
47. Peretz I, Champod AS, Hyde KL. Varieties of musical disorders. The Montreal Battery of evaluation of amusia. *Ann N Y Acad Sci*. 2003;999:58-75.
48. Ayotte J, Peretz I, Hyde K. Congenital amusia: a group study of adults afflicted with a music-specific disorder. *Brain*. 2002;125:238-51.
49. Peretz I. Brain specialization for music. New evidence from congenital amusia. *Ann N Y Acad Sci*. 2001;930:153-65.
50. Peretz I, Ayotte J, Zatorre RJ, Mehler J, Ahad P, Penhune VB, et al. Congenital amusia: a disorder of fine-grained pitch discrimination. *Neuron*. 2002;33:185-91.
51. Hyde KL, Zatorre RJ, Griffiths TD, Lerch JP, Peretz I. Morphometry of the amusic brain: a two-site study. *Brain*. 2006;129:2562-70.
52. Hyde KL, Lerch JP, Zatorre RJ, Griffiths TD, Evans AC, Peretz I. Cortical thickness in congenital amusia: when less is better than more. *J Neurosci*. 2007;27:13028-32.
53. Profita J, Bidder TG. Perfect pitch. *Am J Med Bioeth*. 1988;29:763-71.
54. Zatorre RJ, Perry DW, Beckett CA, Westbury CF, Evans AC. Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. *Proc Natl Acad Sci U S A*. 1998;95:3172-7.
55. Baharloo S, Johnston PA, Service SK, Gitschier J, Freimer NB. Absolute pitch: an approach for identification of genetic and nongenetic components. *Am J Hum Genet*. 1998;62:224-31.

56. Lenhoff HM, Perales O, Hickok G. Absolute pitch in Williams syndrome. *Music Perception*. 2001;18:491-503.
57. Levitin DJ, Cole K, Chiles M, Lai Z, Lincoln A, Bellugi U. Characterizing the musical phenotype in individuals with Williams syndrome. *Child Neuropsychol*. 2004;10:223-47.
58. Wieser HG, Hungerbuhler H, Siegel AM, Buck A. Musicogenic epilepsy: review of the literature and case report with ictal single photon emission computed tomography. *Epilepsia*. 1997;38:200-7.
59. Sidtis JJ, Feldmann E. Transient ischemic attacks presenting with a loss of pitch perception. *Cortex*. 1990;26:469-71.
60. Berrios GE. Musical hallucinations: a statistical analysis of 46 cases. *Psychopathology*. 1991;24:356-60.
61. Fernandez A, Crowther TR, Wieweg WV. Musical hallucinations induced by propranolol. *J Nerv Ment Dis*. 1998;186:192-4.
62. Fukui H. Music and testosterone: a new hypothesis for the origin and function of music. *Ann N Y Acad Sci*. 2001;930:448-51.
63. Pujol J, Rosset-Llobet J, Rosinés-Cubells D, Deus J, Narberhaus B, Valls-Solé J, et al. Brain cortical activation during guitar-induced hand dystonia studied by functional MRI. *Neuroimage*. 2000;12:257-67.
64. Brandfonbrener AG, Robson C. Review of 113 musicians with focal dystonia seen between 1985 and 2002 at a clinic for performing artists. *Adv Neurol*. 2004;94:255-6.
65. Rosset-Llobet J, Fàbregas S, Rosines-Cubells D, Narberhaus B, Montero J. Análisis clínico de la distonía focal en los músicos. Revisión de 86 casos. *Neurología*. 2005;20:108-15.
66. Thompson BM, Andrews SR. An historical commentary on the physiological effects of music: Tomatis, Mozart and neuropsychology. *Integr Physiol Behav Sci*. 2000;35:174-88.
67. Hughes JR. The Mozart effect. *Epilepsy Behav*. 2001;2:396-417.
68. Rauscher FH, Shaw GL, Ky KN. Listening to Mozart enhances spatial-temporal reasoning: towards a neurophysiological basis. *Neurosci Lett*. 1995;185:44-7.
69. Sutoo D, Akiyama K. Music improves dopaminergic neurotransmission: demonstration based on the effect of music on blood pressure regulation. *Brain Res*. 2004;1016:255-62.
70. Kneafsey R. The therapeutic use of music in a care of the elderly setting: a literature review. *J Clin Nurs*. 1997;6:341-6.
71. Koger SM, Chapin K, Brotons M. Is music therapy an effective intervention for dementia? A meta-analytic review of literature. *J Music Ther*. 1999;36:2-15.
72. Hamel WJ. The effect of music intervention on anxiety in the patient waiting for cardiac catheterization. *Intensive Crit Care Nurs*. 2001;17:279-85.
73. Sarkamo T, Tervaniemi M, Laitinen S, Forsblom A, Soynila S, Mikkonen M, et al. Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. *Brain*. 2008;131:866-76.
74. Guétin S, Soua B, Voiriot G, Picot MC, Hérisson C. The effect of music therapy on mood and anxiety-depression: an observational study in institutionalised patients with traumatic brain injury. *Ann Phys Rehabil Med*. 2009;52:30-40.
75. Alain C, Zendel BR, Hutka S, Bidelman GM. Turning down the noise: the benefit of musical training on the aging auditory brain. *Hear Res*. 2014;308:162-73.