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# Neurobiology of Music and its Application in Dementia

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Funding: No specific funding was received for this work.Potential competing interests: No potential competing interests to declare.

## Abstract

Therapeutic music proves to be an excellent alternative to improve the mental performance of elderly residents in longterm care facilities, as it is a non-invasive activity that has physiological and psychological benefits, improving the ability to interact in society and decreasing the individual's stress. This study aims to show the relevance of music as a complementary therapy in the care of the elderly living in geriatric institutions. In this analysis, it was possible to observe several benefits of therapeutic music, such as increased individual comfort, effect on pain, decrease in systolic blood pressure and anxiety, sleep regulation, better social interaction, and reduction of the severity of symptoms of pharmacotherapy increasing the comfort level of these patients. Therefore, its multiple benefits, ease of use, and lack of side effects corroborate that this technique is being used increasingly.

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Keywords: Elderly; Music therapy; Dementia; Aged; Nursing homes; Geriatric.

## Introduction

Music has historically been seen as an ideal tool for exploring emotions, especially since music can constantly evoke strong emotions between people <sup>[1]</sup>. However, until now, very few functional imaging studies have explored emotion with music. A study examined the neurophysiological correlates of the pleasant/unpleasant emotional dimension with

harmonised melody sequences. The stimuli varied in their degree of (permanent) dissonance and were consequently perceived as more or less unpleasant (stimuli with the highest degree of permanent dissonance were rated as more unpleasant by the test subjects). The stimuli were computer-controlled with no musical expression (i.e., no dynamics or agogic). Therefore, these stimuli were suitable for inducing unpleasant rather than pleasant emotions. Increasing levels of distress were observed in stimuli correlated with activations of the right parahippocampal gyrus (and regions of the precuneus), and decreasing levels of distress correlated with activations of the orbitofrontal and frontopolar cortex, as well as the subcallosal cingulate cortex <sup>[2]</sup>. Another study examined changes in regional cerebral blood flow (rCBF) during particularly pleasant emotional experiences when listening to music (so-called "chills") <sup>[3]</sup>. The test subjects listened to their favourite music (as a control condition, they listened to the favourite music of another test person). During the "chills," changes in rCBF in the islet area, right orbitofrontal cortex, right amygdala, and prefrontal cortex were measured, suggesting that these brain regions are involved in the process of rewarding and emotion are involved.) A functional magnetic resonance tomography (fMRI) study showed that emotion was induced by pleasant and unpleasant musical stimuli [4]. Unlike the study by Blood et al., the pleasant musical stimuli were not computer-controlled sounds but natural pieces of music (happy instrumental dance pieces recorded from commercially available CDs). The unpleasant stimuli were electronically manipulated, cacophonous (permanently dissonant) counterparts to these pieces of music. In addition, the stimuli used here should not only induce unpleasant effects but also pleasant emotions (as a response to upbeat music). While listening to unpleasant music, activations of the hippocampus, parahippocampal gyrus, and amygdala (in both hemispheres) were measured. The inverse (pleasant) contrast showed activations of the anterosuperior islet and the anterior frontolateral cortex in the right hemisphere, as well as bilateral activations of the Heschl gyrus and the rolandic operculum (in the central operculum/subcentral gyrus, activity changes were thus measured, on the one hand, in limbic and paralimbic structures (amygdala, hippocampus, parahippocampal gyrus, and anterior islet); These structures are known to be involved in emotional processing <sup>[2][3]</sup>. Current data show that the emotional processing of music can activate a network that encompasses these numerous structures <sup>[5]</sup>. Interestingly, the functional magnetic resonance imaging data from Koelsch et al. also showed strong bilateral activations in the area of Roland's operculum while listening to pleasant (but not unpleasant) music. In this area is the representation of the larynx, the representation of an effector (vowel) involved in producing vocalisations. The larynx contains the vocal cords, whose vibrations produce a vocal sound. The frequency of these vibrations determines the pitch of the vocal sound. Therefore, the available data show the production of vocal sounds (without accompanying motor activity) while listening to emotional musical stimuli previously composed and produced by other individuals. Intriguingly, there is an analogous phenomenon in the visual domain. In small, nonhuman primates, observation of an action leads to activation of premotor areas <sup>[6]</sup>. This activation is identical to the one observed in the actual execution of this action. The premotor cortex (PMC) is involved, among other things, in the preparation and execution of actions that are not necessarily performed by the motor system. This means that PMC neurons are active when an action is performed but also when it is simply presented or observed <sup>[7]</sup>. Physical reactions to music include effects on the vegetative nervous system. There is the possibility of vitalisation of the individual through the activity of the vegetative nervous system in connection with the integration of musical and non-musical information (mental, physical, and emotional), probably in the cortices of multimodal parietal association. The effects of music processing on the vegetative nervous system have so far been investigated by measurements of electrodermal activity

and heart rate <sup>[3][8]</sup>. Processes within the vegetative nervous system (and thus also vitalisation processes) influence processes within the immune system. The effects of music perception on the immune system are measured based on changes in the concentration of immunoglobulin A in saliva <sup>[9][10]</sup>. Interestingly, processes within the immune system are likely to be positively influenced by premotor activity when creating music <sup>[10]</sup>. The neural activities of the later stages of musical perception may be identical to those of the initial action planning stages <sup>[6][11]</sup>. Meanwhile, it has been shown that music perception can interfere with action planning, that just listening to piano pieces can lead to premotor activity of finger performances in pianists, and that only listening to music, even in so-called non-musicians. It can lead to premotor activity in the representation of the larynx <sup>[12][13]</sup>. In addition to the importance to the individual of action induction, the perception of music (rocking, clapping, dancing, or singing) is also likely to have social functions to create bonds between individuals in a group or even between individuals in different groups <sup>[14]</sup>. Interestingly, these evolutionarily beneficial social aspects of making music are accompanied by positive effects on the immune system. These positive effects possibly represent an important origin of cooperative and community music production evolution in human beings. In other words, our organism is designed so that community-oriented social activity regenerates a vital system of our organism, specifically the immune system.

#### Neuroanatomy of Music

The act of listening to music requires the involvement of specific well-differentiated neuroanatomical and neurophysiological processes. Both hemispheres play a fundamental role in the perceptual process. However, the right auditory cortex and a series of highly specialised neural networks undoubtedly play a fundamental role in recognising melodies and notes. In fact, there are areas in the brain that process various components of music, such as pitch, vibration, and harmony, while the cerebellum seems to be in charge of the rhythm <sup>[15]</sup>. The primary auditory cortex, specifically located in the temporal lobe, is responsible for processing auditory information. Music reaches the cochlea in the inner ear, travelling along the auditory nerve through the midbrain to synapse in the cochlear nucleus, from where it is directed to the medial geniculate body or auditory thalamus <sup>[16]</sup>. However, the emotional response is generated in the circuits and projections that run from the thalamus to the amygdala and the medial orbitofrontal cortex).

# Effects on Cognitive Functions and Dementia

Music possesses the property of generating emotional responses, such as the ability to activate reward systems similar to sexual stimuli or food <sup>[17]</sup>. It can also cause changes in the components of emotions and tendencies in activity, such as dancing, singing, clapping, or playing an instrument <sup>[18]</sup>. It also has a direct effect on the regulation of emotional stress since it reduces anxiety by distracting attention from aversive stimuli <sup>[19]</sup>. Furthermore, chronic pain is one of the most frequent and disabling problems of the elderly, resulting in loss of autonomy and social disconnection. Lack of independence increases the predisposition to diseases such as mood disorders, further increasing pain. Music has been shown to induce states of relaxation and distraction from the focus of pain, thereby decreasing anxiety and stress <sup>[20]</sup>. Music has a well-documented effect in relieving anxiety, depression, and pain in somatic diseases <sup>[21][22][23]</sup>. The

responses triggered by music in structures that provide dopaminergic input, such as the ventral tegmental area and the nucleus acumbens (part of the limbic system), as we will see later, suggest that music reduces pain by relieving anxiety and distracting attention from aversive stimuli, thus helping to cope with emotional stress <sup>[24]</sup>. The use of music in critically ill polytrauma patients reduces anxiety and pain levels, increasing the patient's well-being and improving the quality of care <sup>[25]</sup>.

There is evidence in studies of healthy subjects that listening to music that is enjoyable for them can. Temporarily improve performance in tests of temporal-spatial skills, attention skills, verbal fluency, and creativity <sup>[26][27][28]</sup>. Randomised controlled studies in patients with dementia have shown that the use of music therapy or music-based exercises improves cognition and verbal fluency globally <sup>[29][30]</sup>. However, many of these trials suffer from methodological problems, and it is impossible to conclude with certainty a benefit [31]. However, the quality of more recent studies has improved, and benefits have been observed in controlling agitation, mood, anxiety, and global cognitive function <sup>[32][33]</sup>. This study compared the standard of care in 89 patients with mild dementia to singing or listening to music sessions (weekly for 10 weeks in their home with caregivers). The authors found that cognitive function was maintained or improved in both groups in which music was used, in addition to an improvement in guality of life. An immediate post-intervention evaluation showed that music sessions improved overall cognition (measured with the Mini-mental Test), attention, and executive functions measured with a battery of frontal lobe function. The patients who received music were even more oriented at a 6-month follow-up. Patients with frontotemporal degenerative dementia tend to have more difficulty associating emotions with music than those with Alzheimer's, so the etiologic type of dementia may also determine the therapeutic response<sup>[32]</sup>. Musical memory is considered to be independent of other memory systems. This is reflected in the observation that in Alzheimer's disease, more than in other types of dementia, patients retain musical memory. Sacks noted that even very demented patients can become activated by listening to their favourite music <sup>[34]</sup>. It has been assumed that this is because areas of musical memory are affected little or only highly late in the neurodegenerative process. A study analysed 32 normal subjects with functional MRI exposed to unknown, newly known and long-known music and confirmed that the areas that encode the already known musical memory are the caudal anterior cingulate and the presupplementary motor area and also showed that these areas are the least affected in the pathological process of Alzheimer's <sup>[35]</sup>. With all, emphasis continues to be placed on the need for and in an individual, not group, approach, considering the patient's musical preferences.

# Effects of Music in Caring for Institutionalized Older Persons

Music may benefit people at all phases of life, from promoting the growth of close bonds between babies and their parents to offering necessary, sensitive, and compassionate palliative care near the end of life. It has been shown that singing to newborns, a widespread practice worldwide, has several positive effects, including enhancing mother-baby contact and lowering infant discomfort. Similarly, it has been noted that music helps older persons with senile dementia feel less agitated and anxious <sup>[36]</sup>. Living in a long-term institution brings with it several problems in the lives of aged persons, in which they may face physical and psychological disorders, such as suffering, social isolation and sadness, helplessness

and even depression, and predominantly cognitive impairment. In addition, the level of physical comfort is negatively affected due to issues such as chronic diseases, pain, and poor quality sleep <sup>[37]</sup>. One of the alternatives to improve this mental performance is found in music therapy, a healthcare activity that is described as a way of listening to music that has considerable effects on patients, affecting them physiologically and psychologically in a way that improves the ability to deal with people, makes them feel relaxed and takes them away from stressors <sup>[38]</sup>. Framed within the framework of non-pharmacological therapies, music is of great interest as a therapeutic tool complementary to pathologies that are difficult or limited to treat since it activates an extensive network of cognitive areas of the brain and generates structural changes in the brain <sup>[39]</sup>. For therapeutic music, several aspects must be considered, including the fact that people depend on their musical culture and that they benefit in different ways depending on the type of disease. From this, it is possible to enjoy several benefits that therapeutic music has, such as greater comfort for the individual, effect on pain, decrease in systolic blood pressure, anxiety and even reduce the severity of the adverse effects of drugs (usually highly polymedicated patients) simultaneously with the increase in the comfort level of these patients <sup>[37][38][39][40]</sup>. Something possible due to its ability to induce alpha waves in the brain, which are capable of causing relaxation and, with this, can lead to the decrease of negative feelings in depressive disorders. It can also trigger the release of endorphins, causing physiological responses, such as a decrease in blood pressure <sup>[37][38]</sup>. In addition, it has been seen that the effects of disturbed sleep architecture were comparable to hypnotic ones in patients with disturbed sleep architecture. On the other hand, it promotes the secretion of endogenous and natural analgesics in the body and, with a mood-stabilizing effect, reduces pain and anxiety and has a positive effect on cognition, proven by a randomised controlled trial <sup>[39][40]</sup>.

# Conclusion

Music therapy is a type of therapy that has been extensively researched and found to have numerous benefits. As an adjuvant therapy, it can be used in conjunction with other treatments to help improve patient outcomes. One of the most significant benefits of music therapy is its ability to improve cognition. Studies have shown that listening to music can enhance memory and attention, which can be particularly useful for patients with neurological conditions such as dementia. In addition to improving cognition, music therapy has also been found to provide comfort and reduce pain. Listening to music can stimulate the release of endorphins, which are natural painkillers. This can be particularly helpful for patients who are experiencing chronic pain or undergoing painful medical procedures. Another benefit of music therapy is its ability to lower blood pressure. Studies have shown that listening to music can help reduce systolic blood pressure, which can be particularly beneficial for patients with hypertension. Additionally, music therapy has been found to reduce the adverse effects of drugs and anxiety. It can provide a calming effect and help patients cope with the side effects of medication or the stress of medical procedures. One of the most compelling reasons to consider music therapy is its ease of use and lack of side effects. Unlike some other types of therapies, music therapy is non-invasive and does not require any special equipment or preparation. Additionally, no known side effects are associated with music therapy, making it a safe and effective treatment option for many patients. Finally, a deeper understanding of how the brain interacts with music could help us develop the clinical potential of music therapies even further. By exploring the neural mechanisms involved in music perception and enjoyment, we may be able to develop more targeted and effective music

interventions for specific patient populations.

# Other References

• Sloboda, J. A. (1991). Music structure and emotional response: Some empirical findings. Psychology of Music, 19(2), 110-120.

#### References

- <sup>^</sup>Krumhansl, C. L. (1997). An exploratory study of musical emotions and psychophysiology. Canadian Journal of Experimental Psychology, 51(4), 336-352.
- <sup>a, b</sup>Blood, A. J., Zatorre, R., Bermudez, P., & Evans, A. C. (1999). Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. Nature Neuroscience, 2(4), 382-387.
- <sup>a, b, c</sup>Blood, A., & Zatorre, R. J. (2001). Intensely pleasurable responses to music correlate with activity in brain regions implicated in reward and emotion. Proceedings of the National Academy of Sciences of the United States of America, 98 (20), 11818-11823.
- <sup>^</sup>Fuentes-Sánchez, N., Espino-Payá, A., Prantner, S., et al. (2023). Pleasant and unpleasant emotions induced by music: A meta-analysis of functional neuroimaging studies. Authorea. https://doi.org/10.22541/au.167648585.57480949/v1
- <sup>6</sup>Karmonik, C., Brandt, A., Elias, S., Townsend, J., Silverman, E., Shi, Z., & Frazier, J. T. (2020). Similarity of individual functional brain connectivity patterns formed by music listening quantified with a data-driven approach. International Journal of Computer Assisted Radiology and Surgery, 15(4), 703-713. https://doi.org/10.1007/s11548-019-02077-y
- 6. <sup>a, b</sup>Rizzolatti, G., & Craighero, L. (2004). The mirror-neuron system. Annual Review of Neuroscience, 27, 169-192.
- <sup>7</sup> Koelsch, S., Fritz, T., von Cramon, D. Y., Müller, K., & Friederici, A. D. (2006). Investigating emotion with music: An fMRI study. Human Brain Mapping, 27(3), 239-250.
- <sup>^</sup>Khalfa, S., Peretz, I., Blondin, J.-P., & Manon, R. (2002). Event-related skin conductance responses to musical emotions in humans. Neuroscience Letters, 328, 145-149.
- 9. <sup>^</sup>Hucklebridge, F., Lambert, S., Clow, A., Warburton, D. M., Evans, P. D., & Sherwood, N. (2000). Modulation of secretory immunoglobulin A in saliva; response to manipulation of mood. Biological Psychology, 53(1), 25-35.
- 10. <sup>a, b</sup>Kreutz, G., Bongard, S., Rohrmann, S., Hodapp, V., & Grehe, D. (2004). Effects of choir singing or listening on secretory immunoglobulin A, cortisol, and emotional state. Journal of Behavioral Medicine, 27(6), 623-635.
- 11. <sup>^</sup>Janata, P., Tillmann, B., & Bharucha, J. J. (2002). Listening to polyphonic music recruits domain-general attention and working memory circuits. Cognitive, Affective, & Behavioral Neuroscience, 2(2), 121-140.
- <sup>^</sup>Drost, U. C., Rieger, M., Brass, M., Gunter, T. C., & Prinz, W. (2005). Action-effect coupling in pianists. Psychological Research, 69(4), 233-241.
- 13. <sup>^</sup>Drost, U. C., Rieger, M., Brass, M., Gunter, T. C., & Prinz, W. (2005). When hearing turns into playing: Movement induction by auditory stimuli in pianists. The Quarterly Journal of Experimental Psychology Section A, 58(8), 1376-

1389.

- 14. <sup>^</sup>Hagen, E. H., & Bryant, G. A. (2003). Music and dance as a coalition signaling system. Human Nature, 14(1), 21-51.
- 15. <sup>C</sup>*Ustodio, N., & Cano-Campos, M. (2017). Effects of music on cognitive functions. Journal of Neuropsychiatry, 80(1),* 60-69.
- <sup>^</sup>Boso, M., Politi, P., Barale, F., & Emanuele, E. (2006). Neurophysiology and neurobiology of the musical experience. Functional Neurology, 21(4), 187-191.
- 17. <sup>^</sup>Buentello-García, R. M., Martínez-Rosas, A. R., & Alonso-Vanegas, M. A. (2010). Music and neurosciences. Archivos de Neurociencias, 15(3), 160-167.
- 18. <sup>^</sup>Koelsch, S. (2014). Brain correlates of music-evoked emotions. Nature Reviews Neuroscience, 15, 170-180.
- Sarkamo, T., Tervaniemi, M., & Latinen, S. (2008). Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. Brain, 131, 866-876.
- Mitchell, L. A., & MacDonald, R. A. (2006). An experimental investigation of the effects of preferred and relaxing music listening on pain perception. Journal of Music Therapy, 43, 295-316.
- Cassileth, B. R., Vickers, A. J., & Magill, L. A. (2003). Music therapy for mood disturbance during hospitalization for autologous stem cell transplantation: A randomized controlled trial. Cancer, 98, 2723-2729.
- Cepeda, M. S., Carr, D. B., Lau, J., & Alvarez, H. (2006). Music for pain relief. Cochrane Database of Systematic Reviews, 2006(4), CD004843.
- Siedliecki, S. L., & Good, M. (2006). Effect of music on power, pain, depression, and disability. Journal of Advanced Nursing, 54, 553-562.
- 24. <sup>^</sup>Sacks, O. (2006). The power of music. Brain, 129, 2528-2532.
- Contreras-Molina, M., Rueda-Núñez, A., Pérez-Collado, M. L., & García-Maestro, A. (2021). Effect of music therapy on anxiety and pain in the critical polytraumatised patient. Enfermeria Intensiva, 32(2), 79-87. https://doi.org/10.1016/j.enfie.2020.03.005
- Thompson, W. F., Schellenberg, E. G., & Husain, G. (2001). Arousal, mood, and the Mozart effect. Psychological Science, 12, 248-251.
- Schellenberg, E. G., Nakata, T., Hunter, P. G., & Tamoto, S. (2007). Exposure to music and cognitive performance: Tests of children and adults. Psychology of Music, 35, 5-19.
- <sup>^</sup>Thompson, R. G., Moulin, C. J., Hayre, S., & Jones, R. W. (2005). Music enhances category fluency in healthy older adults and Alzheimer's disease patients. Experimental Aging Research, 31, 91-99.
- 29. <sup>^</sup>Van de Winckel, A., Feys, H., De Weerdt, W., & Dom, R. (2004). Cognitive and behavioural effects of music-based exercises in patients with dementia. Clinical Rehabilitation, 18, 253-260.
- Brotons, M., & Koger, S. M. (2000). The impact of music therapy on language functioning in dementia. Journal of Music Therapy, 37, 183-195.
- <sup>^</sup>Vink, A. C., Bruinsma, M. S., & Scholten, R. J. (2011). Music therapy for people with dementia. Cochrane Database of Systematic Reviews, 2011(3), CD003477. https://doi.org/10.1002/14651858.CD003477.pub2
- 32. <sup>a, b</sup>Baird, A., & Samson, S. (2015). Music and dementia. Progress in Brain Research, 217, 207-235.
- 33. ^Sarkamo, T., Tervaniemi, M., Laitinen, S., Numminen, A., Kurki, M., Johnson, J. K., et al. (2014). Cognitive,

emotional, and social benefits of regular musical activities in early dementia: Randomized controlled study. The Gerontologist, 54, 634-650.

- 34. <sup>^</sup>Sacks, O. (2019). Musicophilia: Tales of music and the brain. Anagrama.
- 35. <sup>^</sup>Jacobsen, J.-H., Stelzer, J., Fritz, T. H., Chetelat, G., La Joie, R., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. Brain, 138, 2438-2450.
- <sup>^</sup>Rebecchini, L. (2021). Music, mental health, and immunity. Brain, Behavior, and Immunity Health, 18, 100374. https://doi.org/10.1016/j.bbih.2021.100374
- 37. <sup>a, b, c</sup> Pavlicevic, M., Tsiris, G., Wood, S., Powell, H., Graham, J., Sanderson, R., Millman, R., & Gibson, J. (2015). The 'Triple effect': Towards researching improvisational music therapy in dementia care homes. Dementia, 14(5), 659-679.
- 38. <sup>a, b, c</sup>Ugur, H. G., Aktaş, Y. Y., Orak, O. S., Saglambilen, O., & Avci, I. A. (2017). The effect of music therapy on depression and physiological parameters in older adults living in a Turkish nursing home: A randomized-controlled trial. Aging & Mental Health, 21(12), 1280-1286.
- <sup>a, b, c</sup> Wang, Q., Chair, S. Y., Wong, E. M. L., & Li, X. (2016). The effects of music intervention on sleep quality in community-dwelling elderly. Journal of Alternative and Complementary Medicine, 22(7), 576-584.
- 40. <sup>a, b</sup>Ergin, E., & Yücel, S. C. (2019). The effect of music on the comfort and anxiety of older adults living in a nursing home in Turkey. Journal of Religion and Health, 58(4), 1401-1414.