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MUSIC TRAINING AS A POTENTIAL NEUROPROTECTIVE AGENT

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SUMMARY

A substantial amount of evidence suggest that music training is a powerful means of plastic reorganization of brain structures. Musical training is accompanied by plastic rearrangement of the central nervous system and numerous studies converge in disclosing that the brain differs significantly between musicians and non-musicians. Music-dependent brain changes concern both the grey and the white matter so that musicians possess a neuronal network shaped by type and degree of individual expertise as well as a different connectome than non-musicians. It is reasonable to assume that these plastic changes can provide a more efficient configuration of the neural network and justify an impact on cognition and behaviour in all ages of life. Furthermore, a number of studies suggest the effectiveness of „neurological music therapy" in clinical practice. Based on available literature, music should be considered one of the main activity that can preserve the brain efficiency and can be proposed as a primary non pharmachological agent in promoting a neuroprotective lifestyle. Understanding the variables of musical training that can positively influence brain plasticity might be one of the most exciting and promising areas of future research.

Key words: *brain plasticity – neuroprotection - music training - music therapy - Mozart effect*

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INTRODUCTION

We humans are a musical species
no less than a linguistic one
Oliver Sacks

A substantial contribution to the definition of the peculiar characteristics of the musical experience was provided by neuroscience. Historically, the first issue addressed by the researchers had concerned the representation of music in the brain. From the earliest studies, clinical cases of selective impaired recognition of melodies ("amusia") as well as of preservation of musical abilities in aphasic patients were repeatedly described (Benton 1977). Such a dissociation between verbal and musical skills has been made famous by Luria (1965): the Russian composer Vissarion Shebalin, while severely aphasic, continued to compose at his previous level: in particular, his Fifth Symphony was judged by Shostakovitch a "brilliant creative work, filled with highest emotions [...] the creation of a great teacher" (Sacks 1985).

This clinical dissociation suggested that these two functions were processed in different brain hemispheres. However, the dichotomy between a linguistic left hemisphere and a musical right hemisphere proved to be a not sufficient model to account for the variety of observed phenomena. Better, clinical dissociations highlighted by neuropsychological studies suggested to think of music as a highly complex stimulus. According to Oliver Sacks (2008) "All of us (with very few exceptions) can perceive music, perceive tones, timbre, pitch intervals, melodic contours, harmony, and (perhaps most elementally) rhythm. We integrate all of these and "construct" music in our minds using many different parts of the brain. And to this largely unconscious structural appreciation of music is added an often intense and profound emotional reaction to music." So, the amusic disorders may selectively affect only some components such as only rhythm or musical instruments recognition or the ability to read or write music (Peretz & Coltheart 2003); they may involve only expressive or receptive abilities (for example, according to Alajouanine, 1948, Maurice Ravel, after presenting a permanent Wernicke aphasia, could no longer compose or perform music, but his capacity to perceive and appraise musical pieces remained intact); patient may be able to recognize other non-musical (human, animal, environmental) sounds as well as verbal prosody (Piccirilli et al. 2000); farther, the emotional dimension may be totally independent from the other components of the musical experience to the point that subjects who are unable to identify a piece of music can derive pleasure and satisfaction from his listening (Levitin 2006).

In short, in amusic patients, melody, harmony, rhythm, meter, memory, imagination, emotional response and so on may be compromised independently of each other. These different components are first analyzed independently and only later integrated. Thus, music elaboration requires an ongoing process of decomposition and recomposition of the different components (Peretz & Zatorre 2003).

From the anatomical point of view, these studies suggest that music is distributed throughout the brain (Peretz & Zatorre 2005). Typical musical experience recruits a highly complex neuronal network involving acoustic cortex (perception and analysis of tones), premotor and motor cortex (movement, dance, tapping, playing an instrument), sensory cortex (feedback from playing an instrument and dance), visual cortex (to read music, to look at your own performance or that of others), cerebellum (rhythm and tapping), hippocampus (memory of music and context), amygdala (emotional reaction and memory), nucleus accumbens (reward and motivation), corpus callosum (functional integration of the two hemispheres), prefrontal, orbitofrontal, cingulate cortex (executive functions, expectations, …). Music is a widespread function of the nervous system.

MUSIC AND BRAIN

Clinical, neurophysiological and neuroimaging studies suggest that music training influences the pattern of brain organization. For example, cortical representation of the digits of the left hand of string players was larger than that in controls (Elbert et al. 1995). This finding has been correlated with the peculiar use of the left hand of violin players. Brain differences, concerning both the grey and the white matter, had been repeatedly confirmed by a larger number of studies. In fact, the brain structural and functional organization differs significantly between musicians and non-musicians (Gaser & Schlaug 2003).

These investigations suggest that musical training is a powerful means for reorganization of brain structures (Schlaug 2015). It is important to note that these brain changes are not present in an undifferentiated way but correlate with a number of variables and characteristics linked to the personal history of each individual musician such as the kind of musical instrument played (for example the sensorimotor representation of the hands is different between violinists and pianists), the age of onset (with a detectable threshold at around seven years of age), the duration and intensity of training (which could differentiate the professional musicians and those who just plays for fun) and so on (Merret et al. 2013). These brain changes conform to the different individual experiences and had been interpreted as a result of practice-dependent neuronal plasticity.

Already the link between music skills and brain plasticity had been suggested by Santiago Ramon y Cajal who, in in his "Textura del Sistema Nervioso del Hombre y de los Vertebrados" (1904). wrote "[…] the work of a pianist […] is inaccessible for the untrained human, as the acquisition of new abilities requires many years of mental and physical practice. In order to fully understand this complicated phenomenon it is necessary to admit, in addition to the strengthening of pre-established organic pathways, the establishment of new ones, through ramification and progressive growth of dendritic arborizations and nervous terminals. […] Such a development takes place in response to exercise, while it stops and may be reversed in brain spheres that are not cultivated." (cited in Pascual-Leone 2003). Furthermore, Ramon y Cajal emphasized: "intellectual power, and its most noble expressions, talent and genius, do not depend on the size or number of cerebral neurons, but on the richness of their connective processes, or in other words on the complexity of the association pathways to short and long distances […] Professional dexterity, or rather the perfecting of function by exercise […] were explained by either a progressive thickening of the nervous pathways […] excited by the passage of the impulse or the formation of new cell processes (non-congenital growth of new dendrites and extension and branching of axone collaterals) capable of improving the suitability and the extension of the contacts, and even of making entirely new connections between neurons primitively independent" (Ramon y Cajal 1917).

At the present time, the prediction of Ramon y Cajal has been fulfilled: in fact, in the last twenty years, since neuroimaging studies may be repeated several times in the same subject, it became possible to assess any changes that occur over time and to document what happens in the brain during learning a skill. Many longitudinal studies showing differences between before and after a musical training support the idea of brain plasticity driven by musical exercise (Chang 2014). For example, six-year-old children, followed for approximately two years with a musical training, have a marked development of the right arcuate fasciculus and corpus callosum compared with children not exposed to any musical exercise (Hyde et al. 2009). Likewise, in naive subjects, listening to music activates auditory regions and playing a musical instrument activates sensorimotor regions; however, after a training, listening to music activates auditory but also sensorimotor regions and playing the piano activates sensorimotor but also auditory regions (Bangert & Altenmüller 2003). In other words, through the exercise, the two neural networks had been connected and have begun to operate in an integrated manner so that it becomes possible to say that for a musician to hear music is equivalent to playing it, and vice versa (Baumann et al. 2007).

Ultimately, a substantial amount of evidence converges to suggest that musical training improves the efficiency of the connections between different brain regions. As a result of this music-dependent plastic rearrangement of neuronal networks, musicians seem to possess a different connectome than non-musicians (Schmithorst & Wilke 2002).

It should be noted however that plasticity may be dysfunctional. One example of "aberrant" maladaptive plasticity is the focal hand dystonia, also known as the musician's cramp or Apollo's curse (Altenmüller et al. 2015). The functional neuroimaging studies have documented that the disorder is the result of a disorganization of the sensorimotor cortical representation of the fingers. It is an exercise-induced plasticity that leads to the incorrect functional connection between regions which should remain functionally distinct (Pujol et al. 2000). It would be a mistake to consider plasticity an exclusively beneficial phenomenon. For this reason, one of the most exciting areas of research is aimed at understanding of the variables that can positively influence brain plasticity, leading to a more efficient intra- and inter- hemispheric communication and a better functional integration between brain regions.

In this perspective, as suggested by Patel (2019), music may be considered "a transformative technology of the mind"

MUSIC AND COGNITION

The effect of music on brain plasticity raises the question of whether this effect can be used to enhance cognitive performance. Several investigations are in line with this hypothesis. Further, it becomes legitimate to ask whether these plastic changes have behavioral effects limited to specific domain (such as an improved sound discrimination and localization or greater ability in fine movements of the fingers), or a more general impact on cognitive function and behavior (Oechslin et al. 2013). After the outcry over the so-called "Mozart effect", the hypothesis that music learning implies an improvement in calculation and in verbal and spatial skills has been repeatedly subjected to methodologically rigorous verification but with contradictory results (Rauscher et al. 1995). Interestingly, a possible explanation for this discrepancy in the existing literature calls into question the differences between music listening and music playing: according to some observations, there are reasons to think that generalized cognitive effects can be obtained solely by an active learning to play an instrument (Miendlarzewska & Trost 2014). On the contrary results are more convincing with regard to the relations between learning music and improvement of verbal skills, including phonological awareness, verbal memory, fluency, naming, reading, as well as the ability to distinguish words in a noisy environment and to correctly pronounce a foreign language (Forgeard et al. 2008, Roden et al. 2012).

No less importance has the documentation of a positive influence on social competence of children and adolescents. As may be expected, music education promotes cooperation and socialization, and encourages the development of prosocial skills as establishing relationships, understand the rules and their role in a workgroup, do not use aggressive and violent behavior, taking the overall goal as their own and so on (Trainor et al. 2012). In support of this hypothesis, researchers have also drawn attention to the relationship between musicality and sociability in Williams syndrome (Levitin et al. 2004).

The interpretations of the relationship between music training and cognitive/behavioral improvement are not unique (Schellenberg 2012): the very complex multisensory integration required by musical training could cause a functional rearrangement that possibly can be usefully employed in other non-musical tasks (Piccirilli et al. 2021). Cognitive/behavioural improvement could be the direct result of the skills learned in the music (e.g. the exercise based on the melodic sequence might give rise to an equivalent better ability to master the language sequence) or be related to the needs of activating other cognitive processes to get learning (for example, the working memory and executive functions). Furthermore, music-listening and performance have been shown to affect human gene expression: music increases the activity of the genes involved in learning and memory and the production of the dopamine, while reducing the activity of genes associated with neurodegenerative diseases. Similar observations have led some researchers to think of musical experience as an example of epigenetic factor, that is an event able to modify the expression of individual genes, without modifying the genome. In the interaction between genes and environment, musical training appears to have all the basic features of an epigenetic modifier of brain structures (Nair et al. 2021).

The various processes induced by musical training may justify the protective benefits on cognition documented by current research. This is why, according to Paul Carvel (2000), "Music deserves to be mandatory second language of all schools in the world".

MUSIC AS A POTENTIAL NEUROPROTECTIVE AGENT

The hypothetical beneficial effect of music-induced plasticity can get support from the studies on the behavioral effects of musical training. These effects can be found in all ages of life and current studies provide consistent evidence for a protective influence of music on the developing as well as adult brain (D'Alessandro, 2016). For example, infants, who listen to music for the first time out of the womb, are able to recognize changes made to the original music and show brain activation very similar to that observed in adults (Perani et al. 2010); furthermore, it has been suggested that music therapy can play an important role in providing neuroprotection to premature infants (Standley 2012). In clinical practice, results of studies on the effectiveness of music therapy in different pathological conditions - such as autism, aphasia, neglect, parkinsonism, dementia, epilepsy, learning disorders - justified the introduction of the term "neurological music therapy" (Särkämö et al. 2016, Thaut et al. 2015). Indeed, while the whole brain reacts to music, its different areas may react to different components of music so that its various components can be used in a differentiated manner in relation to the type of pathological disorder. For example, in Parkinson's disease, rhythmic stimuli help to initiate movement and regulate a tread (Thaut et al. 2001). In epileptic subjects, the decrease in the seizure frequency had been related to the synchronization of biological rhythms with musical rhythms through the mechanism of entrainment (D'Alessandro et al. 2017, Lin & Yang 2015). Furthermore, musical training seems to protect aging individuals from age-related cognitive impairment ("Vivaldi effect") and dementia (Mammarella et al. 2007). There is noteworthy inter-individual variability in aging, a finding that has been interpreted in relation to the notion of reserve capacity: brain reserve is thought to be related to the structural characteristics of the individual nervous system, and cognitive reserve to more efficient configuration of the neural network (Stern 2009). In this view, the same number of neurons can form networks that are connected in diverse ways and a well-connected network can more easily mitigate the effects of aging. Thus, the same degree of brain atrophy may manifest itself in distinctly different ways in different individuals (Park & Reuter-Lorenz 2009). A growing body of literature indicates that interventions with the capacity to integrate multiple neural networks may be an effective way to enhance reserve capacity, as occurs with musical training. Through the musical exercise, neuronal networks begin to operate in an integrated manner (Piccirilli et al. 2019). It is reasonable to assume that differences in the efficiency of the configuration of neural networks induced by musical training may lead to the differences in brain-aging profiles found for musicians (Rogenmoser et al. 2017). Musical engagement seems to shape brain structures in such a way as to maintain better reserve capacity (Hanna-Pladdy & MacKay 2011). In a population-based twin study, playing a musical instrument was significantly associated with less likelihood of dementia and cognitive impairment, supporting suggestions that differences observed between musician and non-musician twins are likely due to musical training rather than pre-existing biological differences (Balbag et al. 2014).

Brain plasticity largely depends on experiences that occur over the course of a lifetime and continue throughout the individual's life if adequate incentives are available. Music could be an incentive of this kind and can be proposed as a non-pharmacological agent in promoting a neuroprotective lifestyle.

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All Authors have worked together and contributed equally to this manuscript.

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