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Neural plasticity: The substratum of music-based interventions in neurorehabilitation

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Abstract

Background—The plastic nature of the human brain lends itself to experience and training-based structural changes leading to functional recovery. Music, with its multimodal activation of the brain, serves as a useful model for neurorehabil-itation through neuroplastic changes in dysfunctional or impaired networks. Neurologic Music Therapy (NMT) contributes to the field of neurorehabilitation using this rationale.

Objective—The purpose of this article is to present a discourse on the concept of neuroplasticity and music-based neuroplasticity through the techniques of NMT in the domain of neurological rehabilitation.

Methods—The article draws on observations and findings made by researchers in the areas of neuroplasticity, music-based neuroplastic changes, NMT in neurological disorders and the implication of further research in this field.

Results—A commentary on previous research reveal that interventions based on the NMT paradigm have been successfully used to train neural networks using music-based tasks and paradigms which have been explained to have cross-modal effects on sensorimotor, language and cognitive and affective functions.

Conclusions—Multimodal gains using music-based interventions highlight the brain plasticity inducing function of music. Individual differences do play a predictive role in neurological gains associated with such interventions. This area deserves further exploration and application-based studies.

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Keywords

Neural plasticity; brain plasticity; music; music-based interventions; neurologic music therapy; neurological rehabilitation

1 Introduction

The proposition that the brain is a dynamic structure with the potential to re-organize and re-wire itself in response to intrinsic and extrinsic factors, stated in the early 1900 s (Brown & Sherrington, 1912), is now supported with rigorous scientific research and advanced imaging techniques. The organization, density and strength of neuronal connections in the central nervous system (CNS) have been found to change with learning and experience, or during recovery from injuries and degenerative conditions (Ripollés et al., 2016). This ability of the CNS to create adaptive changes in its morphological and functional aspects, involving neurogenesis, changes in neuronal connectivity and neurochemistry, has been referred to as neuroplasticity (Sasmita, Kuruvilla, & Ling, 2018). Neuroplasticity is broadly defined as the ability of the nervous system to respond to intrinsic as well as extrinsic stimuli by reorganising its structure, function and connections (Cramer et al., 2011). This is described at many levels from molecular to cellular systems to behaviour. A review of literature reveals three prominent patterns of neuronal systems with regards to neuroplasticity: a) neural structures that show little or no change despite extreme alterations of experience, e.g. complete deafness (Hofman & Swaab, 2002); b) certain neural systems that are sensitive to experience induced changes only within particular periods of time known as 'critical periods' (Stegemöller, 2014); c) neural circuits that remain modifiable throughout the life-span (Wan & Schlaug, 2010).

Various perspectives underlying the neuroscience of neuroplasticity (or brain plasticity) has contributed towards the development of therapeutic models guided by its role in functional recovery (Nahum, Lee, & Merzenich, 2013; Sharma, Classen, & Cohen, 2013). One such model is the neuroscientific based approach to utilising music as a therapeutic method for rehabilitating impaired functions.

In the current field of Cognitive Neuroscience, music is not only considered as a powerful tool to study the human brain, but it is becoming more and more evident that engaging in music, actively or passively and music-based interventions have helped us understand neuroplasticity, the veritable nature of the human brain much more in depth (Pacchetti et al., 2000; Reybrouck, Vuust, & Brattico, 2018). Music making and listening incorporates multiple sensory modalities and activates various neural pathways in the brain. This multimodal and multisensory attribute of music explains its role in mediating plastic changes in the nervous system. In the recent past, music-based interventions have been used to facilitate functional improvement through re-organization of neural circuitry in various conditions, e.g. stroke (Ripollés et al., 2016; Särkämö & Soto, 2012; Yakupov, Nalbat, Semenova, & Tlegenova, 2017) and traumatic brain injury (Berit Marie Dykesteen Vik, Skeie, & Specht, 2019).

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In the following sections, we seek to explore how music guides neuroplasticity via neural and neurochemical mechanisms. We also discuss how music has been used to develop certain therapeutic interventions aimed at rehabilitation of functions and comment on the research potential that the field of neuromusicology has to offer.

2 Pathways to music-related neuroplastic changes

Plastic changes in the CNS involve reorganization at both cortical and sub-cortical levels (Sharma et al., 2013). Relevant literature reveals that plasticity subserves multiple phenomena, either limited to early developmental years or operating across the lifespan. Several studies have reported structural differences between the brains of musicians and non-musicians (Wan & Schlaug, 2010). Musical training has been reported to induce structural changes in cortical areas involved in sensorimotor functions (Schlaug, 2001), auditory perception (N. Kraus & Chandrasekaran, 2010) and in white-matter tracts, such as the corpus callosum, the corticospinal tract and the arcuate fasciculus (Reybrouck et al., 2018) and higher grey matter density in the left anterior hippocampus (Groussard et al., 2010; Herdener et al., 2010). The following text discusses the prominent mechanisms underlying music-related plastic changes in the CNS.

2.1 Long-term potentiation (LTP) and long-term depression (LTD) induced changes

The classical explanation of neuroplasticity stems from Hebb’s theory of synaptic strengthening and remodelling by experience and as he had popularly stated “What fires together wires together” (Hebb, 1949). Bliss and Lømo (1973) were the pioneers that discovered how brief high-frequency stimulations enhanced the synaptic activity between two neurons causing persisting change in the strength of the synapse (T. V. Bliss & Lomo, 1973). This explains the mechanism of long-term potentiation (LTP) in a nutshell. LTP was found to occur at specialized synapses that had glutamate receptors called N-methyle-D-aspartate (NMDA) (Bliss, Collingridge, Morris, & Reymann, 2018). While LTP leads to strengthening of a neuronal circuit at synaptic level, the opposite effect has also been discovered which is referred to as long-term depression (LTD).

LTD occurs during low rate stimulation for long periods of time (Mulkey & Malenka, 1992) and also involves NMDA receptors. LTD leads to decreased synaptic activity and weakening of synaptic connections (T. V. P. Bliss et al., 2018). LTP and LTD are the neural mechanisms that underlie learning and memory and mostly occur in the hippocampus of the limbic system. The hippocampus has functional connections with the central auditory pathway, indirectly via the fronto-medial cortex, insula and amygdala and with the amygdala and auditory cortex directly via the entorhinal cortex (K. S. Kraus & Canlon, 2012). This pathway is implicated in the formation of longterm auditory memories (Squire, Schmolck, & Stark, 2001), and auditory cues are involved in the formation of spatial memories (Tamura, Ono, Fukuda, & Nakamura, 1990). Thus, music and sound stimulation induce LTP in the brain, thereby producing plastic changes at the synaptic level through the formation of new neural pathways and strengthening of existing ones. Daily exposure to music (60 dB) has been reported to enhance learning performance and increased BDNF (a neurotrophic factor indicated in LTP and formation of memory) expression in the hippocampus (Angelucci et al., 2007; de Deus et al., 2017; Lu, Christian, & Lu, 2008).

2.2 Neurochemically modulated plastic changes

Neurochemicals released in the CNS mediates behavioural and emotional concomitants in the organism. The activity of neurochemicals in turn progressively remodel the representation and functional importance of sensory stimuli in the cerebral cortex (Bao, Chan, & Merzenich, 2001). One important neurochemical which is implicated in motivational and reward-seeking behaviour, dopamine, is also known to modulate LTP (Gurden, Takita, & Jay, 2000). Music has also been widely discussed as having hedonistic properties and act as a natural reinforcing stimulus (Eckart Altenmüller & Schlaug, 2015; Bao et al., 2001; Chanda & Levitin, 2013). Music was shown to be associated with a significant increase in activity within structures that comprise the mesocorticolimbic system and are critical to reward and reinforcement, such as the ventral striatum [including the nucleus accumbens (NAc)] and mid-brain, as well as the thalamus, cerebellum, insula, anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC) (Chanda & Levitin, 2013). Studies have shown that stimulating the ventral tegmental area (VTA; comprises dopamine neurons that are activated by new stimuli or rewards) together with an auditory stimulus of a particular tone increases the cortical area and selectivity of the neural responses to that sound stimulus (Bao et al., 2001), thereby serving as a mechanism for neuroplastic changes in the reward circuitry of the brain (Traub, Whittington, Stanford, & Jefferys, 1996).

2.3 Cortical reorganization through music

Neuroplasticity at the cortical level occurs through reorganization and remapping of functional representations in the cerebral cortex or cortical maps (Kaas, 1991; Reybrouck et al., 2018). The brain is a malleable or ‘plastic’ structure that undergoes changes in response to experience and repeatedly performed actions through changes in the efficiency, density and connectivity of neural networks (Vik, Skeie, Vikane, & Specht, 2018). Music is one such phenomena which, through multimodal brain activation, can induce plastic changes in cortical pathways. Music making involves the primary auditory and motor regions, their inter-connections, regions that integrate areas involved in auditory and motor operations, as well as areas implied in other multisensory information integration (Schlaug, 2009). Thus, this multisensory activation in the brain involving multiple sensory and association areas may lead to the strengthening of existing neural connections as well as the development of new neural links between cortical areas that were otherwise not connected. This mechanism of cortical remapping, which subserves musical processing in the brain, underlies the rehabilitative function of music via neuroplasticity. Neuroplasticity is a normal developmental phenomenon in the maturing brain as a result of learning new skills, memory formation, recovery from injury and accounting from sensory deprivation or environmental enrichment experiences (Wan & Schlaug, 2010).

Cortical reorganization induced by musical training has been reported across the life-span in multiple studies (Hyde et al., 2009; Wan & Schlaug, 2010). Acquiring the skill to play a musical instrument engages multiple sensorimotor and cognitive functions which stimulates multimodal activation across the brain (Schlaug, Altenmüüller, & Thaut, 2010).

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Researchers have reported music-induced plastic changes in the brain as a function of life stage. Musical training, which occurs early in life, serves as a model for studying the effect of sensitive periods on brain and behaviour (Christopher J Steele, Bailey, Zatorre, & Penhune, 2013). Longitudinal studies on the effect of musical training in children have shown both behavioural changes such as improved auditory processing (Habibi, Cahn, Damasio, & Damasio, 2016), fine motor skills (Martins, Neves, Rodrigues, Vasconcelos, & Castro, 2018), verbal memory and executive functions (Miendlarzewska & Trost, 2014) and structural changes in volume of the primary auditory cortex (Bermudez, Lerch, Evans, & Zatorre, 2009), planum temporale, corpus callosum (Schlaug, Norton, Overy, & Winner, 2005) and in areas of the somatosensory cortex involved in one’s instrument of practice (Pantev, Engelien, Candia, & Elbert, 2001). Such findings suggest that the developing brain can undergo long-lasting structural and functional adaptations in response to early experiences such as intensive musical training and it has traditionally been reported that the earlier the training begins, the more extensive is the cortical reorganization reported (Amunts et al., 1997). Music induced plasticity has also been reported to bring about structural modifications in the adult brain. Ageing and neurological disease-related functional loss have been rehabilitated through music-induced plastic changes in the brain. Interestingly, elderly musicians have been found to have better auditory discrimination abilities, better working memory and stronger visuospatial abilities than age-matched non-musicians (Grassi, Meneghetti, Toffalini, & Borella, 2017). Results from previous studies have also shown a causal relationship between musical training and cognitive improvement in patients of Traumatic Brain Injury (TBI) via reorganization of neural networks (Vik et al., 2018). In cases of chronic stroke, significant restitution of activity and connectivity among auditory-motor regions of the affected hemisphere leading to improvement in motor functions with the use of music-based intervention have also been reported (Ripollés et al., 2016).

3 Music-based neurorehabilitation

The understanding of behavioural expression of complex, multi-level recurrent neural networks is an integral part of neuroplasticity-based neurorehabilitation approaches (Merzenich, Van Vleet, & Nahum, 2014). Stated simply, the functioning of the nervous system is integrated across multiple hierarchically organized levels with complex behavioural expressions being a product of a cascading series of neurological activities in the brain. Thus, impairment of behaviours is reflective of impaired neural circuits and necessitates neurological renormalization or strengthening of alternative circuits that are relatively preserved (Nahum et al., 2013). This ability of the CNS has already been extensively discussed as neuroplasticity and forms the basis of neurorehabilitation approaches using music. Music being a multimodal entity, engaging perception, cognition, and motor control in the brain (Koshimori & Thaut, 2019), serves as an effective medium for rehabilitating impaired neurological functions through employing multiple relevant neural circuits that are relatively preserved in the individual.

Researchers world-wide are focusing extensively on music and rhythm-based intervention strategies; those that are grounded in utilising the brain’s plasticity in promoting rehabilitation and restoration of neurological functions. With years of research in this area of neuromusicology, Neurologic Music Therapy (NMT) emerged as a standardized system of therapy comprising a cluster of 20 techniques. Based on the Rational Scientific Mediating Model (RSMM), NMT techniques grew out of ongoing research which explain the scientific basis of music therapy as founded in the “neurological, physiological, and psychological foundations of music perception and production” (Michael H. Thaut, McIntosh, & Hoemberg, 2014).

3.1 A brief note on neurologic music therapy (NMT)

Music has been applied therapeutically for facilitation of emotional expression, catharsis and social integration across various schools of psychotherapy (Michael H Thaut & Thaut, 2005). With the advent of neuroscience techniques such as MRI and PET scans, it has been possible to study the neural underpinnings of music and rhythm in the human brain. This paradigm shift from social to scientific modalities have engendered the NMT system as a scientific and standardized core therapeutic approach. NMT has been formally defined as “the therapeutic application of music to cognitive, sensory, and motor dysfunctions due to neurologic disease of the human nervous system” (Hegde, 2014). This is supported by neuroscientific evidence underlying music and brain functions which explains the influence of music on neural processes related to the control of movement, attention, speech production, learning, and memory, which can aide in retraining and recovering lost functions in the injured or diseased brain. A discussion on NMT necessitates a brief mention of the scientific models on which the system evolved: The Rational Scientific Mediating Model (RSMM) and the Transformational Design Model (TDM). The RSMM forms a connecting link between music and therapy via the neurological, physiological and psychological functions activated by music perception and production. The elements of this model are: the neurological, physiological and psychological response to music; parallel shared processes between musical and nonmusical functions sub-served by similar brain areas; the mediating role played by music in activating these non-musical but overlapping functions and behaviours; and, finally the clinical application of this mediating model in therapy and rehabilitation (Hegde, 2018; Michael H. Thaut et al., 2014).

As the name suggests, the TDM guides translation of knowledge gathered through the RSMM into functional music therapy practice. The TDM leads the researcher from assessment of the patient to application of music therapy and generalization of skills in activities of daily living (ADL). The role of music therapy in enhancing an individual’s chances at engaging in ADL through improvement in functioning and increasing independence is the fundamental aim of any rehabilitative program (Michael H. Thaut et al., 2014). Assessment serves an important part in standardized treatment protocols and in quantifying the efficacy of music-based interventions, lending itself to the conduct of randomized clinical trials (Eckart Altenmüller & Schlaug, 2015) which further strengthens the evidence base for NMT techniques.

Several techniques subsumed under the NMT system have been used across various neurological conditions (Michael H Thaut, McIntosh, & Hoemberg, 2015) for rehabilitation of impaired functions in stroke (Altenmüller, Marco-Pallares, Münte, & Schneider, 2009; Ripollés et al., 2016; Särkämö & Soto, 2012), mobility and stability in movement disorders (Bukowska, Kręzalek, Mirek, Bujas, & Marchewka, 2016), speech and language dysfunctions (Jungblut, Huber, Mais, & Schnitker, 2014; H. A. Lim, 2010; K.-B. Lim et al., 2013), cognitive and affective dysfunctions (Wendy L Magee, Clark, Tamplin, & Bradt, 2017; W. L. Magee & Davidson, 2002; Raglio et al., 2015). Thaut et al., have discussed the application of NMT techniques to three broad clusters of neurologic deficits or impairments, namely: Sensorimotor, Speech and Language and Cognitive functions (Michael H. Thaut et al., 2014). In the following section, a look has been taken into the various studies that have addressed neurological deficits using NMT techniques or other music-based interventions aiming at rehabilitation of lost or impaired functions.

3.2 Music-based interventions for sensorimotor functions

Neuroscientific methods have explored the link between the auditory and motor systems and has discussed the ability of the auditory system to detect temporal rhythmic patterns in stimuli and entrain the motor system by synchronizing the motor response to the temporal feature of the stimuli, i.e. matching motor behaviour to beat (Michael H Thaut et al., 2015; Michael H Thaut et al., 1996). NMT-related motor improvements in neurological conditions have been attributed to this sensorimotor coupling between auditory and motor activity due to the strengthening of neural connections between the auditory and motor cortices (Buard, Dewispelaere, & Kluger, 2019).

Several studies attempting to explain the neural mechanism of motor entrainment have attributed the activation of the reticulospinal pathways via richly distributed fibre connections from the auditory to motor centres from the spinal cord upward on brain stem, subcortical, and cortical levels (Felix, Fridberger, Leijon, Berrebi, & Magnusson, 2011). Neural oscillatory patterns in the auditory system have been linked to the time and frequency of sound stimulus (Fujioka, Trainor, Large, & Ross, 2012) and have been found to activate brain auditory areas, motor areas (sensorimotor cortex, supplementary motor area) as well as the inferior frontal gyrus and the cerebellum (Tierney & Kraus, 2013). It is through the neural activation and entrainment of sensorimotor pathways of the brain to rhythmic patterns in music that the rehabilitative function of music therapy in neurologic conditions has been established.

A case study used somatosensory-related NMT techniques comprising auditory beat (produced by a metronome or a musical instrument) cued motor exercises on a keyboard, castanet and other objects in a cohort of 3 patients with PD. Findings revealed clinically significant improvements in one or more areas of fine motor functioning across the subjects. The researchers further reported that neuroimaging data on the same cohort while performing a cued finger tapping task showed simultaneous activation in the auditory and motor cortices leading to an increase in evoked power in the beta-range (Buard et al., 2019). While the study lacked both a control group or a control condition, it does provide preliminary evidence on the effect of NMT techniques in entrainment of motor functions at an objective level with neuroimaging evidence implicating auditory-motor coupling in music-based neurorehabilitation. Another study using the musically-cued gait training (MCGT) program based on Rhythmic Auditory Stimulation (RAS) of NMT with 14 hospitalised PD patients reported increased gait speed and stride length in non-cued gait post-training, however some individual differences in responsiveness to intervention were prominent (Dalla Bella et al., 2017). Arias and Cudeiro (2008), used an auditory and visual rhythmic sensory stimulation on Freezing of Gait in PD and reported significant improvement in gait parameters when the frequency of stimulation matched the preferred walking cadence of patients (Arias & Cudeiro, 2008).

One of the frequently studied conditions for music-based neurorehabilitation is stroke, which is supported by imaging studies that observe music-related activation in motor brain regions such as primary motor cortex, premotor cortex (PMC) and supplementary motor area (SMA) (Baumann et al., 2007), the same regions that show abnormal activations in stroke (Li et al., 2016). In a study 20 individuals with chronic stroke, suffering from a slight to moderate upper extremity hemiparesis, received music-supported therapy (MST) for rehabilitation of motor functions. Findings revealed significant improvement in motor activity in the paretic hand and was supported by a concordant restitution of connectivity in auditory-motor pathways on functional magnetic resonance imaging (fMRI) (Ripollés et al., 2016).

In a case series report, balance and ambulation deficits in three neurologic cases suffering from stroke, PD and cerebrovascular accident (CVA) respectively, were found to show significant improvement in gait, increased cadence, decreased frequency of falls, and independent ambulation following individually tailored treatment protocols with various elements of NMT such as Patterned Sensory Enhancement (PSE), Therapeutic Instrumental Music Performance (TIMP) and RAS (Rice & Johnson, 2013). Such intervention modules mobilize various elements of music, such as pitch, dynamics, harmony, meter, and rhythm to enhance and aid motor activity, muscle coordination, strength, balance, postural control and range of motion implicated in adaptive activities (Cheong, 2019; Clark, Baker, & Taylor, 2012; Wang et al., 2013). Another study with 7 left-hemisphere stroke patients with ideo-motor apraxia reported significant improvements in upper-extremity functioning and activities of daily living (ADL) following gross and fine motor exercises through drum and keyboard playing under the TIMP paradigm of NMT (Yoo, 2018). Musical instrument playing in TIMP facilitates adaptive motor functioning by strengthening the range of motion, endurance, finger dexterity and limb coordination in motor impairments seen in patients with neurologic disorders.

3.3 Music-based interventions for language functions

Entrainment of functions to rhythmic cues applies to functions beyond motor control. Researchers have shown varied elements of speech and language control being positively affected by rhythmic entrainment (Natke, Donath, & Kalveram, 2003). Motor speech disorders where NMT techniques have been implicated can mainly be discussed in cases of dysarthria: speech disturbance due to disruption of muscles required for speech production, apraxia: sensorimotor disturbance resulting in dysfunctions in directing movements necessary for volitional speech production (Lee, Thaut, & Santoni, 2018) and, aphasia: a communication disorder which can affect a person’s use of expressive and receptive language, despite their cognitive ability.

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In a pilot randomized controlled study in chronic post-stroke aphasia, melodic intonation therapy (MIT) of NMT was done using melodic intonation and rhythm to restore aphasic speech. The study reported significant improvement in adaptive speech, but only in repetition of items ($\beta = 13.32$, $p = 0.02$) that were used for training during the research and were not generalizable to functional communication beyond the trained items. The researchers explained that MIT is more beneficial in cases of aphasia in earlier stages post stroke than in chronic cases (Van Der Meulen et al., 2016). MIT works on the hypothesis that music processing regions of the right cerebral hemisphere has language capabilities, and that they could potentially compensate for damaged left hemisphere language regions in individuals with speech production disorders (Zumbansen, Peretz, & Hébert, 2014). However, other studies have reported significant, lasting improvements in language production using MIT or MIT based techniques such as a relatively recent study by Wan et al., (2014) where 11 chronic aphasic post-stroke patients underwent an intensive intonation-based speech therapy showed structural right hemisphere white matter changes in the inferior temporal gyrus accompanied by improved communication and verbal fluency (Wan, Zheng, Marchina, Norton, & Schlaug, 2014). MIT has been reported to be beneficial in apraxia of speech, which is cited as a defining component of Broca's aphasia (Zumbansen et al., 2014). Longitudinal studies have also been reported that have found MIT efficacious in individuals with speech disorder as compared to a control therapy designed to resemble MIT but without the pitch and rhythmic components (Schlaug, Marchina, & Norton, 2008) or a palliative version of MIT (Stahl, Henseler, Turner, Geyer, & Kotz, 2013; Wilson, Parsons, & Reutens, 2006).

NMT has also been used with the child and adolescent population. In a study comparing the effect of music-based therapy, speech training and no-training on verbal production of 50 children with autism spectrum disorder (ASD), The Developmental Speech and Language Training through Music (DSLM) of NMT was used and findings indicated a significant improvement in speech following both music ($d = 1.275$) and speech training ($d = 1.141$) as compared to no training condition with low functioning ASD performing better on verbal production following music training (H. A. Lim, 2010). DSLM uses developmentally appropriate musical materials and experiences to aide speech and language development in children with developmental delays.

Other NMT techniques such as Rhythmic Speech Cueing (RSC), Therapeutic Singing (TS) and Oral Motor and Respiratory Exercises (OMREX) have also been shown to be effective in addressing speech and language sequelae of neurological conditions (Mainka & Mallien, 2014; Michael H Thaut & Thaut, 2005).

3.4 Music-based interventions for cognitive and affective functions

The clinical implications of NMT through entrainment of cognitive functions have only recently started emerging as a therapeutic model of change. In their work, Conway et al., explain how the inherent temporal and sequential characteristics of music may serve as a "scaffold" for cognitive functions, such as memory. In other words, non-musical cognitive functions may be enhanced through bootstrapping with temporal elements of music. The rhythmic feature of music may create a pattern or structure to which information may be mapped leading to better encoding and retrieval (Conway, Pisoni, & Kronenberger, 2009).

Thaut et al., (2014) in their seminal work, studied the influence of music mnemonics using spoken and sung versions of Rey's auditory verbal learning test (RAVLT) on verbal memory in patients with multiple sclerosis (MS). Findings suggested that patients underwent learning-related brain plasticity and showed better word memory and word order memory for the sung as compared to the spoken RAVLT (two-way ANOVA: $F(1.52) = 4.12$; $p = 0.45$; mean squared error 0.057). The findings were mirrored in electroencephalography (EEG) data which showed stronger learning-related activation in prefrontal areas in patients during word learning trials (Michael H Thaut, Peterson, McIntosh, & Hoemberg, 2014). Music's inherent temporality helps in sequencing and in chunking of large arrays of information into smaller, easily encoded clusters, thereby reducing the memory load and allowing deeper levels of encoding. The researchers in the study explained that the use of musical mnemonics was successful in both encoding by aiding deep level processing and in retrieval by providing critical cues embedded in music's temporal structure.

Impairments in attention and concentration following Traumatic Brain Injury (TBI) have been addressed by researchers using various elements of the NMT paradigm. One preliminary quasi-experimental study with TBI patients in a group-setting used a multi-faceted NMT protocol comprising musical attention control exercises, musical mnemonics, musical executive function training and therapeutic singing exercises to address various aspects of the dysexecutive syndrome as well as affective dysregulations in TBI patients. Findings showed that NMT effectively improved functioning in the domains of executive functions, particularly in mental flexibility (d = 1.21), and significant decrease in depressed mood (d = 0.52) and anxiety (d = 0.28) (M. Thaut et al., 2009). The study however did not report any significant effect of NMT on attention and memory, thereby highlighting the need for studies with longer durations of intervention. Another recent study using MST on behavioural and cognitive deficits in patients following mild TBI reported improved cognitive performance including attention and concentration as well as enhanced well-being and social interaction. These findings were supported by neuroimaging data using both simple task-based and resting-state fMRI which gave evidence of significant functional neuro-plastic changes in the OFC's networks that are often damaged following a TBI (Berit Marie Dykesteen Vik et al., 2019).

Gait deficits in PD provide a prototypical area for the application of music-based interventions owing to the connectivity of the auditory-motor cortices and rhythmic entrainment of motor functions as discussed above. However, behavioral data give evidence of such gait-related interventions in PD as having more than a motor benefit and extending into rehabilitating cognitive functions as secondary outcomes. Particularly, in a study using the musically cued gait training (MCGT) paradigm of NMT not only reported improvements in gait parameters but also showed beneficial effects on perceptual and sensorimotor abilities in patients with PD (Bella, Benoit, Farrugia, Schwartze, & Kotz, 2015). Another study using RAS, which is the standard NMT paradigm for motor training in PD, showed improvement in not only functional gait ($p < 0.001$) and overall gait quality ($p < 0.001$) but also reported increased fronto-temporal conncectivity in the RAS group which is

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strongly linked to cognitive functioning in PD (Calabrò et al., 2019). The RAS technique has ideally been found to involve cognitive faculties through activation of the cerebellar-thalamocortical network during RAS training thereby enhancing cognitive performance (specifically working memory and processing speed) as reported in Parkinson's Disease (Lesiuk, Bugos, & Murakami, 2018).

A common neurological sequela of stroke, sensory neglect and inattention, have shown positive improvement with the Musical Neglect Training (MNT) in a study on two individuals with persistent chronic unilateral visual neglect. Both the patients showed significant improvement for exploratory visuomotor neglect on the Albert's test (screening tool for unilateral spatial neglect). Despite having a small sample of only two subjects and thereby posing poor generalizability of findings, this study may provide potential area for future research into NMT based MNT paradigm in post-stroke cases with neglect (Kang & Thaut, 2019).

Music has been hailed as a facilitator of well-being and emotional health since ancient times. Scientific evidence supporting this claim have focused upon the role of the functioning of the hypothalamic-pituitary-adrenal axis (HPA) and levels of the human stress hormone, cortisol, which have been reported to show reduced levels on exposure to relaxing music (Koelsch et al., 2011). In patients with neurological conditions such as Dementia, music-based interventions following the NMT rationale have been found to improve affective as well as cognitive functioning. In a recent study by Ray and Gottell (2018), singing and music-with-movement exercises were used with small groups of 4 to 6 in-patients with moderate dementia. Findings indicated significant reduction in depressive symptoms ($p \leq 0.001$) and improvement in well-being ($p = 0.003$) following the music-based intervention which used an array of musically cued movement exercises (Ray & Götell, 2018). In another study assessing the efficacy of MST on motor recovery in individuals with stroke, it was found that the NMT paradigm not only restored motor deficits but also showed positive effects on mood as assessed on the Beck Depression Inventory (BDI; $t(17) = -3.532$, $p < 0.003$) implying a reduction in depressed and negative mood post-therapy (Ripollés et al., 2016).

4 Conclusion

The role of music in mediating plastic changes in the mouldable brain is well documented and presents itself as a prominent area of research. With more advanced imaging techniques, the exact sequelae of music-brain relationship are beginning to gain scientific clarity. The use of music-based interventions is not only implicated at the neuronal level but also known to have motivational salience and to foster positive emotions. The empirically supported understanding that the brain is mouldable to the experience of music guides the domain of music-based neurore-habilitation. The core of this rehabilitative function lies in music's polymodal brain activation ability which may alter effectiveness of cortical pathways and positively affect task performance across various domains. Thus neuronal adaptations in the brain is finding increasing application for music-based interventions in rehabilitation of neurological deficits and in making the brain more receptive to acquiring new learning in a relatively shorter time-frame, a concept referred to as 'metaplasticity'(Herholz &

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Zatorre, 2012). Music-induced plasticity has been successfully explored following varied experimental paradigms ranging from music listening, musical training, systematically developed therapeutic techniques such as NMT to studying structural and functional aspects of a musician’s brain.

The longevity and effectiveness of the neuroplastic changes induced by music demands more systematic and rigorous scientific attention. Several longitudinal studies have commented on the long-lasting nature of neuroplastic changes induced by musical training and music-based interventions (Herholz & Zatorre, 2012; Christopher J. Steele & Zatorre, 2018; White, Hutka, Williams, & Moreno, 2013). There are certain prominent factors that have been reported to influence the strength of this brain-behaviour relationship. There exist individual differences in responsiveness to music-based activities and interventions. In the area of experience-based neuroplasticity, researchers have not ruled out the possibility of predisposing factors that might make a particular individual more receptive to neuroplastic benefits than others. It has been shown that higher grey matter concentration and cortical thickness in right Heschl’s sulcus (primary auditory cortex) and bilateral anterior intraparietal sulcus (the cortical region important for pitch-processing) are predictive of better pitch task performance in musicians, after factoring out musical training based changes (Foster & Zatorre, 2010). Another study reported individual differences in sensorimotor synchronization abilities before exposure to a musically cued gait training (MCGT) paradigm as a potential determinant of success of intervention with spared synchronization abilities at baseline being predictive of better treatment outcome (Dalla Bella, Benoit, Farrugia, Schwartze, & Kotz, 2015).

This field has collected compelling evidence of the rehabilitative potential of the art and science of music. Contemporary experimental paradigms and imaging techniques need to be further advocated to further this emerging understanding. Researchers studying role of music-based intervention techniques in neurorehabilitation would further the understanding of the neuroplastic nature of the brain and the application of this in enhancing overall well-being and functioning.

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