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ALZHEIMER'S DISEASE AND TREATMENT

Alzheimer's Sound Health

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Abstract

There is an emerging interest in using music as a non-invasive non-pharmacological therapy for various mental disorders. The study of music and medicine is a rapidly growing field which had been largely focused on the use of music as a complementary therapy. Despite its evident universality and high social value, the ultimate biological role of music and its connection to brain disorders is poorly understood. This communication is an attempt to link known facts about the potential of music as a non-pharmacological therapy in treating neurological disorders with special emphasis on Alzheimer's disease.

Introduction

The ancient Greek classic Juvenal's dictum "*Mens sana in corpore sano*" (a sound mind in a sound body) is an ideal description of a happy state of human being that has never lost its resonance [1]. Music experts profound effect on human mind since brain is the first organ affected by music [2-4]. Music is a unique feature of human civilization that exists in every culture around the world [5,6]. Listening to music is an experience where an individual immerses oneself perceiving internal focus/mediation/spiritual awareness [7]. The human relationship to sound begins with the development of an auditory system during the pre-natal stages between seventeen and nineteen gestational weeks [4,8,9]. Recent experimental findings indicate that music has the potential to guide attention towards sensory cues and prevent fatigue-related signals [10,11]. The medicinal use of music dates back to ancient times with historic records of various cultures [12,13]. Music is a drug without side effects and is considered a type of "Yoga" which acts upon the human body, mind and soul through the medium of sonorous sounds [14].

The use of music as a medicine started with the second world war when music was used to expedite the recovery of wounded soldiers [13]. Ancient Indian classical music maestros affirmed that, ragas-the basis of Indian classical music, influence emotions of human being by changing the resonance of the human body [14,15]. The experiment conducted by Balkwill and Thompson (2000) where they asked 30 Western listeners to judge the expression of 12 Hindustani ragas intended to express anger, joy, peace, and sadness, found that despite being culturally unfamiliar, listeners were sensitive to the intended expression of the ragas [16]. The “Raga Chikitsa” constituted one of the treatment options of Ayurveda [14,17]. Music has been found to induce relaxation and alter pain perception, blood pressure, and respiratory and heart rates [18-20]. Soft, slow, non-lyrical music significantly decreased systolic blood pressure, heart rate, respiratory rate and oxygen saturation [17,19]. Music with a faster tempo significantly increased heart rate, ventilation, blood pressure and sympathetic nervous activity [21]. Cognitive processing of music is hypothesized under two mechanisms: Affective or indirect mediation and non-affective or direct mediation. Affective mediation (but not non-affective or direct mediation) refers to an induction of specific cognitive networks through emotional music processing networks [22]. Thus, music plays a significant role in maintaining sound mind in a sound body. This communication discusses how music can be a valuable tool to probe multifold cognitive functions and its potential as a candidate therapy for treating neurological disorders such as Alzheimer’s disease.

Music and brain

Neuroanatomical correlates of music

The very first organ influenced by music is the brain. The auditory brainstem processes the neural signals from cochlea and sends them to the thalamus, which projects them to the auditory cortex [23]. The transduction of music into a neural signal occurs in the cochlea where music signals are perceived through shearing of hair cells within the cochlea and encoded into neuronal firing patterns in the thalamus and auditory cortex [17,23,24].

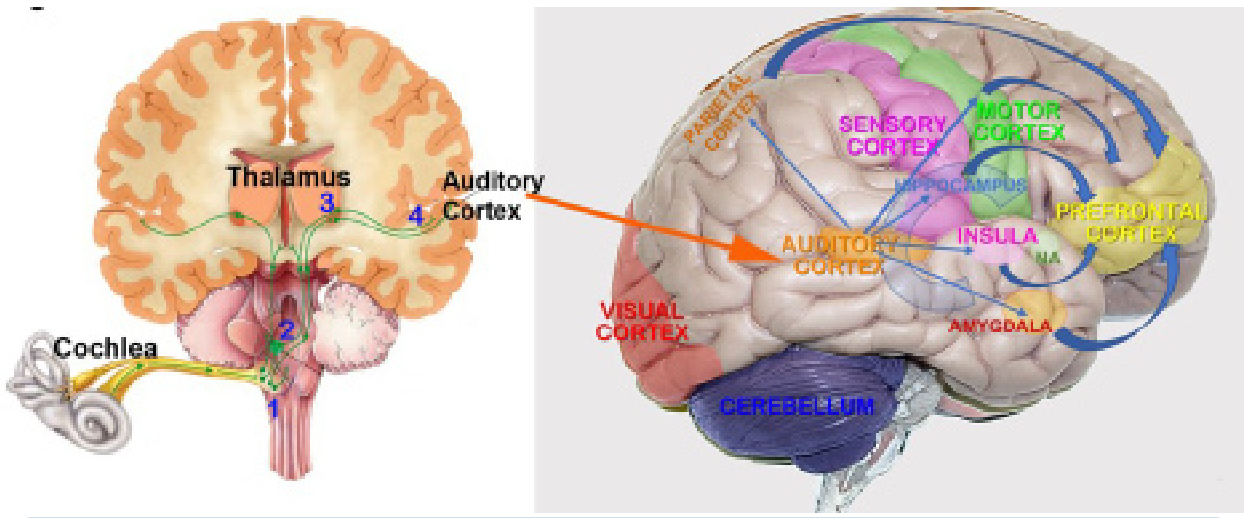


Figure 1: Left Panel: ross section of the brain through auditory cortex showing acoustic signal flow from cochlea to auditory cortex. [1] Sensory axons from cochlear ganglion terminating on the cochlear nucleus located in brain stem; [2] Axons form cochlear nucleus projecting to the inferior colliculus; [3] Axons from inferior colliculus projecting to the thalamus; [4] Thalamic neurons projecting to the auditory cortex. **Right panel:** Different regions of the brain receiving acoustic signal-inputs from auditory cortex (Straight arrows), eventually projecting to the frontal/pre-frontal cortex (Curved Arrows) where all signals are integrated; NA (Nucleus Accumbens).

The auditory cortex carries out perceptual analysis in terms of pitch (generally tones are physically referred to as frequencies, but with respect to music they are referred as pitches), timbre (the quality of a musical sound that distinguishes different types of sound production), rhythm (the organizational pattern of sound in time or the timing of musical sound), intensity and roughness [25]. The music, particularly vocal sounds, activate auditory neurons in the primary auditory cortex during the informational processing of music tones. During this process, music is encoded into neuronal signals propagated through the thalamus ultimately reaching to auditory cortex [24].

The firing rates of auditory neurons triggered by auditory rhythm and music, entrain the firing patterns of motor neurons, thus driving motor system into the frequency levels [26]. The auditory stimulation primes the motor system to a state of readiness to move by facilitating motor response quality [24]. The auditory system has a wide distribution of neural connections to motor centers in the spinal cord and brain stem at the cortical and sub-cortical levels [27,28]. The frontal lobe is involved in integrating auditory and motor information, imitation and empathy [25]. Imamura et al. have implicated that the sound processing occurs between cochlea and auditory cortex where pitch recognition for melody, rhythm and timbre occurs, emotional processing occurs in insula and limbic area, working memory for rhythm occurs in parietal cortex, and finally integrative information processing for harmony, emotion, working memory and behavioral output occurs in frontal/prefrontal cortices [24]. The emotive network of cingulate gyrus, amygdala, hippocampus and midbrain plays an important role in any musical activity and underlies the motivation to listen to music [29]. Integrative emotional processing for harmony, emotion, working memory and behavioral output occurs in the pre-frontal cortex [24]. Thus, the neuronal excitation caused by music stimuli although first hits the auditory cortex, goes much beyond to a widespread network of frontal, temporal, parietal and subcortical areas related to attention, memory and motor functions, as well as to the limbic and paralimbic brain regions related to emotions and cognition, forming a basis for music perception and brain functioning [13].

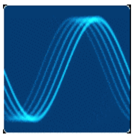
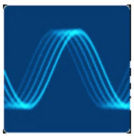
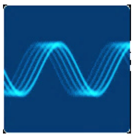
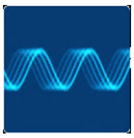
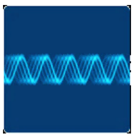
Neurochemical correlates of music

Music has been found to affect neuroendocrine system [13, 30]. Research has established a role for music in the regulation of the hypothalamic-pituitary axis, the sympathetic nervous system, and the immune system, which have key functions in the regulation of metabolism and energy balance [31]. Studies have shown that endogenous opioids are released from pituitary on exposure to music [13]. Another study conducted to see the effect of music on constitutively expressed opiates and cytokines found that with regard to mu-opiate receptor expression, mononuclear cells showed significantly increased opiate receptors in subjects exposed to music compared to control group [32,33]. In addition, plasma morphine 6 glucuronide levels increased while plasma morphine levels decreased implying morphine's conversion to morphine 6 glucuronide, along with significant reduction in inflammatory cytokine-interleukin-6 (IL-6) after music exposure [34]. There are also reports showing significant reduction in stress-hormones i.e. Adreno-Corticotropin Hormone (ACTH) releasing and adrenocorticosteroids (Cortisol) after music exposure [30,35]. Another study showed significant enhancement of Brain-Derived Neurotrophic Factor (BDNF) after music exposure [36,37]. Dopamine is postulated to be involved in the enjoyment of music [30,38]. Dopamine is demonstrated to be released from the ventral striatum and in the ventral tegmental area in subjects listening to pleasant music [30,39]. In addition, role of endorphins/endocannabinoids and nitrous oxide in emotional perception of music and in producing physical effects such as vasodilatation, local warming of the skin and a reduction in blood pressure as a response to listening music respectively are described [25]. Listening to techno-music resulted in a significantly increased plasma norepinephrine, ß-endorphin, adrenocorticotropic hormone, cortisol and growth hormone, however, while listening to classical music, no significant changes were detected in hormonal concentrations [30]. These studies emphasize Indian classical music-induced hormonal balancing without increasing stress hormones.

Activity correlates of music

The language of the brain is nothing but electrical activity. Electroencephalography (EEG) is the tool for measuring brain's electrical activity as an index of neuronal oscillations. The EEG signal records electrical field generated by neural oscillations. Neural oscillations or brainwaves are rhythmic patterns of neural activity. In individual neurons, oscillations appear as action potentials which are then propagated to post-synaptic neurons while synchronized activity of large number of neurons in a group can be measured in EEG. EEG signals are characterized in specific frequency bands defined as cycles per second or Hertz (Hz) i.e. Delta (δ) (0.5-4Hz), Theta (θ) (4-8Hz), Alpha (α) (8-12Hz), Beta (ß) (12-30Hz), Gamma (γ) (>30Hz), which are associated with different brain functions such as deep sleep (δ), inward focus, episodic memory (θ), wakeful relaxed state but alert / attentive mind (α), busy and active mind (ß), fast information processing and problem solving linked to intelligence, memory and cognition (γ) [40,41] (Table1).

Table 1: Neurobiological effects of brain waves.

Brain frequency band	Hertz (Hz) (Cycles per second)	Functional significance	Representative EEG	AD Dementia
Delta (δ)	0.5 – 4 Hz	**Deep sleep / healing** • Originate from thalamus and cortex • Indicate deep stage 3 of Non-Rapid Eye-Movement (NREM) sleep, also known as Slow Wave Sleep (SWS) • Suspend external awareness, promote deepest meditation		↑
Theta (θ)	4 – 8 Hz	**Relaxation / creativity / restorative sleep** • Originate from hippocampus and cortex • Senses are withdrawn from the external world, inward focus • Co-occur with gamma waves and play important role in synaptic plasticity and episodic and spatial memory retrieval		↑/↓/None
Alpha (α)	8 – 12 Hz	**Stress relief / restful but alert** • Originate from occipital lobe • Alpha is 'the power of now' being in current resting state • Indicate alert calmness, mind/body integration • Restful but reflective, passive but alert brain waves		↓
Beta (ß)	12 – 30 Hz	**Busy and active mind** • Originate from occipital lobe and replace alpha waves • Beta wave is a 'fast' activity associated with active, busy and anxious thinking and concentration		↓
Gamma (γ)	>30 Hz (30–150) Hz 40 Hz-of interest	**Fast information processing, problem solving** • Originate from thalamus • Fastest waves, faster than single neuron firing • Gamma activity is correlated with large scale brain network activity such as working memory and long-term memory		↓

Music-induced measurable neurological responses in the form of EEGs have been well documented [42]. One study analyzed the effects Indian classical music on brain activity during normal relaxing conditions using EEG [43]. Sanyal et al. have studied the effects of two sets of Indian classical music "Ragas" with opposing emotional effects on alpha and theta EEG index in 20 subjects who volunteered in this study [44]. The results showed that the complexity of the brain rhythms varied significantly when the emotion of the music was changed from happy to sad, where Ragas indicative of sadness/sorrow (Darbari Kanada and Miyaki Malhar) increased theta waves while the Ragas indicative of joy/pleasant mood (Chhayanat, Bahar) decreased theta waves [45]. Another investigation by the same group analyzed alpha and theta EEG rhythms in 10 participants using a simple acoustic stimuli i.e. Tanpura Drone, using Multifractal Detrended Fluctuation Analysis (MFDFA), showed that Tanpura Drone increased both alpha and theta complexity [15,46,47]. An EEG study of Ragas with its impact on brain waves suggested that ragas like Khamaj and Puriya may relieve mental tension and raga Malhar may pacify anger and excessive mental instability [43]. Schalles et al. studied synchronization of moving and listening behavior with brain waves via hand-drumming and found that cortical connectivity during auditory tapping task indicated increased coherence from brain waves between auditory, parietal and motor areas with dominant frequency bands centered around 10-20Hz (α/ß) [48]. These reports, although limited, indicate theranostic use of music-induced EEG activity.

Neurorehabilitative effects of music

Neurologic Music Therapy (NMT) has become distinct rehabilitative science that has shown promising recovery from many neurological diseases and hence has been approved by the World Rehabilitation Federation as an effective evidence-based method of treatment [29]. Listening to music can reduce epileptiform discharges enhancing brain plasticity [49]. Bandera et al. showed that singing helped recovery from cerebral palsy by improving gait with reduced time and number of steps [50]. Jaschke et al. suggested that music has a beneficial influence on brain development and exerts positive effects on cognitive, communicative and social skills in persons with Intellectual Disabilities (ID) including Autism Spectrum Disorder (ASD) [12]. Incorporating music into a rehabilitation program was observed to foster recovery of cognitive functions, mood, co-ordination and memory [51].

Among musical components, a repetitive rhythm appears to play a significant role in regulating physiologic and behavioral functions through the synchronization of biological rhythms with musical rhythm based on acoustic resonance [51]. Additionally, regular rhythmic patterns facilitate memory encoding and decoding of non-musical information making music as an efficient mnemonic tool [51]. Music with its unique ability to access motivational systems in the brain, provides time-structure enhancing perception process for language, motor and cognitive learning [51]. The evidence from basic and clinical neuroscience suggests that listening to music involves many cognitive components with distinct brain substrates [52]. The effect of music on specific brain regions, as measured by neurophysiology and neuroimaging techniques, have unfolded functional neuronal network connectivity and activation of target brain regions between the auditory cortex, the reward brain system and the learning/memory brain system [7]. Musical stimuli have been shown to activate specific pathways in specific brain regions including nucleus accumbens, amygdala, hippocampus, hypothalamus, insula, cingulate/pre-frontal/orbitofrontal cortex, critically involved in emotions and cognition [53,54]. In addition, neurochemical studies have suggested that music stimulates the secretion of several hormonal mediators such as endorphins, endocannabinoids, dopamine, serotonin and melatonin which are known to play significant role in emotional and cognitive integrity [53,54].

As the world's population is rapidly aging, it is imperative to find avenues that would promote successful aging while simultaneously preventing age-associated cognitive impairments that are typical of normal or pathological aging. Recent research has increasingly considered music as a promising tool for improving cognition and promoting well-being. Music activates a broad network of brain rather than a single "music area", particularly while listening to familiar music [55]. Classical music has an ability to enhance cognition beyond the music listening session [56]. Music has been shown to improve autobiographical recall [57,58] which can be automatically retrieved by a musical cue, indicating that music can be used to evoke specific involuntary autobiographic memories [59]. Music interventions have been shown to improve sleep disturbances by increasing melatonin levels [60], and by balancing steroid hormones without the adverse effects of hormone replacement therapy [61,62]. Generalized music interventions involve the use of music with the goal of improving general well-being of the person to stimulate verbalization, memories or to encourage relaxation and neurorehabilitation [63,64]. Adults age 60 to 85 without previous musical experience exhibited improved processing speed and memory after just three months of weekly 30-minute piano lessons and three hours a week of practice, whereas the control group showed no changes in these abilities [65]. Cognitive and neural benefits of musical experience continue throughout the lifespan, and counteract some of the negative effects of aging, such as memory and hearing difficulties in older adults [66]. Research shows that music activities (both music listening and music making) can influence older adults' perceptions about the quality of their lives. Some research has examined the effects of music listening on biological markers of health and subjective perceptions of wellbeing. Other studies on the psychological and social benefits associated with music making activities have demonstrated that participants often place considerable value on these "nonmusical" benefits of music activity [67]. Playing music reduces stress and has been shown to reverse the body's response to stress at the DNA-level [68]. Blood samples from participants of an hour-long drumming session revealed a reversal of the hormonal stress response [69]. Stanford University School of Medicine conducted a study with 30 depressed people over 80 years of age and found that participants in a weekly music therapy group were less anxious, less distressed and had higher self-esteem [Friedman, "Healing Power of the Drum," 1994]. Music has been found to stimulate parts of the brain, and studies have demonstrated that music enhances the memory of Alzheimer's and dementia patients, including a study conducted at UC Irvine showing improved memory of Alzheimer's patients after listening to classical music (Cheri Lucas, Education.com, "Boost Memory and Learning with Music," pbs.org). Thus, mental health effects of music are increasingly recognized.

Music and alzheimer's disease

With the rapidly aging population of the world, there is a sharp upward trend for the prevalence of Alzheimer's Disease (AD) and AD Related Dementias (ADRD) all around the globe with limited treatment options. Studies have documented that conversion rate from Mild Cognitive Impairment (MCI) to AD is about 10-15% every year [70]. Epidemiological and clinical studies confirm that MCI predicts a transition state towards mild AD and warns early identification of the disease that can facilitate treatment interventions to halt the disease progression [71]. Alzheimer's Disease (AD) is a global epidemic and public health crisis currently afflicting ~6 million Americans (and ~40 million people worldwide). By the middle of the century, these numbers will escalate to ~16 million Americans (and ~152 million people worldwide) suffering from AD, if effective disease-modifying treatments are not discovered [72]. Current FDA-approved pharmacotherapy for Alzheimer's disease include

Acetylcholinesterase inhibitors (AChEi) (Rivastigmine, Donepezil, Galantamine) and N-methyl-D-aspartate (NMDA) glutamate receptor modulator (Memantine) [73]. Investigational therapies for AD include antihypertensive drugs, anti-inflammatory drugs, secretase inhibitors, insulin resistance drugs, brain-derived neurotrophic factor, and immunization. Nutritional and botanical therapies include huperzine A, polyphenols, Ginkgo, Panax ginseng, Withania somnifera, phosphatidylserine, alpha-lipoic acid, omega-3 fatty acids, acetyl L-carnitine, coenzyme Q10, melatonin along with various vitamins and minerals. Other alternatives include cognitive training, leisure activities and socialization [74]. FDA-approved symptomatic pharmacotherapy provides only modest benefits without halting the progression of the disease and is associated with adverse effects [73,75] while other investigational therapies are not conclusive [74]. Given the lack of effective disease-modifying treatment(s) for AD [76], there is an unmet medical need in validating alternative treatments with greater therapeutic efficacy and virtually no side effects in treating AD, such as a non-invasive non-pharmacological music therapy [55,75-79].

Lyu et al. explored the effects of music therapy on cognitive functions and mental well-being of patients with AD and showed that music therapy was effective in enhancing memory and language ability in patients with mild AD while reducing the psychiatric symptoms in patients with moderate to severe AD [80]. Chevreau et al. conducted a study showing music as a mediator for improving autobiographical memory in AD, in which the authors developed “index music” method based on “index word” where subjects had to remember their choice of word(s) from the music presented. Results showed that the autobiographical memory scores of AD patients were significantly improved after subjecting them to “index music” [81]. An exploratory randomized trial consisting of “Kirtan Kriya (KK) mediation or Music Listening (ML) program conducted for 12 min/day for the duration of 12 weeks, showed that KK and ML treatment modulated plasma levels of beta-amyloid (Aß) (a key seeding molecule fundamental to AD pathogenesis), Telomer Length (TL) and Telomer Activity (TA) associated with improved cognitive functions and quality of life [82]. A study that examined the effect of music encoding on the recognition of associated verbal information in which lyrics of unfamiliar songs were presented either as sung or spoken recordings, demonstrated better recognition accuracy for the sung-lyrics than the spoken-lyrics in patients with AD [83]. A sample study consisting of 25 patients with mild Alzheimer’s disease that examined a short protocol of 60 min music therapy, lowered cortisol (stress-hormone) levels, and significantly reduced stress, anxiety and depression [84].

Accumulating evidence shows that the ability of music is relatively well preserved in aging and dementia, even during the late stages of dementia when verbal communication may have deteriorated [85]. A systematic review performed using PubMed and ScienceDirect data bases between 2006-2016, indicated beneficial impact of music therapy on cognition (memory, attention, language), emotion, and behavior (anxiety, depression, and agitation) [79].

There is evidence to suggest that music for memory can remain intact in persons with AD, even while experiencing rapid cognitive decline [86,87] because musical memory networks are independent of traditional temporal lobe memory networks, both within and outside of the temporal lobes including frontal and parietal cortices [88-90] and are spared until the later stages of AD [91]. These observations suggest that music perception forms “islands of cognitive reserve” in otherwise cognitively impaired person, and hence music can be utilized as an effective intervention even in late stages of dementia [92] and in treating age-related neurological disorders such as Alzheimer’s disease [85]. A study that utilized positron emission tomography (PET) scanning to investigate which music listening brain areas are affected by Alzheimer’s pathology in relation to amyloid deposition and glucose metabolism found that music listening brain areas experienced less pathology [91]. Simmons-Stern et al. have observed that music enhanced verbal encoding and memorial awareness in AD patients [83, 93, 94]. And lowered stress in AD as indicated by reduced salivary cortisol levels [84]. A systematic review mentioned that the music interventions were best at reducing behavioral symptoms of dementia such as agitation and anxiety [95]. Studies which used individualized playlists improved cognitive outcomes in both active music therapy and music listening compared to methods that used music chosen by an experimenter [55,96]. Another systematic review reported that music therapy was effective in reducing depressive behavioral symptoms in dementia patients [97,98]. Although, sizable reports have examined beneficial effects of music in AD, further investigation(s) and more evidence in this field are warranted to claim the significance and utility of music therapy in treating AD and other neurological disorders.

EEG is the direct correlate of brain functions [99] that gets gradually modified during physiological aging. Over the course of “natural” aging, the power decrease of occipital alpha rhythms might be associated with changes in the basal forebrain cholinergic system functioning, which sustain the excitatory activity in the cholinergic brain stem pathway [100]. When compared to the resting state EEG rhythms of healthy normal old, AD patients showed an amplitude increase of widespread delta and theta sources and an amplitude decrease of alpha (8-13Hz) and/or beta (13-30Hz) brain waves [101-104].

These EEG abnormalities were associated with altered regional cerebral blood flow/metabolism along with impaired global cognitive function as evaluated by mini-mental state examination (MMSE) scores [99]. Early/pre-clinical stages of AD are typically associated with slowing down of resting occipital alpha rhythms [105]. In this regard, several studies have shown a relationship between apolipoprotein 4 (ApoE4) genetic risk factor has been found to affect EEG rhythms in AD patients, which are found to be associated with higher delta and theta power along with lower alpha and beta powers [106]. Most EEG studies in AD have shown prominent decrease of alpha band coherence which are hypothesized to be associated with cholinergic deficits [107]. On the other hand, changes in the theta band coherence in AD are not found to be homogeneous, as some studies show increase/decrease/no change [108]. One study showed that the total delta coherence is higher in AD than in the MCI and higher in MCI than in normal old Delta Coherence, Normal old>MCI>AD), confirming that the functional coupling of resting EEG rhythms becomes progressively abnormal [109].

Loss or a significant drop in EEG synchronization in faster rhythms has been correlated with MMSE scores in MCI and AD patients [110]. Few studies have studied EEG index over the course of progression of dementia where significant increase of delta and theta power in conjunction with decrease of alpha and beta power have been observed [111]. The physiological mechanism at the basis of abnormal brain rhythms in MCI and AD have been postulated to originate form impairment in the cholinergic neural projections from basal forebrain which is a crucial factor of AD [112]. An evidence supporting this fact showed that resting EEG alpha power is decreased from experimental damage to cholinergic pathways [113].

Increase of slow EEG power along with decreased alpha activity is linked to cognitive decline in MCI correlated with negative MMSE scores compared to normal age-matched controls [114]. As mentioned earlier, the relative decrease of alpha power in MCI may be related to an impaired index of cholinergic basal forebrain [115] and may further suggest a progressive impairment of the thalamocortical and corticocortical system [71]. Studies have demonstrated that increased delta/theta activity and deceased alpha/beta/gamma activity may be the predictors of convergence from MCI to AD/ADRD [103,107,116].

Available Alzheimer's clinical data indicate overall decreases in the faster brain waves (alpha, beta, gamma) with simultaneous increases in the slower (delta, but not theta) brain waves, collectively resulting in declined brain activity [55,99,117]. As mentioned earlier, the coherence of theta brain waves is not homogeneous, as some studies show either decrease or increase [99,118] or no change [119] of theta brain waves in AD/MCI. Mounting evidence indicates that theta and gamma oscillations are closely related to spatial and episodic memory processing [116,117,120]. The gamma co-occurs with theta rhythm in the hippocampus and plays important role in the formation and retrieval of episodic and spatial memory [120], indicating that theta and gamma oscillations are closely related to cognitive processing [116,121]. In addition, rhythmic synchronization of all brain waves is critical in reviving memory [116,122,123]. Thus, EEG indices could be utilized for preclinical assessment of AD/ADRD and for therapeutic manipulation of targeted EEGs to prevent, halt or reverse AD/ADRD. Although many studies have demonstrated beneficial effects of music in AD, further investigation(s) and additional evidence(s) in this field are warranted to claim the significance and utility of music therapy in treating alzheimer's disease and/or other neurological disorders.

Conclusions

This review unravels the concept of musical brain and neurorehabilitative potential of music as a safe and non-invasive alternative therapy for treating neurodegenerative disorders with special emphasis on Alzheimer's disease. The structural, neurochemical and physiological basis of brain in exerting the health effects of music have been discussed detailing how structured sound language of music stimulates and integrates brain neuronal structures/pathways in a music-specific way. The role played by music in healing variety of health conditions has been reviewed along with supporting key anecdotal evidences. An improved understanding of the scientific foundation of music and its application using new technologies such as electroencephalography to monitor and modulate brain function(s) with musical exposure have been discussed. Although scientists and musicians have contributed significantly in these areas of investigation, clear correlation of Eastern/Western music compositions with neurooscillatory activity of normal and abnormal brain functions for its theranostic potential is not well-established yet. Further studies are warranted in proving music as a safe, non-invasive and effective therapy for neurodegenerative diseases including Alzheimer's disease.

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