The Neuroscience of Music Processing and Music Interventions for Mental Illness

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Abstract-Growing research on music and language processing in recent years has simultaneously enabled us to understand its uses and promise in therapeutic settings. This review used recently published peer-reviewed literature to study the neurobiology of music processing, which includes the auditory processing hierarchy and engagement with language processes. Results showed that music has an impact on emotion systems, particularly the reward pathway and the Hypothalamic-Pituitary-Adrenal (HPA) axis. Furthermore, listening to music or music therapy for the treatment of neurological diseases psychiatric and demonstrated effectiveness in improving patient outcomes. Overall, music processing is a sophisticated process with some similarities to language processing. Future randomized controlled trials are required to shed light on the neurocognitive aspect of music processing.

Keywords—music processing, music therapy, emotion, psychiatric disorders, neurological disorders, stress

I. INTRODUCTION

Music is one of the most complex sensory processes the human brain can understand. Research into the inner mechanism of music perception, its similarities and differences with language perception, and neurocircuitry associated with emotional and reward systems is still in its infancy, and many studies investigating the complexity of music suggest it may have therapeutic uses [1]. Recent findings have demonstrated many therapeutic uses, including regulation of mood, enhancement of concentration, decreased neurodegeneration, and management of stress [2]. The number of published research and interest in music's therapeutic uses has increased in recent years, as shown in Fig. 1, demonstrating the importance of the topic

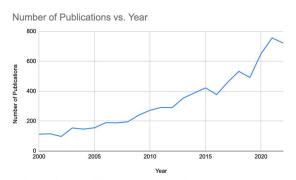


Fig. 1. The number of publications on PubMed using the search term "music therapy". A general upward trend is observed, starting from the year 2000 (112) and ending in 2022 (721).

Any auditory stimuli involve the auditory processing hierarchy, where lower structures pass information to higher structures to decipher increasingly complex sounds. This process starts with sound waves, which are funneled into the ear canal and reach the tympanic membrane to activate mechanoreceptors called hair cells, eventually passing a signal up to the primary auditory cortex through the cochlear nerve [1]. It is passed to the cerebral cortex where the sound as a whole is processed; parts of the sound, such as tone, pitch, and timbre, that were analyzed separately are combined and processed as a whole [1]. This signal is then transferred to various emotional pathways to influence mood, finally causing a behavioral effect, such as autonomic responses [1, 3].

While music and other auditory stimuli have similarities with regard to signal transduction and processing, music has additional complexity compared to other auditory stimuli: lyrics and melody. Currently, research supports that lyrics increase the emotional impact of sad music, but in happy music, the acoustic cues are more important compared to the lyrics [4]; this finding demonstrates how lyrics can influence the effects of music on behavior. Other studies have also investigated where different combinations of music are tested (changing the lyrics with the same melody, changing the melody with the same lyrics, etc.) and showed that different melodies influence word processing, suggesting that the processing of music and its lyrics are intertwined [5]. While processing lyrics might differ, understanding speech is a multi-step process: the stimuli from hair cells are delivered to the auditory cortex, which simply processes differences in speech frequencies and patterns; afterwards, this is sent to Wernicke's area, associated with language comprehension [6]. The auditory cortex also recognizes differences in pitch and tone, which helps analyze a song's melody [3]. Other aspects important to the comprehension of music include rhythm, memory, musical performance, and anticipating a certain pattern. All this information is processed as a whole by the cerebral cortex, where a potential emotional and/or physiological response is generated [1].

Many different systems are implicated in emotions, particularly the limbic system—a network that comprises the amygdala, hippocampus, thalamus, and hypothalamus [1]— and neurotransmitters. The amygdala is one of the most heavily researched, receiving sensory information, assigning an emotional value, and based on that sending signals to other parts of the limbic system, while also regulating anxiety, fear, aggression, and fear conditioning [7, 8]. It connects to the hypothalamus and the hippocampus, which play a role in homeostasis/neuroendocrine output and long-term memory respectively. Through these connections, the amygdala, based on the emotional intensity of a stimulus, can impact the body's hormones (physiological responses) and play a role in memory formation (high emotional value encodes the memory stronger) [8].

The mesolimbic pathway, also called the reward pathway, is part of the limbic system responsible for motivation. The Ventral Tegmental Area (VTA) activates dopaminergic neurons to multiple areas of the brain, most notably through the mesolimbic or the mesocortical pathway [9]. Here, a signal initiated at the VTA is passed through the dopaminergic neurons to the Nucleus Accumbens (NAc), the amygdala, the hippocampus, and the prefrontal cortex when performing or seeking a rewarding action (Fig. 2). The NAc encourages action (seeking out the rewarding action), the amygdala creates a sense of pleasure, and the hippocampus enables the brain to remember what or how to repeat the rewarding experience. Overall, this circuit assigns values to certain activities and prompts individuals to continue performing activities they find rewarding [10].

In this review of the published literature, the mechanisms by which music is processed and its promise in medicine will be investigated.

Dopamine Pathways

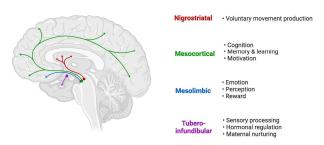


Fig. 2. An overview of dopaminergic pathways in the brain. The mesolimbic pathway, also called the reward pathway, connects the VTA to the NAc and the amygdala. The mesocortical pathway also plays a role in reward, connecting the VTA to the cerebral cortex [10].

II. METHODS

The research was conducted from scholarly sources including Google Scholar, the National Center for Biotechnology Information (NCBI), the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), Frontiers, and the National Institutes of Health (NIH). The search was mostly limited to papers published in English over the past 20 years that were focused on the following keywords for research: "music", "music therapy", "emotion", "auditory processing", "language", "language processing", "speech", Studies were included within the following criteria: (a) focused on language and music in human subjects, (b) focused on emotion and music, (c) auditory processing, (d) language processing, (e) music and neurological disorders, (f) music and psychiatric illness. The exclusion criteria were: (a) animal studies, (b) non-English papers, (c) theoretical papers, and (d) conference abstracts.

The figures were created using Biorender and Google Sheets.

III. DISCUSSION

A. Emotion

Studying emotional responses to music remains challenging due to discourse surrounding the meaning of emotion, and how to differentiate music-evoked changes in emotion from everyday life experiences. While emotion is difficult to define due to its subjectivity, here it is understood as the combination of affect systems (the brainstem, diencephalon, hippocampus, and orbitofrontal cortex) and effector systems (motor systems and physiological responses) [11]. A growing amount of evidence supports that music affects subjective feelings, physiological arousal, and motor responses (smiling, dancing, tapping, etc.) [12, 13]. A common consensus partly attributes the emotions evoked by music to the instinctual response activated by acoustic changes, such as a sudden change in volume or a fast rhythm [13]. Some studies suggest that the acoustic changes in music activate the 'brain stem reflex' and tap into our survival system, due to the similarities between acoustic changes (pitch, tempo, loudness, etc.) and acoustic signals in dangerous situations (predator noises, sudden loud noises, etc.) [13]. This triggers physiological responses and actions related to emotions (chills, goosebumps, tears, etc.). In support of this, a study where participants identified which music passage invoked the most physical emotional responses showed that new or unexpected harmonies and appoggiaturas (an unexpected note that delays an expected one) had the most effect, supporting this idea that unexpected changes affect emotion through our survival instincts [14].

Regardless of the underlying reason, much research supports that music affects regions that underlie emotion. A meta-analysis of functional neuroimaging studies reported certain activities in different parts of the emotional system, such as the amygdala, the hippocampal formation, the NAc, and the orbitofrontal cortex, while listening to music. In particular, the superficial amygdala, connected to human communication, responds to joyful or energetic music, which could be because music is seen as socially significant. Other brain regions include the hippocampal formation—which regulates the HPA axis and memory, the nucleus accumbens—part of the reward pathway that encourages action to obtain rewards, and the orbitofrontal cortex—which assigns the reward value of goals and is involved in controlling emotional behavior [12, 15].

Other research has focused on the effects of music on the dopaminergic pathways, most specifically the mesolimbic pathway [1]. Multiple studies using neuroimaging techniques have tried to investigate the activation of reward systems while listening to music, which have shown that pleasurable and chill-inducing music activates similar neural networks as other rewarding stimuli, such as food or sex [2].

Three studies used PET to investigate regional Cerebral Blood Flow (rCBF) during musical pleasure. In one study, rCBF of self-selected pleasurable music that induced chills was compared to neutrally-rated music, and the pleasurable music reported higher rCBF within mesocorticolimbic structures necessary for reward and reinforcement, such as the ventral striatum (importantly the NAc), the midbrain, the thalamus, cerebellum, and Orbitofrontal Cortex (OFC). The two other studies also reported NAc activation in unfamiliar pleasant music compared to rest, and in singing compared to speech [2]. Although PET has a low spatial resolution, these studies suggest that music that is considered pleasant or chillinducing activates the reward pathway in the brain.

Studies using functional Magnetic Resonance Imaging (fMRI) corroborate this conclusion. Some studies observed

activation of the VTA, NAc, and interactions between the VTA and other brain structures that regulate emotional, autonomic, and cognitive functions [2]. Ventral striatum activation was found in pleasurable and familiar music with deactivation of the amygdala and hippocampus [2]. While the hippocampus is known to regulate the HPA axis and inhibit stress [16], it's possible that this observed deactivation could relate to the modulation of cortisol by pleasant music. However, it's important to note that some of these PET studies reported increased rCBF in the hippocampus, contradicting the fMRI results, and thus this field requires more investigation. An upside to these studies is that both experimenter and self-selected music were used for pleasurable music, which allows for corroboration between studies that are "controlled" and studies that take personal preference into account.

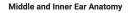
Besides neuroimaging studies, a limited number of studies have investigated neurotransmitter changes due to listening to music, which can contribute to therapeutic settings. Music has been shown to stimulate the release of dopamine in the reward system [2], and another study has directly observed the relation between dopamine and musical pleasure, where giving participants a dopamine precursor (levodopa, which increases dopaminergic availability) increases musicinduced pleasure [17]. Additionally, ligand-based PET scanning has enabled the measurement of dopamine during passages that reliably induced chills, where dopamine release was seen in the NAc, and dopamine release within the caudate was seen immediately before the passage that caused chills [18]. These suggest that not only is music related to pleasure, but also directly to neurotransmitter release, and thus music can directly modulate neurotransmission. Lastly, music has also been shown to modulate serotonin release; pleasant music releases more serotonin in the brain, while unpleasant music reduces the level of serotonin [19]. Many mental illnesses show relation to problems in neurotransmission, particularly depression and low serotonin [20], and methods to modulate synaptic neurotransmitter levels or stimulate more frequent neurotransmitter release should be investigated thoroughly.

Additionally, some studies show that relaxing music reduces stress levels, and can potentially be used for the treatment of anxiety and depression. Stress is defined as a neurochemical response to disruption in the system's homeostasis. This is caused by stress hormones, such as corticoids, released from the Hypothalamic-Pituitary-Adrenocortical (HPA) axis, which can be mediated by the hippocampus [21]. Heightened activity in this system is anxiety. associated with stress and Additionally, cardiovascular changes (elevated heart rate and faster breathing) help increase oxygen and glucose supply to both the brain and muscles, which starts the "fight or flight" response triggered by the catecholamines norepinephrine and epinephrine, regulated by the brainstem, central, and peripheral autonomic nervous system [2]. While stress and the fight or flight response are essential to human survival, prolonged stress might cause the activation to be chronic, linked to impaired cognitive functioning, higher susceptibility to infectious disease, anxiety, depression, and dementia [2], therefore mechanisms to regulate stress levels by effective means, such as music, can be beneficial. Across

many different studies, relaxing music has reduced cortisol [2] and norepinephrine [19], and a few studies have also measured the effect of energizing music. In three studies, energizing music increased cortisol and norepinephrine levels, corresponding to an activated HPA axis [2], but some studies show conflicting results. This, in part, could be attributed to the lack of standardization in experimenter-selected music, highlighting the necessity of clearer standardization in future research.

B. Hearing

Comprehension of music requires the transmission of signals from the other environment to the brain cortex. The outer ear funnels sound waves into the eardrum, stimulating the ossicular lever system which moves fluid inside the cochlea of the inner ear (Fig. 3). This stimulates the mechanoreceptors' hair cells which transduce the mechanical stimuli into electrical pulses [22]. Action potentials travel through the cochlear nerve towards the auditory brainstem, via the thalamus, and finally to a part of the temporal lobe called the primary auditory cortex [23]. Before the signal is sent to the primary auditory cortex, basic aspects of audio, including frequency, pitch, timbre, roughness, duration, and loudness of individual notes in a melody, are encoded [1, 23]. Music then engages with the higher parts of the auditory hierarchy in the primary auditory cortex. Successive processing stages include determining pitch height and pitch chroma, linking the current music to stored musical memories and knowledge, and deciding the behavioral response [1, 24]. A distinction between the lower and higher levels of processing can be shown through pitch: at the lower levels, the pitch is just the noise that correlates to a frequency, but at the higher levels, it could sound either 'bright' or 'dull', not to mention how the perception of that pitch might change once placed with many other sounds (in a chord, with patterns, etc.) [1, 24].



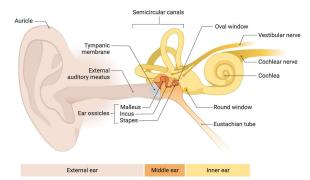


Fig. 3. A schematic overview of the middle and inner ear anatomy. Sound waves are funneled into the ear canal by the outer ear, hitting the tympanic membrane, vibrating the ear ossicles, and vibrating the fluid in the inner ear through the oval window. This reaches the cochlea where the organ of Corti (which sits above the basilar membrane) is disturbed by the vibration. Inside the organ of Corti, the inner hair cells vibrate and transmit the signal through the cochlear nerve to the brain.

C. Language Processing

Some recent research has found that music and language processing share many neural processes [25], and this review will summarize current findings with a focus on the relationship between language and musical processing. Anatomical regions responsible for language include Broca's area in the inferior frontal gyrus, Wernicke's area in the superior temporal gyrus, parts of the middle temporal gyrus, and some gyri in the parietal lobe (inferior parietal and angular gyrus) [26]. Across studies using different methods, all propose subdivisions of Broca's area into Brodmann areas 44 and 45. The inferior frontal gyrus, most importantly Broca's area, is known to support both language production and comprehension, but its specific role is not well understood. Results from different neuroimaging, neurophysiological, and behavioral studies have demonstrated that Broca's area supports action observation and execution, linking it to motor-based speech production and comprehension [26]. On a more specific level, neuroimaging studies also revealed that Broca's area supports verbal working memory because of increased brain activity in complex sentences. Lastly, some research attributes different roles in language processing to the two subdivisions of Broca's area, Brodmann areas 44 and 45, but those specific roles are also heavily debated [26].

Contrary to previous understanding that the Wernicke's area, commonly associated with the left posterior Superior Temporal Gyrus (pSTG), and Supramarginal Gyrus (SMG), is responsible for language comprehension, recent research has suggested it may rather play a role in speech production [27], a more specialized aspect of language comprehension [28], or concurs with previous convention. A study using PET analyzed brain activation during phonological processing, finding that there was greater activation of the left superior temporal gyrus, and other research suggests the Wernicke area is involved in speech production and barely involved in language comprehension [27]. Before language production, phonological retrieval must be done, which is where the speaker accesses knowledge about consonant and vowel speech sounds (phonemes) that form the spoken words. Studies using neuroimaging methods, such as fMRI, PET, and magnetoencephalography have evidence suggesting that the Wernicke area is involved in phonological retrieval, playing a large role in speech production [27]. Additionally, it highlights that lesions in the left pSTG and SMG impair a test of phonological retrieval, where patients were unable to differentiate if words that looked similar rhymed or not (e.g., snow and blow vs. plow), and notes that lesions in this same area weren't associated with a loss in word comprehension. However, it's important to note that this review focuses on lesions in the same area, the left pSTG and SMG, and thus may not be true for all of Wernicke's area [27].

While it was previously believed that Wernicke's area is exclusively involved with language comprehension and Broca's area with language production (though debates are ongoing), modern imaging techniques and research have shown that both areas are intertwined, possibly sharing the two roles between them [29]. The dual stream model proposes that Wernicke's and Broca's areas are connected through two fascicles: a dorsal and ventral pathway [26]. The ventral pathway processes speech to comprehension while the dorsal pathway supports sound to articulation [30]. Additional findings have suggested that there are two ventral pathways (ventral I and II) that run parallel and two dorsal pathways, from the temporal cortex to the premotor cortex (dorsal pathway I) and from the temporal cortex to BA 44 (dorsal pathway II). Dorsal pathway I is thought to mainly support sound-to-motor skills, while dorsal pathway II is involved in higher-level language processes [26]. This strongly suggests that Wernicke's and Broca's areas work in tandem to perform both language production and comprehension, rather than work individually on one each, which could help to explain the confusion surrounding the roles of Wernicke's and Broca's areas individually. Studies geared towards the more recent dual-stream model can clarify whether Wernicke and Broca's areas truly have individual functions, or they rely on each other to execute speech and language comprehension.

Current research examining the connection between music and language focuses mainly on musical ability and its relation to language perception. In a review done by Jäncke [31], two papers report that phonological awareness and musical ability are closely related and that musical training can increase phonological awareness. Other studies highlighted that native tone language speakers (e.g., Mandarin) are more sensitive to small pitch changes, tone deafness hinders pitch perception in language (especially in aforementioned tonal languages), and professional musicians process language differently than control groups [31]. A study by Wong et al. [32] found that in an unfamiliar language (Mandarin), musicians show a significantly more accurate encoding of pitch in the brainstem, showing that there's a subcortical connection and that musical training can affect linguistic capability. Still, research on this topic is limited, more so about passive engagement with music rather than active and how music listening may impact language processing or language acquisition. However, current research strongly supports an existing connection between the two processes, and further studies may be able to indicate an effect of passive listening on language, an interplay between language (lyrical) processing and music processing, or a three-way connection between music, emotion, and language that can be used to further the field of music therapy.

IV. MUSIC IN THERAPEUTIC SETTINGS

Current research supports that psychiatric disorders such as depression and anxiety would benefit from the emotional effect of music. Depression is a disorder often attributed to a lack of neurotransmitters leading to problems in neuron communication [20] and presenting with depressed mood, apathy, feelings of low self-worth, sleep difficulty, or anorexia, and in severe depression, suicidal ideation or attempt. Although its exact etiology remains unknown, as a common mental health problem, the World Health Organization reported that 350 million people have depression worldwide. Mossie, Kindu, and Negash [33] warranted investments to develop effective and non-invasive methods. Music listening differs from music therapy, not requiring a trained professional, and so can be done easily and inexpensively. Music listening has been shown to lower stress levels in depressive disorders [34], but much of current research's focus lies on music therapy as an alternative treatment or a supplement to other methods. While casual music listening may not be enough to treat depression, music therapy is a professional approach, where a qualified music therapist uses music to both improve mental health and boost the effects of concurrent treatments, such as medications [35]. Multiple studies show that music therapy is well-accepted

and successful for short-term mood improvements using the Hamilton Rating Scale for Depression [23], and significant effects are seen when paired with standard care [35]. Generally, music therapy for depression seems to be well-tolerated, shown through low dropout rates and improvements in mood, but a systematic review by Maratos *et al.* [36] suggests that current research struggles with a small number and low methodological quality of studies, decreasing confidence in its effectiveness as an alternative therapy. Therefore, more studies of higher quality on music therapy and depression, as well as further research to determine the cause of these effects, are needed.

Different anxiety disorders affect an estimated 33.7% of the population [37], but the most prevalent one is Generalized Anxiety Disorder (GAD). Anxiety is believed to result from abnormally heightened activity in the limbic system, specifically the HPA axis [38]. Relevant parts of the limbic system include the hippocampus, which modulates the HPA axis, the amygdala, and the hypothalamus, which regulates homeostasis and connects the nervous system to the endocrine system [39]. These hormones can control growth, metabolism, and mood, among other things. While anxiety is the most prevalent diagnosed disorder in the EU, only an estimated 20% of patients receive treatment, highlighting the need for cost-effective and self-administrable treatments [40]. In two systematic reviews and meta-analyses, the results suggested that music listening reduced anxiety with a large effect size, owing to music's capabilities as an emotion regulator [40, 41]. These findings suggest that music listening can be considered as an alternative treatment, and further research into its mechanisms of emotional regulation could help develop specific interventions.

While many different kinds of music interventions exist, the differences highlighted in Table 1, this review will focus on the therapeutic effect of passive music engagement (music medicine/listening and music therapy) rather than active (playing an instrument or group singing).

Table 1. Types of music interventions, a brief description, and the methods
of delivery

Type of Intervention	Description	Mode of Delivery	Reference
Music Medicine	Listening to pre- recorded music to improve health	Given by healthcare professionals	[42]
Music Therapy	A systematic intervention where the therapist helps the client using tailored music experiences	Given by a certified music therapist	[43]
Other Music Interventions	Musical activities for health promotion or recreation	Healthcare workers, non- professionals, self-administered	[42]

V. CONCLUSION

Music, with its ability to activate the reward system and reduce stress, holds promise as an alternative noninvasive treatment for many psychiatric disorders; passive music engagement is inexpensive, has a low chance of negative effects, and is easily integrated for patients which reduces the chances of discontinuation. Besides being used on its own as treatment (music therapy) it can also be used concurrently with other therapies like medications to heighten the effects. Current research outlines that while music affects emotion, and newer studies demonstrate a music-language relation, there exists no established pathway that connects music, emotion, and language. More research into their relations might reveal additional uses of music therapy, such as in language development disorders.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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