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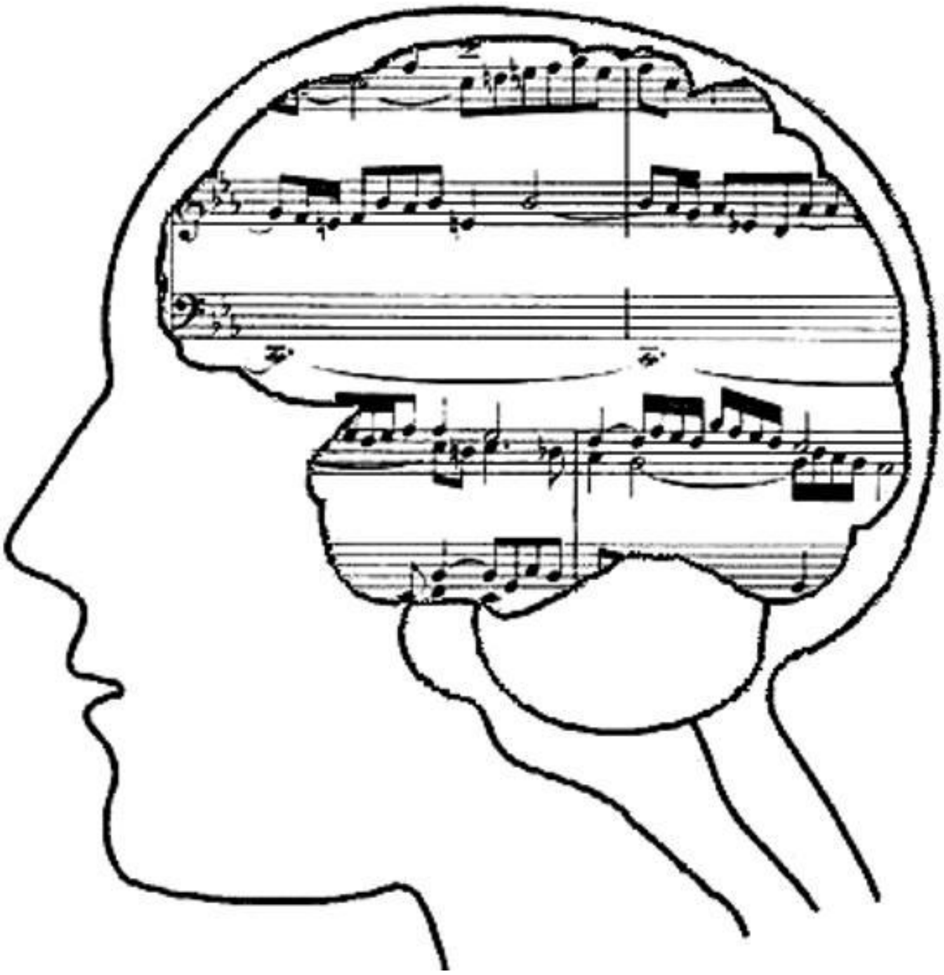
The musical brain

How music evokes emotions and related positive feelings



Without music, life would be a mistake.
–Friedrich Nietzsche

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Abstract

The power of music in eliciting physical reactions has been known since the ancient Greek cultures. The mechanisms behind it however, have long been unclear and are only just recently being unraveled. Numerous brain imaging studies have shown an increase in regional cerebral blood flow in the limbic system during self reported pleasure and strong physiological reactions, called chills, while listening to music. Actual feelings of reward can be evoked by music via dopamine release related activity in the nucleus accumbens, part of the limbic system. Different mechanisms could be responsible for eliciting feelings of reward and pleasure, such as violations of expectations of musical syntax, associative mechanisms or musical contagion. The idea that the strong positive effects of music can be of therapeutic use has lead to music being used as therapy in the Unites States since the forties. The ability of music therapy to relieve depressive symptoms as well as sustaining active patient involvement makes it an interesting method for treating depression. But the current main issue in depression is not necessarily failure of recovery, but the risk of relapse after recovery. Deficits in the hippocampus, amygdala and prefrontal cortex are suggested to correspond to deep-seated cognitive vulnerability, which is an important factor contributing to relapse. Music has been shown to modify these brain structures. Therefore, in the current review, music is proposed as source of self therapy for ameliorating depressive symptoms in order to prevent relapse.

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Introduction

"Music is all around us, all you have to do is listen"[1]. These words illustrate how simple it can be to benefit from the beauty of music. Everybody knows that listening to music can be fun. But not many people realize the effects it can actually have. It can ruin the atmosphere, when slow and sad sounding, or it can give a boost during rave parties, where music is often fast and happy sounding. If you have ever watched a thriller with the sound turned off, you know how important music is in creating suspense.

However, even if you were not aware of this, music is most probably a part of your life. As it has been part of human life ever since the first person started making drum sounds, thousands of years ago. Since it is has been around us for so long and it can be useful as well as pleasant, it comes as no surprise that extensive processing occurs in many different parts of the brain when one listens to music. Certain characteristics of music can rapidly activate structures in the brain stem. This activation triggers the sympathetic nervous system which has physiological effects such as a rise in blood pressure and an increased heart rate. Other features of music can lead to dopamine release in the limbic system, thereby triggering feelings of happiness. Those evoked emotions can be very strong, intense feelings of pleasure accompanied by bodily sensations such as shivers down the spine. By activating the limbic system, listening to music can actually be rewarding, similar to the rewarding effect of drinking water after a long period of thirst. [2-4]

In fact, the power of music in eliciting physical reactions has been known since the ancient Greek cultures.[5] The mechanisms behind it however, have long been unclear and are only just recently being unraveled with the use of brain imaging techniques. The idea that the strong positive effects of music can be of therapeutic use dates many years back. The earliest known reference to music therapy in the United States was in 1789 in an unsigned article in the Columbia Magazine titled "Music Physically Considered". Although not solely for its effect on affect, music is already being used as therapy in the Unites States since the forties.[6] It is applied with different objectives in many different disorders, such as ameliorating social skills in autism, relaxing the body in mentally disabled people with movement disorders and reducing depression in various mental disorders. Music therapy has been found to be particularly appropriate to treating major depression disorder, because patients are less likely to drop out in this kind of therapy.[7] Absence of will to participate in and accept therapeutically intervention is a major problem in this disorder.[8] The ability of music therapy to relieve depressive symptoms as well as sustaining active patient involvement makes it an interesting method for treating depression. Although clinical improvement by music therapy in depressive disorders has been shown, it is hard to establish what exactly causes this improvement. Confounding factors such as social interaction and the act of making music make it difficult to measure the effect of music itself. Also, music therapy alone has not been shown to ameliorate symptoms, it is always in combination with medicines and/or speech therapy.[7]

Moreover, treating major depression in the acute phase is not the essence of the problem anymore. Many patients benefit from existing anti-depressive drugs and therapies. After full remission, they are able to recover and function again in society. The issue that needs attention here is the matter of high risk of relapse after recovery. Three quarters of patients suffering from depression experience more than one episode of depression. And the more episodes are suffered, the more likely patients are to relapse again after recovery.[9] After full remission from depression, people will have to participate in society again, as before. Not seldom, they will have to deal with more stress inducing events than they are able to cope with, leading to depressive symptoms such as depressed mood, low energy and loss of interest. Without the help of a therapist or therapy they need to find a way to ameliorate those symptoms in order to prevent themselves to relapsing into a true depression. As Bockting, Spinhoven, Wouters, Koeter & Schene (2009)[10] report, an important modifiable predictor of relapse was a lesser capacity to refocus on positive matters. The quality of music to induce positive feelings, in combination with the fact that one can apply it at anytime, anywhere and that it has no detrimental side-effects, in contrast to the only alternative self-therapy of anti-depressive drugs, makes it an interesting source of self-therapy.

Interventions targeted towards prevention of relapse have recently received increasing attention. But current interventions targeting prevention of relapse, such as cognitive-behavioral and mindfulness-based therapy, are indicated to only influence the surface-level of negative thinking. These are automatic thoughts developed through assumptions about and attitudes towards the environment. As the thoughts are integrated into a depressed scheme about the world, which serves to distort reality and allows the person to maintain negative thoughts, influencing only the automatic thoughts, will ultimately not help the person.[11] In contrast, music has been shown to evoke activity changes in certain brain regions and neural circuitry implicated in emotional processing.[12] Deficits in these regions are suggested to correspond to deep-seated cognitive vulnerability, because they contribute to maladaptive behavior such as affective processing bias or feedback sensitivity, ultimately causing the mentioned depressed scheme.[13] And it is exactly this deep-seated cognitive vulnerability that should be targeted, as this is an important factor contributing to relapse or even worse, suicide.[8]

From sound to music perception

Up until now, music has been referred to as a homogenous entity that is able to evoke emotions in the listener as such. Yet, music is composed of several properties that together define the style of a musical piece. These properties are processed separately in (sub)cortical areas of the brain. In order to elaborate on the physiological and psychological effects that music can have on people, an overview of the different parts of the brain that are involved in processing the different aspects of music is needed. Subsequently, the properties most important for influencing affect can be defined.

The French composer Edgard Varèse invented the term “organized sound”, to describe music. As such, music is a composed of multiple simultaneous and/or sequential tones. The sound of a tone is propagated through air as a sequences of waves of pressure. This mechanical energy of sound is translated into electrical signals by the inner part of the ear, the cochlea. In an ascending path from the cochlea to the primary auditory cortex (see figure 1), all the basic acoustic properties of music such as pitch, duration and loudness of the individual notes are encoded (for a more detailed explanation of the central auditory pathways from cochlea to the auditory cortex, see Kandel, Schwartz & Jessell, 2000[14]). After reaching the primary auditory cortex, the different properties of music are processed more specifically in distinct parts of the brain. These are located around the primary auditory cortex. Music is thus processed as sound with distinct characteristics. Only after integrating the different elements again, one is able to perceive music as such and be aware of the effects it has on oneself.

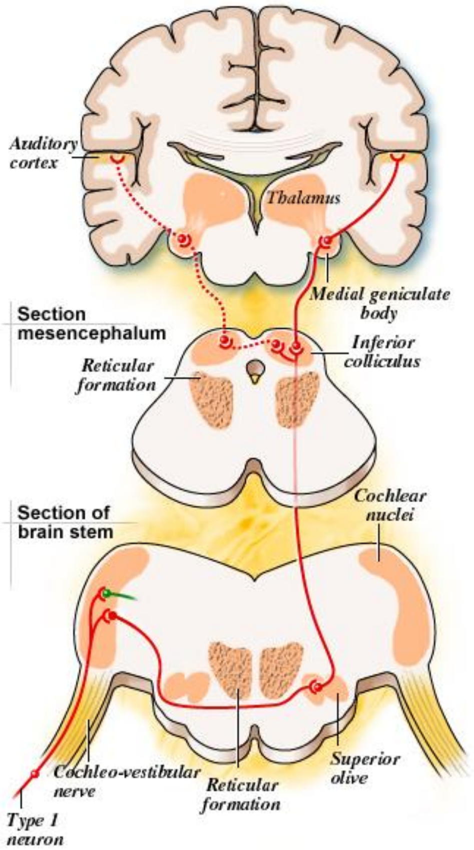

Figure 1.[15] Schematic picture of ascending auditory pathway from brainstem via midbrain and thalamus to auditory cortex.

The primary auditory cortex is situated in the superior temporal lobe in Heschl's gyrus (HG). Surrounding it are several secondary auditory fields. From these first and secondary auditory areas, two-way connections exist throughout the brain. This complex network makes association and feedback possible between different perceptional and motor areas.[16]

The property of music that is probably most extensively investigated is pitch. Together with timing aspects (tempo, rhythm), it defines the melody of music. Furthermore, one can distinguish loudness or intensity and timbre.[7, 16] Pitch will be described in more detail because it is the most important factor in the evoked emotional responses by music. The remaining three features will be briefly explained, since they can contribute to eliciting responses as well.

Pitch

Pitch is the perception of the frequency of a sound. The primary and secondary auditory areas of most mammals contain a tonotopical organization, where pitch is organized from low to high,[17] similar to the tonotopical map in the cochlea.[14] In figure 2, a tonotopical map generated in the chinchilla, is depicted. A similar organization exists in humans. This allows for the encoding of sound frequency, or pitch height. Pitch perception comprises not only absolute pitch of individual tones, but also relative pitch toward other tones.

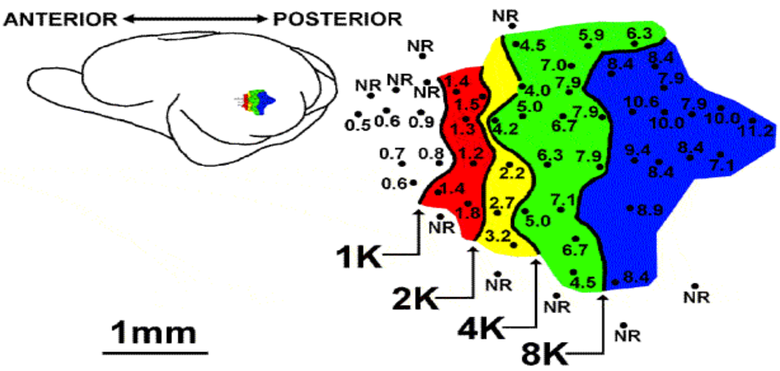

Figure 2.[18] Recorded voltage spikes from neurons responding to specific frequencies, generating a tonotopical map in the brain of a chinchilla. The numbers represent the frequency of stimulus to which the neurons in that immediate area are most sensitive. 1-8K = 1000-8000 Hertz. NR = not reported

Absolute pitch is processed in *Heschl's gyrus* and *posterior regions of secondary auditory regions.*[17] Whereas tonal relations such as intervals, which are distances in pitch height between tones, as well as pitch contour, which are the up- or downward movements of tones, are processed in the *superior temporal gyrus (STG) and planum temporale (PT).*[19] Pitch also defines the tonality of a musical piece. In Western music, the most important distinction is between major and minor tonalities. The major tonality is usually seen as happy or cheerful and minor as sad or unhappy. The pitch relations between the tones of a chord determine the tonality. Minor and major tonalities elicit activation in the *inferior frontal gyri*, *the dorsal cingulate cortex* and in a part of the ascending pathway, the *medial thalamus*. The dorsal cingulate cortex is suggested specifically to be involved in differentiating the modalities.[17]

Several areas have been shown to be selectively active during minor tonalities: *the amygdala, retrospenial cortex, cerebellum, parahippocampal gyrus, ventral anterior cingulate cortex, left medial prefrontal cortex and* in the *brain stem*.[17]

Pitch furthermore defines whether composed tones or sequences of tones are consonant of dissonant. In a consonant composition of tones, the tones are in harmony. Harmonic relationships of tones are described in the circle of fifths (see figure 3). The closer the keys, the closer their harmonic relationships. This is because they have most of the scale notes in common, causing the least interference of the tones. This is experienced as pleasant to hear. Consequently, dissonant compositions are experienced as unpleasant.

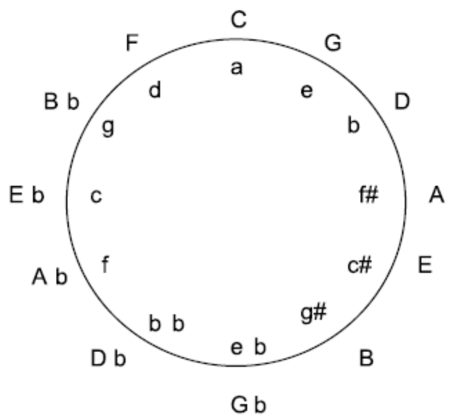

Figure 3.[20] Circle of fifths. The letters in the outer circle represent the major keys and the adjacent letters in the inner circle represent the minor keys. b = flat, meaning depression of the tone by half a degree, # = sharp, meaning elevation of the tone by half a degree.

Timing aspects

The perception of rhythm involves structures in the *cerebellum, (pre)supplementary motor area (SMA) and the basal ganglia.*[16] The cerebellum also attributes to our sense of tempo. Additionally, when rhythms with accents at regular intervals are perceived, the *anterior superior temporal gyri* show greater activation as well.[17] Pitch and the duration of a tone together define the melody of music. After they are processed seperately, they are integrated together with loudness to give us the impression of a fully realized musical piece, as stated by Levitin & Tirovolas (2009).[17]

Loudness

Loudness or intensity is a contextual aspect that contributes to evoking chills (a physical, as well as an emotional reaction to music that will be discussed to more detail later on) in listeners. This feature is already pre-processed in *the brain stem*,[19] but it is not clear what area, if any, of the auditory cortex is involved in processing it further.

Timbre

The distinctive sound of a voice or instrument is called timbre, or tone quality. The *STG* and *PT* are implicated in the processing of timbre.[7, 16] These are overlapping areas with the processing of pitch.

True emotions?

Before elaborating on how emotions are evoked in the brain, an issue that needs some attention first, is the ongoing debate about whether music can evoke actual emotions. Some researchers, referred to as 'cognitivists' consider the responses to music as purely aesthetic and rarely, or never, emotional. According to them, one can appreciate a musical piece, which will give pleasure, but this will not elicit a true emotion.[21] Others, the so-called 'emotivists', claim that music can elicit true, basic emotions such as happiness or sadness.[22] Yet another group are of the opinion that music can indeed evoke emotions, but that these are not the same emotions as the ones we experience in everyday life. As they claim, basic emotions occur only in reaction to an event that is to influence one's goals. For instance, a good grade for a test would elicit happiness, since it will contribute to the goal of graduating. According to these 'non-emotivists', listening to music could not evoke such a response, because it does not have any capacity to further or block goals.[22] A view that Koelsch (2010)[2] challenges by pointing out the social functions of music, some of which are to facilitate making *c*ontact, to engage social *c*ognition and being a means of *c*ommunication. As Koelsch (2010)[2] states, music does serve a goal in this regard, namely the goal to fulfill social needs that are of vital importance for the individual.

To be able to recognize and reliably research emotional responses, a clear description of emotion is needed. Lundqvist, Carlsson, Hilmersson, & Juslin (2009)[23] state that emotions are manifested in three different, measurable components: experience, expression and physiology. A view on which many researchers agree and one that therefore will be adopted here. Experience is the component that is least easy to objectify, since it is defined as subjective feelings such as happiness or pleasure described by the listener. Expression is the behaviour that the emotion leads to. Examples are facial expressions such as smiling or frowning. The physiology comprises bodily functions that are (dis)activated. This component is the most reliable representative of emotion, since it are mostly responses of the autonomic nervous system, under unconscious control. Changes in skin conductance and heart rate are some examples. Also, brain imaging techniques such as position emitron tomography (PET) and functional magnetic resonance imaging (fMRI) make it possible to visualize activity in the brain, which is part of the physiological response as well.

In the discussion about the ability of music to evoke actual emotions, the fact that music processing employs an extensive network in the brain in which many different brain areas are involved is not a point of debate. However, the suggestion of a clear division in the brain between music perception and emotional processing of music, is an emotivists view. A double dissociation between music perception and emotional processing is found in brain damaged patients. A patient has been described that had impaired recognition of music but still had a affective response to music.[24] Inversely, a patient whose musical processing was intact after brain damage, but who did no longer have the emotional response appears in the clinical literature as well.[25] These cases point to the existence of two different pathways. A music processing pathway that involves parts of the temporal and frontal lobes. And a emotional pathway involving limbic structures, insula, ventral striatum and thalamus.

It should be noted however, that the affective response of the first patient was not an emotional response in the patient evoked by the music. The research only tested whether the patient was able to recognize happy versus sad emotion in the music. And this represents the aesthetic response of which the cognitivists speak. This does not necessarily mean that the music did not evoke a true emotional response in the patient, only that none is mentioned.

In contrast, the results of Lundqvist et al. (2009)[23] do seem to reflect true emotional responses in listeners. They show that happy music generated more activity in the facial muscle that is used when smiling, greater skin conductance, lower finger temperature, more self reported happiness and less sadness than sad music. Several others have reported changes in pulse, respiration, heart rate, skin conductance, motor patterns, neuroendocrine response, and even immunological function induced by music.[26] However, as Konečni (2008)[21] points out, these emotional reactions are not necessarily evoked by the music directly. The measured responses could be influenced by confounding factors. Musical pieces could be familiar for instance, evoking a response to a memory associated with the music. Or the responses could be a reflection of the emotion perceived in the music and not an evoked response in the listener itself. But what he does conclude, is that emotions can be evoked, even though he prefers to call it moods and be it via key cognitive events. So even if it starts as an aesthetic experience, music can influence your mood and evoke emotions, through mechanisms such as association in which a musical piece brings back a memory with associated feelings. This will be explained in more detail in the section 'How music evokes emotion'.

Despite the ongoing debate whether music is able to evoke emotions directly and if these emotions are actual real life emotions or rather changes in mood, much research has been done concerning activation in the brain during listening to music.

Numerous brain imaging studies have shown increases in regional cerebral blood flow (rCBF) in the *limbic system*, an extensive circuit thought to be involved in reward and emotion during self reported pleasure and strong physiological reactions called 'chills', feelings as shivers down the spine, while listening to music.[27] These chills are frequently used in research to objectify experiences of pleasure, because they are accompanied by an activation of the autonomic nervous system, measurable as increases in heart beat and respiration frequency for example. The limbic system includes areas in the *dorsal midbrain, ventral striatum* (mainly the *nucleus accumbens (NAc*)) and *insula.* The *orbitofrontal cortex* is strongly associated with it, as a paralimbic cortical area[27] (see figure 4).

Salimpoor, Benovoy, Larcher, Dagher, & Zatorre (2011)[33] showed that intense pleasure in response to music can lead to dopamine release in *the striatum,* particularly the *NAc,* which is in the *ventral striatum*. As Menon & Levition (2005)[4] showed in their study, the *VTA* mediates activity in the *NAc, hypothalamus, insula,* and *orbitofrontal cortex* (see figure 4) while participants reported pleasurable experiences during music listening. Hence, activation of the *VTA* in response to music leads to dopamine release in the *NAc*, through the mesolimbic pathway. Activation in the *NAc* correlates with motivation- and reward-related experiences of pleasure elicited by biological drives such as sexual activity or drinking water when dehydrated.[2] Thus listening to music could elicit actual feelings of reward via biological responses.

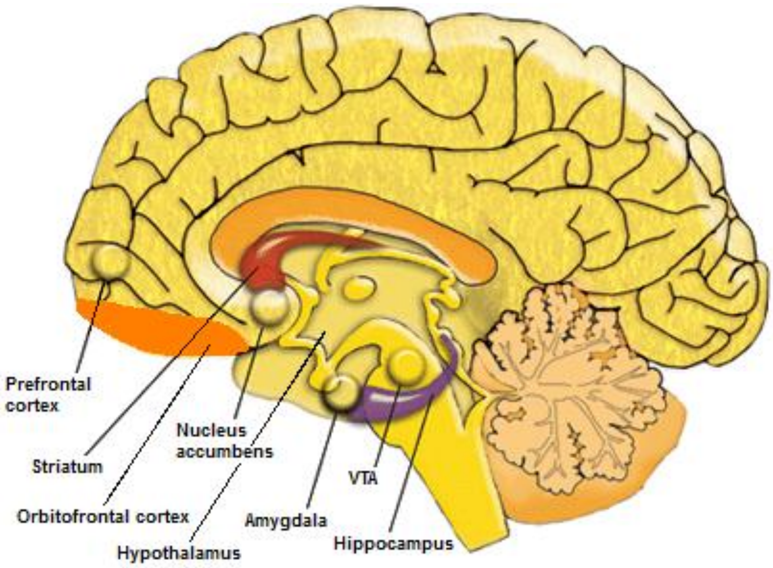

Figure 4 (adjusted from Clapp, Bhave, & Hoffman, 2009[28]).
Schematic picture of (sub)cortical structures of the limbic system.

The activation of the core structures of emotional processing in the brain, in response to listening to music, together with the strong physiological chill responses and self reported feelings of happiness show a definite effect on emotion, whether it is similar to a real life emotion or not. And for the sake of this article, perhaps it is not so much a matter whether actual genuine emotions are evoked, as long as positive feelings are evoked and an uplift of mood is accomplished. The point of debate that has implications though, is how exactly these positive feelings arise. In the next section several mechanisms via which music can evoke emotions are outlined.

How music evokes emotions

Now that a definite effect of music on emotions is demonstrated, the question arises, how could this effect be employed in order to accomplish an uplift of mood? Simply listening to happy music does not necessarily effect negative affect positively.[7] To be able to benefit from the mood uplifting effects of music, the mechanisms underlying the ability of music to evoke feelings will have to be clarified.

Direct, strong reactions evoked by potential danger signals

Before reaching the conscious level where tonal information is perceived as music, this information can already evoke physical reactions and emotional responses because some pre-processing occurs during the ascending path. *The superior olivary complex* in the brain stem and the *inferior colliculus* in the midbrain (see figure 1) show different neural responses to elements such as pitch, timbre, intensity and interaural disparities.[19] Certain sound qualities are indicative of change, such as sudden or extreme sounds, and therefore interpreted by the brain stem as a sign of a potentially important and urgent event. The reticular formation, comprising of several nuclei in the brain stem, can quickly cause an aroused state of the body so that the organism can respond accurately to the potential danger that is indicated by the sound. The increased activation of the sympathetic nervous system will lead to several physiological reactions such as increased heart rate, and increased motor responses.[22]

From the thalamus, all the basic acoustic properties of music are projected to the auditory cortex. But the thalamus is also directly connected to the *amygdala*, an area involved in processing of emotion and control of emotional behavior[19] (see figure 5). This direct connection will lead to an activation of emotions already before cognitive processes have taken place. Feelings of tension or unpleasantness may be evoked.

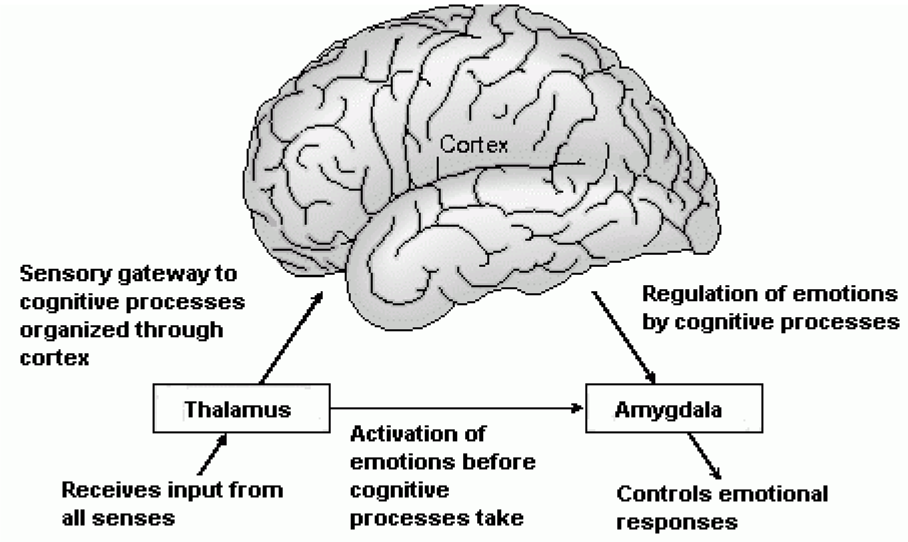

Figure 5.[29] Schematic representation of the direct connection between thalamus and amygdala.

Activation and relaxation

Still, the evoked arousal by music is not always experienced as unpleasant. Several studies have reported concurrent self reported pleasure and strong physiological reactions called ‘chills’, feelings as shivers down the spine, while listening to music. These chills are accompanied by an increased activation of the sympathetic nervous system, showing an aroused state of the body.[27]

The increased activation is probably the result of interaction of the thalamus with the hypothalamus-pituitary-adrenal-axis (HPA-axis). Apart from influencing the sympathetic nervous system, this interaction can affect the parasympathetic nervous system as well.[30] That way, musical input can lead to activation as well as relaxation.[31] Although not directly responsible for evoking an emotion, these responses can give rise to positive feelings. Either through feeling activated when one felt passive and apathic before or through feeling more relaxed when one felt highly stressed before.

Wish, expectation and reward

As mentioned before, music has the potential to elicit feelings of reward. Combining the temporal resolution of fMRI and the spatial resolution of PET scanning, Salimpoor et al. (2011)[3] were able to visualize dopamine release in the Nucleus accumbens (NAc) during peak emotional response, showing the underlying neurobiology. But if a sense of pleasure towards a reward is evoked, one would expect a sense of wanting or expectation to precede these feelings. Salimpoor et al. (2011)[3] showed interesting results regarding this issue. In his study, participants listened to music that induced chills while five indicators of activated sympathetic nervous system were measured: skin conductance, temperature, blood volume pulse amplitude, heart rate and respiration frequency. Participants had to indicate when they felt chills as well as the intensity of the chills. Results show a correlation of all five measurements with reported intensity of chills, suggesting that the report of the highest intensity of chills can be used as a marker of peak emotional responses. This makes a relative accurate timing of brain activation measurements possible. This way, he was able to indicate a release of dopamine anticipating this peak pleasure moment. The dopamine activity was demonstrated to be in the caudate, part of the dorsal striatum. Which makes it relevant, since the dorsal striatum has been associated with expectation and anticipation of a reward. The structure has connections with sensory, motor and associative regions of the brain and has been typically implicated in learning of stimulus-response associations.[33] Studies have shown release of dopamine in the dorsal striatum upon exposure towards contextual cues for rewards such as food and smoking.[32, 33] In conclusion, there seems to be a distinction between a wanting and a liking phase. Certain aspects of a musical piece may trigger a sense of expectation and the wish for resolution (wanting). As the music continues in the expected way, this brings feelings of relief and satisfaction (liking).

But why would music elicit a feelings of expectation and reward? For something to be rewarding, it should first be desired. Drinking water does only evoke feelings of intense pleasure if you were dehydrated before. The answer can be found in the structure of the music itself.

Music is composed of sentences where notes and chords are grouped in an orderly fashion, giving rise to a musical grammar or syntax. Harmonic regularities and meter are some examples of such orderly grouped elements.[17] The musical style used in musical pieces is culture bound. In Western culture for example, we are used to the harmonic relatedness of tones described in the circle of fifths.[20] After being exposed often enough to the musical style of one's own culture, people are conditioned to it. They implicitly learn which tones or sounds are most likely to follow each other in musical sentences. Already at age 5 a child is able to detect changes in key and harmony.[17] Neurophysiological studies using EEG and MEG have shown that music-syntactic violations elicit anterior brain responses called "early right anterior negativity" responses or ERAN, and negative voltage responses approximately 500 ms after the event, known as the N5.[17, 19] The outcome of this measurable syntactical processing is important for processing meaning (see 'meaning' below) and emotion. The violation or delay of expectations of the syntactical structure in music can evoke surprise for example.[19] The subsequent resolution of the violation or delay can lead to feelings of relief, relaxation and pleasure.

As the dorsal striatum is interconnected with many associative regions of the brain, the release of dopamine could be an indication of something other than a detected violation of expectation and associated will for resolution. It could also reflect the associative mechanism mentioned before, that is needed to evoke positive feelings according to Konečni (2008).[21]

Associative mechanisms

A musical piece may evoke positive feelings because it has been paired repeatedly with something that makes you happy.[22] Hearing the theme song of a series might make you happy for example, because the series does. As such, the dopamine release prior to peak pleasure might represent the reactivation of previously made connections between music and event.

The repeatedly pairing of music with positive events and related positive feelings is called evaluative conditioning.[22] This is a mechanism that can occur on a subconscious level, with the person being unaware of the coupled music and event. When listening to music evokes the conscious recollection of an event preserving much contextual information, this is seen as a different mechanism by some,[22] involving episodic memory. Activation of the hippocampus, indicative of memory processing, has been associated with it.

These associative mechanisms do *not* represent processes in which elements of the music itself evoke feelings in the listener, which does apply to the violation of expectations in musical syntax described before. Two more mechanisms where it *i*s the music itself that is thought to evoke feelings in listeners, are emotional contagion and meaning.

Emotional contagion

In the process of emotional contagion the listener is thought to mimic the emotion that is carried out by the music internally, which could lead to the actual induction of emotions.[22, 23] This process has been experimentally shown in the visual field, where people watching pictures with different facial expressions activated the same facial muscles in themselves needed to mimic the emotions.[3434] So called "mirror neurons" are suggested to be involved in emotional contagion. These specific neurons have been found in monkeys to be active when performing an action as well as when looking at another monkey performing the action.[35] Koelsch, Fritz, Cramon, Müller, & Friederici (2006)[36] showed in an fMRI study that brain areas related to a circuitry involved in vocal sound production where activated in response to music listening. This could represent a neural mirror-function mechanism responding to certain expressive acoustical patterns often found in music. These patterns are similar to patterns that occur in emotional speech. Possibly these voice-like aspects could evoke emotions in us by means of such a mirror mechanism.[22]

Meaning

All of the four aforementioned properties of music, timing aspects, loudness or intensity and timbre, contribute to the impact or influence a musical piece has on its listener. They can, individually or in certain combinations, give meaning to music. Usually, meaning is a concept that is given to something by someone. But music can be inherently meaningful because certain combinations of the basic elements can trigger reactions in the listener. The combination of slow rhythm, relatively high pitch and soft, warm voice used in lullabies for instance can be southing and consolidating.

Different mechanisms are responsible for the meaning music might have to someone. Patterns in music can imitate common gestures or prosodic features (patterns of stress and intonation used in language), combinations of tones and chords can mirror an emotion, it can be associated with something (an anthem for instance) or an expectation pattern in syntax is disrupted and resolved[19] (as explained before).

Some think that part of the reason why music can be meaningful, is because it is used as a way of communication between the creator and the perceiver of the music. Structures such as *anterior medial frontal cortex, superior temporal sulcus and the temporal poles* are automatically engaged while listening to music. These are areas normally involved in social and emotional perception, so called 'mental state attribution',[17, 37] indicating an attempt of the listener to understand the intentions the music creator had with the music.[7]

Similarities have been shown in music processing and language processing, as well as overlapping brain areas involved in it. This also suggests that music may have communicative features that contribute to the meaning music can have. For instance, in a recent EEG study,[38] short musical excerpts were followed by the presentation of a target word that was semantically either related or unrelated to the musical excerpt music. Activation in the *right temporal lobe* was measured and an event-related potential, N400, elicited by the musical excerpt followed by the unrelated target word. The N400 is a classic electrophysiological marker of semantic processing.

As mentioned before, violations of musical expectations in music can evoke emotional reactions. These violations invoke the activation of *Brodmann area (BA) 47* and *Broca's area*; areas of the brain implicated in linguistic syntax. Likewise, *BA 47* and *the anterior insula* have been shown to be involved in the perception of musical disruption.[17] The emotional reactions elicited by it, could make music meaningful.[19]

Some musical tunes have meaning because they are well known and perhaps associated with certain context (in the case of a song used in a commercial for example). When it comes to recognizing a familiar tune the anterior superior temporal gyrus and insula are involved.[16] Furthermore, it is not only combinations of tones that can be meaningful. Even a single tone could convey meaning information, sounding bright, dull, or warm for example.[19]

In sum, many different mechanisms involving varies parts of the central nervous system as well as endocrine components are responsible for the emotion evoking effects of music:

- Pre-processing in the brain stem can lead to fast physical reactions to loud and unexpected sounds. These sounds trigger activation of the HPA-axis trough connections with the thalamus, inducing the sympathetic nervous system. Next to these activating effects, music can have relaxing effects as well, affecting the parasympathetic nervous system. The thalamus functions as a relay system and can therefore also trigger emotional responses via its short wired connection to the amygdala, before the sound reaches consciousness.
- Release of dopamine in the dorsal striatum and shortly after in de ventral striatum supposedly reflects a sense of wishing, expectation and reward that is triggered by music. The activation of the striatum might also be linked to activation in the hippocampus, implying associative mechanisms in which music is connected with context or events in the past that are experienced as pleasant.
- So called mirror neurons could be involved in a neural mirror-function mechanism responding to certain expressive acoustical patterns often found in music, leading to emotional contagion.
- Finally, the frontal and temporal lobes are engaged when meaningful features of music are attended to. Such features could be patterns in music that imitate common gestures or prosodic features, combinations of tones and chords mirroring an emotion, or the disruption of an expectation pattern in syntax for example.

As should be clear by now, music can influence a person's mood in many different ways. Even though many people are aware of the eventual uplifting effect musical pieces can have, this effect is mostly established by processes in the brain they are unaware of. A resemblance can be found in depression. Depressed people know that they are down but they are not aware of the altered brain processes that make them vulnerable for depression. Pathophysiology has been implicated in multiple sectors of the PFC, the striatum, amygdala and hippocampus. [13, 39]

This altered processing contributes to maladaptive behavior such as affective processing bias or feedback sensitivity.[13] Affective processing bias in this context means the tendency to focus on negative aspects of the environment. Feedback sensitivity exhibits itself as exaggerated responses to negative feedback and ruminating over perceived failures and criticism. One can easily deduct how such maladaptive behavior can make someone vulnerable for depression. Constantly focusing on negative components in the outside as well as the inside world, is not constructive and will have its effect on ones mood. Functional changes in mentioned brain areas, contributing to this behavior, are shown in depressed patients.[13] Indeed, these regions are targeted in established treatments for depression such as pharmacotherapies and pshychotherapies. What's more, those functional changes can also persist into periods of remission,[13] making them a target for relapse prevention. Especially since activity changes in response to music have been shown in mentioned areas. In the next section, the main areas that are thought to be involved in depression will be outlined, followed by the effect music can have on them.

Considerations for future research

- The release of dopamine in the dorsal striatum anticipating peak pleasure might be representative of the ERAN response that is measured by EEG and MEG. As a suggestion for future study it would be interesting to measure the ERAN as well as the dopamine release in the dorsal striatum to see if both represent the same response of surprise.
- In order to determine which part of the brain could be ascribed to the emotions evoked by associations, responses including ERAN, dopamine activation and chill intensity, from participants listening to known musical pieces associated with positive events could be compared to responses to unknown musical pieces.

Depression: definition and brain areas thought to be involved

According to the WHO, depression is among the leading causes of disability worldwide. It is a common disorder, with a prevalence of 121 million people worldwide, affecting all genders, ages, and backgrounds. Although antidepressant medications and psychotherapy are effective in 60-80 % of the cases,[40] the disorder has a high risk of mortality and a tendency towards chronicity.[9] This is due to the high chance of relapse. Three quarters of patients suffering from depression experience more than one episode of depression. And the more episodes are suffered, the more likely patients are to relapse again after recovery.[9] In order to define the applicability of the beneficial effects of music listening towards depression, some insight into the disorder and the brain areas suggested to be involved is necessary.

The symptoms of a depression, according to DSM-IV[41] are:

- Depressed mood most of the day, nearly every day
- Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
- Significant weight loss, when not dieting or weight gain
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- Diminished ability to think or concentrate, or indecisiveness, nearly every day
- Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide
- attempt or a specific plan for committing suicide

The brain areas that are thought to be involved in depression and therefore extensively studied are the prefrontal cortex (PFC), the amygdala and the hippocampus. The amygdala have been implicated in the tendency to ruminate, a characteristic feature that is often seen in depressed patient. Also, abnormal activation of the amygdala would correlate with the severity of the depression.[42, 43] Depressed patients tent to either overreact or barely react to stimuli in their surroundings. The hippocampus is involved in forming and storing context-dependent information. This hippocampal representation of the environment is used to appropriately adapt our responses to stimuli. Dysfunction of the hippocampus, found in depressed patients, could supposedly contribute to the inappropriate emotional responses seen in depressed patients.[44]

Several structural differences have been shown in the brains of depressed patients compared to healthy subjects. EEG findings show greater activation in the right frontal cortex than in the left frontal cortex in depressed patients. This asymmetry is thought to reflect their negative moods, since relative greater right activation is associated with negative affect.[45] MRI studies[46] show a reduction in the brain volume of depressed patients in the anterior cingulate cortex, orbitofrontal cortex, the hippocampus, the putamen and the caudate nucleus (see figure 6). Moreover, remitted patients have larger hippocampal volumes compared to non-remitted patients, implicating the possibility of the reversal of structural changes. Finally, PET studies[42] have shown abnormalities in regional cerebral blood flow and glucose metabolism in multiple prefrontal cortical and limbic structures implicated in emotional processing.

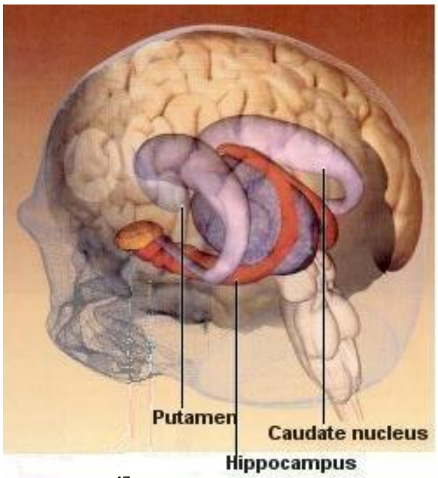

Figure 6.[47] Subcortical structures that are affected in depression.

In response to damage, some neurogenesis can occur in the hippocampus. This can be activated by brain derived neurotrophin factor (BDNF) which is normally present in high amounts in the hippocampus. BDNF synthesis and signaling can be chemically induced by adrenergic and serotonergic agonists such as antidepressants.[48] In a post-mortem study of patients depressed at the time of death significant differences were present between the BDNF concentrations in the hippocampus of antidepressant-treated and untreated subjects.[48]

In depressed patients, serum BDNF concentrations are lower than in healthy subjects, the level correlating with the severity of the depression.[48, 49] This may have several causes. First of all, stress causes a suppression of BDNF synthesis.[48] Severe depression is associated with immune activation and in particular with raised cytokine concentrations. Raised proinflammatory cytokines stimulate the HPA axis.[9] In depressed patients, a dysfunction of the hypothalamo-pituitary-adrenal (HPA)-axis is established.[50] This part of the neuroendocrine system controls the reactions to stress and regulates body functions such as the immune system and mood and emotions. The dysregulation of the HPA axis leads to higher baseline cortisol values and an overactive response to psychological stressors.[51] Second, depression is associated with decreased monoamine (serotonin and noradrenaline) neurotransmission,[52] causing a downregulation of BDNF synthesis as well.[9]

In healthy people, the hippocampus integrates stress signals via its abundantly present corticosteroid receptors and provides inhibitory feedback to the HPA axis. Because of the structural brain changes in the hippocampus in depressed patients, this regulatory feedback is disturbed as well, leading to even more severe dysregulation of the HPA-axis.[9]

In summary, a reduced activity in noradrenergic and serotonergic neurotransmission, a reduction in brain neurotrophins and hyperactivity of the HPA axis and the inflammatory response system are associated with functional abnormalities and structural deficits within the cortico-thalamic-striatal-limbic neurocircuit, disrupting the system balance. The functionally and structurally impaired PFC is not able to regulate the overactivity within the cortical/limbic regions, resulting in the clinical manifestation of the depression (see figure 7).

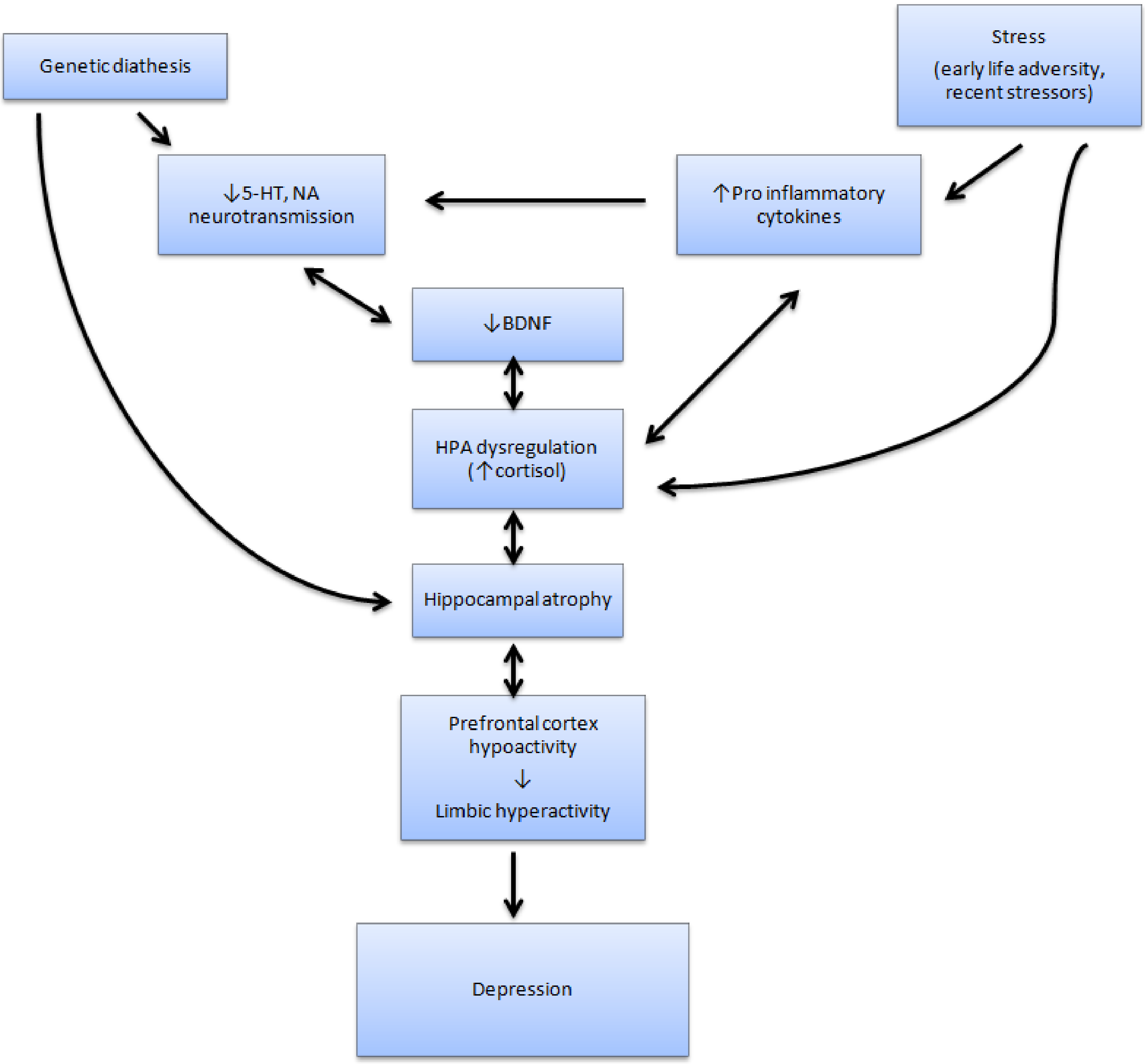

Figure 7 (adjusted from Palazidou, 2012[9]). A schematic overview of the neurobiology of depression. A genetic predisposition and external stress could lead to depression via influence on hormonal and neurological systems. 5-HT = serotonin, NA = noradrenaline, HPA = hypothalamus-pituitary-adrenal axis

In the aforementioned neurobiological pathways of depression, only the monoamines serotonin and noradrenalin play a role. These monoamines have been the center of research around depression for a long time. However, over the past decade, dopamine (DA) dysfunction contributing to the disorder has gained gradually more attention. A great collection of data from animal models, genetics, neuroimaging, and human clinical trials strengthen the case for DA dysfunction in the pathophysiology of major depression, at least in a significant subgroup of patients.[53] DA signaling in the dorsal and ventral striatum indirectly influences an extensive brain circuit involving the hippocampus, amygdala, thalamus, and prefrontal cortex.[53]

Many of the neurobiological mechanisms mentioned to be involved in depression have been shown to be influenced by music. In the next section, the beneficial effects of music on the dysfunctional brain regions will be outlined.

Musics effects on ameliorating depressive symptoms

Patients have frequently been shown to experience the beneficial effects of music on mood, by results of self-reports.[54-57] For instance, in a study among depressed patients by Hsu & Lai (2004),[58] a group of patients that listened to music recreationally in addition to standard treatment had significantly better scores on a self-rated depression scale than the control group that only received standard treatment. But what are the underlying mechanisms of this effect? As said before, several studies using functional neuroimaging have shown that music can modulate activity of all major limbic- and paralimbic brain structures. Since dysfunction of these structures are partly the cause of depressive symptoms, the effects might have their origin here. But apart from the effect on limbic structures, music has an effect on other brain areas and hormone levels as well, possibly contributing to the amelioration of depressive symptoms. Many studies have been done, aimed at researching the effects of music as well as clarifying the neurobiological mechanisms that could be responsible for the effects. The results of which will be discussed next.

Induced activity changes in the amygdala

The amygdala are believed to be involved mostly in detecting emotional valence. Stimuli with negative emotional valence in other perceptional dimensions than auditive (such as fearful facial expressions) have been shown to induce activity changes in the *amygdala.*[36] Also, they have been implicated in the tendency to ruminate and abnormal activation of the amygdala would correlate with the severity of the depression.[42, 43] Numerous functional neuroimaging studies show activity changes in the amygdala evoked by music listening (for a complete overview of these studies, see, Koelsch, Offermanns, & Franzke (2010)[59]). Koelsch et al. (2006)[36] observed increases of BOLD signals in the amygdala in response to unpleasant music. More importantly though, they observed decreases in these structures in response to pleasant music as well. In a PET study by Zatorre (2003),[27] decreases of rCBF were also observed in the amygdala during chill experiences in music listening. These decreases in amygdala activation could be explained by inhibitory presynaptic input from cholinergic neurons in the *NAc* to the *amygdala.*[2, 4]

So, since the amygdala play an important role in the processing of detecting emotional valence, the inhibiting effect on amygdala activation may lead to a decreased response towards negative stimuli. This could result in a change in the aforementioned depressed scheme, ultimately contributing to the amelioration of depressive symptoms.

Restoration of disturbed balance in the hippocampus

Many studies report activity changes in the hippocampus in response to music listening.[2, 60, 61] Koelsch (2010)[2] argues that the hippocampus plays an important role for the generation of tender positive emotions such as joy and happiness. As outlined before (see 'Depression: definition and brain areas thought to be involved'), the hippocampus is one of the brain regions that is suggested to correspond to deep-seated cognitive vulnerability to depression. Depressed patients show a diminished activity of and a reduction in brain volume in this structure, as well as a lower BDNF concentration compared to healthy subjects. And its dysfunction may be the cause of inappropriate emotional responses as seen in depression.[9] It is conceivable then, that music listening can be used to ameliorate the dysfunctions within the hippocampus and the dysbalances between the hippocampus and other brains structures such as the striatum and the amygdala.

Moreover, apart from functional changes evoked by music in the hippocampus, music is implicated in influencing structural changes in the hippocampus as well. In different animal studies,[62-64] mice showed increased BDNF, increased neurogenesis and changed neuronal signaling of BDNF in the hippocampus after being exposed to music. Together, these results demonstrate that exposure to music can modulate the activity of the hippocampus by influencing BDNF production.

In sum, music might restore the disturbed balance in the hippocampus by reactivating it and via increasing BDNF synthesis and signaling it could contribute to the upregulation of neurogenesis in the hippocampus. Also, it could prevent death of hippocampal neurons, since BDNF has a protective effect on neurons as well.[62]

A rise in serotonin levels

In a study by Evers & Suhr (2000)[65] a higher serotonin content of platelets was found in healthy subjects after listening to a classical piece or preferred music. As control, the serotonin content of platelets was measured as well during listening to unpleasant music or during resting without music. No change in serotonin content was observed in these cases. The serotonin content of platelets has been linked to serotonin content of central neurons. Therefore, the results implicate that listening to pleasant music may influence central neural serotonergic transmission.

Since depression is associated with decreased serotonin neurotransmission,[52] this study points towards yet another way in which music may contribute to ameliorating depressive symptoms.

Effects on dopamine release

Since the effects of music on dopamine release followed by emotional responses have already been discussed extensively, it will not be elaborated on further here. However, it should be briefly mentioned that the mechanism is relevant for ameliorating depressive symptoms, since dopamine dysfunctioning may play a role in the origin of depressive symptoms as well.

Restoration of asymmetry in frontal cortex activation and reduction of cortisol levels

Field et al (1998)[66] tested the effects of music listening on frontal cortex activation among two groups of depressed patients, because depressed adults are noted to have greater right frontal activation.[45] EEG was recorded during music listening in the music group and in the control group during sitting while instructed to relax. Saliva samples were made before and after the session as well, to measure and compare cortisol (stress hormone) levels, because depressed patients show abnormalities in the HPA-axis with higher cortisol concentrations.[51] During and shortly after the music listening, shifts in frontal activation symmetry was shown, from relative right frontal activation to relative left frontal activation. The cortisol levels were decreased after the music session compared to before.

The results thus show that music could alter electrophysiological and biochemical measures of depression.

In contrast to the effects of Hsu & Lai (2004),[58] no difference in mood was reported in the music group. This is a surprising effect, giving the object measurements showing a definite effect. These contrasting results might be due to the fact that a difference in affect may only be felt after some time, while EEG and cortisol level measurements are ways to register an immediate effect. The effects shown by Hsu & Lai (2004)[58] where indeed results over the course of weeks, rather than minutes.

Reduction of the poststress response of the HPA-axis

A dysregulation of the HPA-axis and increased cortisol levels lead to chronically heightened stress levels in depressed patients. This contributes to a vulnerability towards depression by resulting in an overactive immunesystem and overactive responses to psychological stressors for example.[9] Therefore, the effects music can have on reducing stress levels, even though it does not necessarily directly have an effect on mood, is an important feature concerning ameliorating depressive symptoms.

The effect of music listening on circulating stress hormones was studied by Conrad et al. (2007)[67] by comparing blood samples from clinically ill patients that listened to slow classical music for 1 hour to a control group that did not have such an intervention. The results showed lower levels of interleukin-6 (a cytokine that stimulates the immune response) and epinephrine in the blood samples of the music group. The reduction in circulating stress hormones was also associated with a drop in blood pressure and heart rate. The study suggests a neurohormonal beneficial effect of music, dependent on the HPA-axis.

As Field et al. (1998)[66] showed, cortisol levels were decreased during and after listening to musis in depressed patients. Suda, Morimoto, Obata, Koizumi, & Maki (2008)[68] studied the effect of music on cortisol levels as well, but in healthy subjects. The results showed that major mode music, which induced happiness, decreased cortisol levels significantly.

Thus, music effectively relieves stress and as Conrad et al. (2007)[67] suggest, it may act by decreasing the poststress response of the HPA-axis.

Considering this mood uplifting effect, several brain areas have been mentioned: release of dopamine in the *dorsal striatum* and shortly after in de *ventral striatum* supposedly reflects a sense of wishing, expectation and reward that is triggered by music; the *frontal cortex, superior temporal gyrus* and *insula* are engaged when meaningful features of music, that can trigger reactions in the listener, are attended to. Fitzgerald et al. (2008)[39] aimed at synthesizing the results of a large number of studies that used variable methods to establish brain areas involved in depression. Only few brain regions were consistently identified among the studies. Among them were the *inferior prefrontal cortex, insula*, *superior temporal gyrus*, and *basal ganglia*, precisely those brain areas that have been experimentally shown to be involved in the emotion evoking effects of music. By acting upon these areas then, music could play a role in restoring a balance in emotional processing and the concurrent mood disorder.

Thus, the ameliorating effects of music on depressive symptoms seem to come forth from two types of processing. First, music can lead to functional and structural changes in several brain areas implicated in depression. By influencing cognitive processes then, an eventual effect can be seen on emotional processing. Now, a parallel can be drawn with the discussion mentioned earlier between the emotivists theory and the cognitivists theory. A synthesis between the theories, as one might recall, is that emotions can indeed be evoked by music, but via key cognitive events. A similar interrelation may be responsible for the eventual mood enhancing effects of music. It is proposed here, that the restoration of the disturbed balance in brain areas such as the hippocampus, amygdala and frontal cortex allows for mechanisms through which music evokes emotions to have an effect, ultimately leading to an uplift of mood.

Since most of these processes are beyond awareness, the beneficial effects of music are not limited to those people that like music or are involved in music making. On the contrary, people who claim not to be moved by music or are not interested in it, might initially benefit most from music as means of self therapy, since they were not aware of the strong mood elevating effects of music yet.

How different aspects of music evoke different responses

So far, different mechanisms by which music can induce emotions and the underlying neurobiology have been reviewed. For the sake of music as self-therapy, it is useful to investigate what aspects of music seem to trigger the mechanisms leading to emotional responses and eventual optimal arousal. Already in 1970, the arousal-inducing properties of music were theorized by Berlyne.[69] According to his theory, listeners will prefer musical stimuli that induce an optimum level of physiological arousal.

As outlined in the previous section, many neural and chemical processes throughout the body are influenced by music listening. Inducing positive feelings seems to be an activating effect at first glance, through evoking chills for example. The opposite effect however, decreasing stress and induce relaxation turns out to play a major role in ameliorating negative affect as well. This may be explained by the fact that when the body is exposed to high amounts of stress, it is being prepared for fight or flight reactions.[70] This results in a constant state of vigilance. This supposedly contributes to a lesser capacity to refocus on positive matters, which is a predictor of relapse.[10] Consequently, in order to ameliorate depressive symptoms and induce positive feelings, one needs to get in a relaxed state first. Then, when the body is receptive to stimuli other than only signs of danger in the surroundings, happy sounding music might contribute to an uplift of mood. Likewise, Suda et al (2008)[68] suggested that the processing of happiness could be correlated to music's ability to reduce stress.

Several musical elements are perceived by listeners to be relaxing (see table 1). As an example, in a study by Conrad et al. (2007)[67] slow movements from Mozart's Sonatas lead to relaxation: decreased circulating stress hormones were measured. Another feature often associated with relaxation is major mode. Suda et al. (2008)[68] reported a minor decrease in cortisol levels in response to music in minor mode as well, but the resulting cortisol levels after listening to major mode were much lower.

As reported by Schafer & Sedlmeier (2010)[71] as well, music induces different levels of arousal and people appreciate music that helps to balance their arousal at a comfortable level. The decrease of stress levels induced by relaxing music, could already induce feelings of pleasure.[68] If subsequently happy music is listened to, an actual mood lifting effect may be the result.

The induction of chills lead to intense feelings of pleasure as well, as stated before. Several musical features that evoke chills are listed in table 1. For instance, a violation or delay of expected tones in musical sentences could lead to chills and rewarding feelings if the violation is resolved. Changing from major to minor to major mode is an example of such an effect.[72] Music that is associated with happiness is mostly in major mode. According to Peretz (2010)[73] we associate major mode with happiness because we tend to prefer familiar over unfamiliar music and major mode is the musical style most used in Western music. Similarly, we prefer consonance over dissonance.

Some musical components, which are all features frequently used in techno-music, could lead to further arousal.[31] Participants of a study by Gerra et al. (1998)[31] experienced tension, anxiety, and a sense of urgency accompanied by a significant increase in systolic blood pressure, heart rate, and plasma hormones, including plasma norepinephrine, and cortisol after listening to techno-music.

Thus, the music was a powerful stimulus for the activation of the noradrenergic system and the HPA axis. Although this level of arousal is experienced by many as pleasant, judging by the high amount of people attending rave parties, this is supposedly not the level of arousal that recovered depressed patients should aim for, as it would expose the body to even more stress.

Table 1. An overview of musical features that have been shown to induce reactions in listeners.

Reactions induced by music	**Musical features evoking the reactions**	**References**
Relaxation	• Slow and stable tempo • Low volume level and soft dynamics • Consistent texture (combination of sounds and instruments) • Absence of percussive and accented rhythms • Gentle timbre (sound or tone color) • Legato (connected) melodies • Simple harmonic or chord progressions • Major mode	Staum & Brotons (2000)[74]; Radocy & Boyle (2003)[75]; Wigram, Pederson, & Bonde (2002)[76]; Krout (2007)[30]; Conrad et al. (2007)[67]; Suda et al. (2008)[68]; Juslin & Lindström (2010)[77]; Bresin & Friberg (2011)[78]
Feelings of pleasure (chills)	• Harmonic sequences • The entrance of a voice • The beginning of a new part • Sudden increases in loudness • The entry of additional • Instruments • The expansion of the frequency range • Violations of expectations	Grewe, Nagel, Kopiez, & Altenmüller (2005)[72]; Blood & Zatorre (2001)[60]; Nusbaum & Silvia (2011)[79]
Happiness	• Fast tempo • Major mode • Staccato articulation • Large articulation variability • Low pitch • Soft timbre • Bright timbre	Khalfa, Schon, Anton & Liégeois-Chauvel (2005)[80]; Suda et al. (2008)[68]; Hunter, Schellenberg, & Griffith (2011)[81]; Lin et al. (2011)[7]; Peretz (2010)[73]; Juslin & Madison (1999)[82]; Juslin & Lindström (2010)[77]; Hunter, Schellenberg & Schimmack (2010)[83]; Bresin & Friberg (2011)[78]
High level of arousal	• High frequency • Continued fast tempo • Strident (dissonant) tone clusters	Gerra et al. (1998)[31]; Juslin & Lindström (2010)[77]

Other factors that have an influence on music responses

Apart from the aforesaid features of music itself, other factors could enhance the emotional experience and consequently lead to an ever bigger uplift of mood. Several factors will be described here: individual differences between listeners, contextual factors and the influence of individual preferences.

For a start, there are differences between listeners considering the way music is listened to. Musical experts perceive music differently and on a different depth than naïve listeners do. But as Mozart said about his own work: "here and there only experts can gain satisfaction but even non experts will feel pleasure without knowing why".[84] This is because even non-musicians (i.e. individuals who have not received formal musical training) have a highly sophisticated (implicit) knowledge about musical syntax,[85] causing the emotional responses, such as surprise and reward towards violations of expectations, as previously outlined. However, as results of Koelsch, Fritz, Schulze, Alsop, & Schlaug (2005)[86] show, areas in the brain involved in music-syntactic processing are activated more strongly in musicians than in nonmusicians. The more specific representation of musical regularities in musicians presumably makes them react more sensitively to the violation of these regularities. This implicates that musical experts might benefit more from the emotion evoking qualities of music.

Furthermore, as suggested by Gabrielsson & Lindstrom (2003),[87] one individual's deepest appreciation of music may be based on the structural features of a musical work, whereas for another individual the emotional content of a piece of music may elicit strong experiences. Likewise, Kreutz, Schubert, & Mitchell (2008)[88] propose different styles of music listening: *music systemizers* tend to focus on music as an object and *music empathizers* process music as emotional communication. Still, both strategies may serve a common goal of cognitive stimulation or emotional reward for both types of listeners. So in spite of differences in musical education or listening styles between individuals, music can induce emotions, be it through different processing mechanisms.

Regarding contextual factors, the way music is presented has been shown to affect the emotional response. An interaction between visual and acoustic systems appears to exist, as apparent for example by the fact that the enjoyment of music is more complete when someone looks at the playing and/or singing musicians than when someone listens to recorded music.[5] As Eldar, Ganor, Admon, Bleich, & Hendler (2007)[89] state, emotions have evolved as evaluations of events in the world that guide adaptive behavior. The concurrent sound and corresponding vision of music would lead to more intense emotions because they correspond more to the real world. For instance, watching a film accompanied by film music elicits more intensive reactions than when the music is listened to alone. This is exactly what Eldar et al. (2007)[89] demonstrated in an fMRI study. Great activation of the amygdala, the hippocampus, and the lateral prefrontal was shown when music was associated with a film showing real actions, whereas this differential activation did not occur if the emotion was provoked only by music. In another study by Baumgartner, Lutz, Schmidt & Jäncke (2006)[90], activity changes in these structures were also stronger during the combined presentation of photographs with music, compared to when only visual information was presented.

In terms of ameliorating depressive symptoms then, combining music with either relaxing or happy visual images could enhance its mood uplifting effects.

Another contextual factor with which music is often combined is exercise. Apart from the beneficial effects of exercise on depression, which are beyond the scope of this review, physical exercise has been found to increase the sensitivity to music.[91] Ironically, the opposite effect, music triggering a drive to move, holds as well. The Nac, activated in response to music as shown by Menon & Levitin (2005)[4], projects to compartments of the *basal ganglia*, which play an important role for the learning, selection and execution of actions.[22] Mitterschiffthaler et al. (2007)[61] observed activation in the caudate nucleus, a structure within the basal ganglia, in their study, only when participants listened to happy music. These results might be an explanation for the drive to move to or dance in response to pleasant music.

Together, these results suggest that moving, in the form of dancing or exercising, and music reinforce each other. Therefore, it is suggested here, to combine the two in order to enhance the beneficial effects of music.

Apart from how and where music is listened to, the frequency of exposure to music plays a role as well, since emotion processing in response to music listening has been found to have a temporal aspect. The results of a study by Krumhansl (1997)[92] suggest that the intensity of an emotional experience may increase over time during the perception of a musical excerpt. Koelsch et al. (2006)[36] found that activations of all structures, except the hippocampus, involved in music processing were stronger during the second block of the musical excerpts. They also suggest that this is explained by increased intensity of emotional experiences in listeners during the perception of the musical excerpts. Considering the relaxation effect of music, Pelletier (2004)[93] found something similar, concluding that the more the listener is exposed to specific music, the greater the relaxation response. These results suggest a certain dose-response effect, implicating that the more often music is listened to, the higher the effect on ameliorating depressive symptoms will be. It should be noted however, that nothing is known about a possible ceiling effect. It is not likely for this effect to keep increasing. Moreover, the possibility of the opposite effect should be considered as well, the intensity of emotional experiences might decrease overtime, due to habituation.

The final factor of influence on music responses attended to here, are individual preferences. As Krout (2007)[30] concluded, the consideration of music preferences of a person is vital, as music that is preferred by the listener may have the most beneficial effects. Several musical components that have been shown to evoke relaxation, feelings of pleasure or happiness have been outlined. But associative mechanisms have been stressed in this review as playing a role in evoking emotions as well. Accordingly, each individual should remember which musical pieces are associated with pleasant memories and concurrent feelings of happiness. If one does not know any music that has such strong associations, it is suggested here to create them. Persons could pair music with something that makes them happy. Maybe a certain place, event, or person. If done often enough, the music will be associated with this happy trigger and listening to the music alone will eventually evoke positive feelings.

A similar mechanism is applied in the field of bio-feedback. Dong et al. (2010)[94] did several experiments in order to design a mobile platform that can record user's EEG in real time, analyze the emotion state, and choose a suitable music track to play. That way, users can adjust their emotion at anytime and anywhere. This is an example of a design in which the feedback is automated, but exactly such mechanisms could be employed personally.

In sum, individual musical education and listening styles may lead to different processing of music, but every person could benefit from the positive feelings evoked by music. Several factors could enhance the mood uplifting effects of music, such as attending life concerts or watch images that contribute to making the music more corresponding to the real world, exercising, frequent exposure to the music and taking into account personal music preferences such as musical pieces that are associated with events that evoke feelings of pleasure.

Considerations for future research

- Perhaps, after frequent exposure to a certain musical piece, one is not moved, surprised or rewarded anymore, because of an continued exposure, adaptation effect. Future studies should investigate this possibility and whether alternating between different musical pieces would prevent such an effect.

Conclusion

In the current review the mechanisms through which music evokes emotions were explored by means of reviewing the existing literature. After a brief overview of the ongoing debate on whether music can elicit actual emotions, several mechanisms responsible for the evoked responses are outlined. Furthermore, the possibility of applying music as a means of self therapy in ameliorating depressive symptoms is investigated.

Regarding the modulation of emotions, several neuroimaging studies as well as studies measuring physiological effects have contributed to our understanding of music evoked emotions. Music has been shown to evoke activity changes in the limbic system, an extensive circuit thought to be involved in reward and emotion, while listening to music.[12] Intense pleasure in response to music can lead to dopamine release in the striatum.[3] Activation of the ventral striatum is reported to be connected to activity in the ventral tegmental area (VTA).[22] The VTA mediates activity in the NAc while participants report pleasurable experiences during music listening.[4] Activation in the NAc correlates with motivation- and reward-related experiences of pleasure elicited by biological drives such as sexual activity or drinking water when dehydrated.[2] Thus listening to music could elicit actual feelings of reward via biological responses.

Next to these feelings of reward and pleasure, music can have a relaxing effect on the body. By decreasing the poststress response of the HPA-axis, it reduces stress.[67] The continued state of stress people vulnerable to depression are in, due to an overactive HPA-axis, contributes to their being less able to focus on positive matters.[10] The relaxing effect of music then, makes the body more receptive to positive stimuli. Whereupon happy sounding music can contribute to an uplift of mood.

Concerning the ameliorating effects of music on mood, much research has been done as well. Music induces activity changes in the amygdala,[27, 36, 59] which have implicated in the tendency to ruminate and abnormal activation of the amygdala would correlate with the severity of the depression.[42, 43] Music can lead to a restoration of disturbed balance in the hippocampus.[2, 60-64]. And it can restore the asymmetry in frontal cortex activation, shown to be associated with depression.[66] The fact that music influences these structures is relevant, because deficits in these brain areas are suggested to correspond to deep-seated cognitive vulnerability.[13] This vulnerability arises because the altered processing in mentioned brain structures contributes to maladaptive behavior such as affective processing bias or feedback sensitivity.[13] As this cognitive vulnerability is an important factor contributing to relapse or even worse, suicide,[8] the need to restore the balance becomes clear. It is proposed in this review that the restoration of the disturbed balance in brain areas such as the hippocampus, amygdala and frontal cortex allows for mechanisms through which music evokes emotions to have an effect, ultimately leading to an uplift of mood.

Based on the evidence thus far, it can be concluded that music is a powerful source of modulating emotions. As such, it can be applied for stimulating feelings of pleasure and an uplift of mood. Moreover, as it is a source of self-therapy with low costs, no side-effects and one that patients are willing to commit to,[7] it is suggested here as a promising approach to preventing relapse to major depression.

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