

Musical anhedonia: a review

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SUMMARY

Objectives

Anhedonia, or the inability or the loss of the capacity to experience pleasure, is a core feature of several psychiatric disorders. Different types of anhedonia have been described including social and physical anhedonia, appetitive or motivational anhedonia, consummatory and anticipatory anhedonia. Musical anhedonia is a rare condition where individuals derive no reward responses from musical experience.

Methods

We searched the PubMed electronic database for all articles with the search term “musical anhedonia”.

Results

A final set of 12 articles (six original research articles and six clinical case reports) comprised the set we reviewed.

Conclusions

Individuals with specific musical anhedonia show normal responses to other types of reward, suggesting a specific deficit in musical reward pathways. Those individuals are not necessarily affected by psychiatric conditions, have normal musical perception capacities, and normal recognition of emotions depicted in music. Individual differences in the tendency to derive pleasure from music are associated with structural connections from auditory association areas in the superior temporal gyrus to the anterior insula. White matter connectivity may reflect individual differences in the normal variations of reward experiences in music. The moderate amount of heterogeneity between the reviewed studies is a limitation to the generalizability of our conclusions.

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Conflict of interest

The Authors declare no conflict of interest

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Introduction

Anhedonia means “without pleasure” and is derived from the Greek an-, “without”, and hēdonē, “pleasure”. The term was coined by Ribot¹ to describe the inability or the loss of the capacity to experience pleasure. Progress in affective neuroscience challenged Ribot’s concept of anhedonia², for example Thomsen and colleagues³ suggested it as “impairments in the ability to pursue, experience, and/or learn about pleasure, which is often, but not always accessible to conscious awareness”.

Anhedonia is a psychopathological feature of several psychiatric disorders. It is a core feature of major depressive disorder and a prominent negative symptom of schizophrenia. Anhedonia has also been identified in substance-related and addictive disorders, eating disorders, maladaptive and risky behaviors, and Parkinson’s disease⁴.

Anhedonia has been differently considered as a pre-morbid personological characteristic (trait anhedonia) or as an acute symptom (state anhedonia) of the clinical picture of schizophrenia and major depressive disorder⁵. Recent investigations highlight the importance to distinguish between the differential effects of chronic, trait-like anhedonia and acute, state-like anhedonia on suicidal ideation and behaviors⁶.

Different types of anhedonia include social and physical anhedonia, sexual anhedonia, musical anhedonia, appetitive or motivational anhedonia, consummatory anhedonia, and anticipatory anhedonia. Physical anhedonia is an inability to feel physical pleasures while social anhedonia is an incapacity to experience interpersonal pleasure⁷. The hedonic process encompasses both anticipatory and consummatory components⁸. Consummatory pleasure reflects the momentary pleasure that is experienced while engaged in an enjoyable activity, while anticipatory pleasure revolves around pleasure from future activities. So, consummatory anhedonia is not enjoying the activity itself, while anticipatory anhedonia is the inability to experience any excitement about the future. In order to explore this two components of the experience of pleasure Gard and colleagues⁹ developed the Temporal Experience Pleasure Scale, consisting of a subscale of anticipatory pleasure and a subscale of consummatory pleasure¹⁰. Other investigators differentiated deficits in the hedonic response to rewards (consummatory anhedonia) and a diminished motivation to pursue them (motivational anhedonia)¹¹.

Our review focuses on musical anhedonia. Music is not considered to be a primary reward even if its role as a pleasurable stimulus is widely established^{12,13}. Music is celebrated and valued in every human culture, and different hypotheses about its origins and cultural roles remain a subject of debate. Music perception and cognition researchers¹⁴ posit that music serves many adaptive functions^{15,16}, serving as an auditory channel for interpersonal communication, possibly preceding speech and language¹⁷. Thus, individual differences in the capacity to enjoy music could also have an evolutionary role for communication. Music is a form of communication incorporating strong emotional signals conveyed by the auditory channel.

In human evolution, music may have served to directly link auditory inputs and outputs with social and emotional reward centers¹⁴. Music may have also served a selective advantage in mate selection¹⁸. There are tremendous individual differences in the reward value of music and some individuals find music more pleasing than others¹⁹. At one extreme end of the spectrum is musical anhedonia, a rare condition where individuals derive no reward responses from musical experience^{20,21}.

Further, individual differences in anhedonia occur in clinical and non-clinical populations^{21,22}.

As reported by Oliver Sacks²³ in his book *Musicophilia*, loss of interest in music (finding it emotionally flat while retaining all of their musical perceptions and skills) is common after strokes, and such losses or distortions of musical emotion are more common with damage to the right hemisphere of the brain.

By reviewing available literature about music anhedonia we aim to clarify whether such a rare clinical condition could give us additional information on the complexity of the functioning of the musical phenomenon and its neural bases, in particular how the brain circuits that process the sound relate to the circuits that process the emotions, or how music can become an emotional experience.

Methods

We searched the PubMed electronic database for all articles up to December 21st, 2018 with the search term “musical anhedonia”. The search included all languages. We compiled articles that (1) were published in English, Italian or French (2) provided empirical data (as opposed to reviews or commentaries). Two blind investigators (FB and LA) performed the literature search, title/abstract screening, full-text review. The selected references were cross-checked and the reference list of relevant articles was screened in order to search for additional literature. In addition we performed an independent review of other sources (e.g. books). Discrepancies were resolved through consensus.

Results

Sixteen articles^{12-14,20,24-35} were identified. We excluded two articles that were unrelated to the topic^{24,30}, one comment²⁷, one review article²⁹, one article in Japanese³⁵, and one article translating and validating a questionnaire to assess musical anhedonia³¹.

In addition to the PubMed search, two other relevant clinical case reports^{36,37} of patients presenting musical anhedonia were identified. A final set of 12 articles, six original research articles^{12,13,20,26,33,34} and six clinical case reports^{14,25,28,32,36,37}, comprised the studies reviewed.

Five original research articles^{12,13,20,26,34} focused on healthy individuals, while one³³, the largest sample-sized study, focused on 78 patients with focal brain damage without pre-morbid neurological or psychiatric conditions. Table I summarizes the six original research articles.

All six single-case reports^{14,25,28,32,36,37} described patients presenting musical anhedonia after focal brain damage, including one¹⁴ which described “severe musical anhedonia” in a subject without clearly identifiable cortical lesions but a lower white matter abnormality between auditory system and reward connectivity. Table II summarizes patients’ characteristics and abilities, the clinical features of their musical anhedonia, diagnosis and site of lesions.

TABLE I. Summary of the original research articles on Musical Anhedonia (MA).

Article	Sample characteristics	Study characteristics	Main findings
Keller et al., 2013	21 healthy adults (M = 9, F = 12, ages 18-52) without current or past Axis I psychiatric disorders	fMRI with musical stimuli was used to examine brain responses and effective connectivity in relation to individual differences in anhedonia	Trait anhedonia was negatively correlated with pleasantness ratings of music stimuli Trait anhedonia was negatively correlated with activation in right NAc, basal forebrain and bilateral hypothalamus. Significant negative correlations were detected in the OFC, anterior insula, anterior and posterior cingulate cortex, and ventromedial prefrontal cortex Effective connectivity between NAc, VTA and paralimbic areas, that regulate emotional reactivity to hedonic stimuli, was negatively correlated with trait anhedonia. Trait anhedonia were not correlated with auditory cortex responses
Mas-Herrero et al., 2014	3 groups of 10 healthy individuals without depression or generalized anhedonia, each with high, average, or low sensitivity to musical reward, assessed using the Barcelona Musical Reward Questionnaire (BMRQ)	Participants performed a music task in which they had to rate the degree of pleasure while listening to pleasant music and a monetary incentive delay task In order to have objective physiological measures of emotional arousal, skin conductance response (SCR) and heart rate (HR) were recorded Music emotion recognition were tested 1-year later a follow-up session were performed with 26 out of the 30 participants	No differences among groups in the ratings (evaluation of pleasure for sex, food, money, exercise and drugs, but a significant effect on the music scale ($p < .001$) Individuals with low BMRQ scores had the fewest high-pleasure or chill responses while listening to pleasant music. Similar results were obtained during the follow-up session. This result was also reflected by their relative lack of physiological responses (SCR and HR) Differences among groups could not be explained by deficit in music perception (amusia), in familiarity, nor in recognizing emotions in music
Martinez-Molina et al., 2016	3 groups of 15 university students (8 females and 7 males each), each with high, average, or low sensitivity to musical reward assessed using the BMRQ. All participants were nonmusicians and matched in age, general anhedonia, sensitivity to punishment and reward scale, and amusia score	SCR were recorded while participants listened to excerpts of pleasant, neutral, and unpleasant music fMRI was scanned while subjects performed a music listening test and a monetary gambling task	The music anhedonic participants showed selective reduction of activity for music in the NAc, but normal activation levels for the monetary gambling task. This group also presented decreased functional connectivity between the right auditory cortex and ventral striatum (including the NAc) In contrast, individuals with greater than average response to music showed enhanced connectivity between these structures
Mallik et al., 2017	15 healthy adults (M = 6, F = 9)	Naltrexone (50 mg) or placebo was administered on 2 different days in a double-blind crossover study Participants' responses to music were assessed using both psychophysiological (objective) and behavioral (subjective) measures	Naltrexone caused decreased physiological reactions to music for both pleasurable and neutral music compared to placebo Naltrexone caused a decrease in self-report measures of pleasure for pleasurable music but not neutral music



TABLE I. *continue*

Article	Sample characteristics	Study characteristics	Main findings
Belfi et al., 2017	78 patients with focal brain damage (M = 37, F = 41, mean age = 59.2) without premorbid neurological or psychiatric dysfunction, and no history of alcohol or drug abuse	Musical anhedonia, anhedonia for different behaviors, and music perceptual abilities were assessed with mailed questionnaires and in-lab task	5 patients showed signs of MA. None of these patients had signs of general anhedonia. The lesions locations for these patients were varied and included: ventromedial prefrontal cortex, posterior cingulate cortex, left temporal pole, and striatum No clear or consistent neuroanatomical correlates of MA were identified One patient with damage to the right hemisphere putamen and internal capsule displayed specific and severe acquired MA
Mas-Herrero et al., 2018	39 healthy subjects, classified into three groups of 13 individuals, according to their Barcelona Music Reward Questionnaire (BMRQ, Mas-Herrero et al., 2013): – 13(6)ANH_specific musical anhedonics, BMRQ < 65 – 13(7)HDN_musical hedonics, 65 < BMRQ < 87 – 13(9)HHDN_musical hyperhedonic, BMRQ > 87 (number of female in parenthesis) The subject were matched in sex and age; They presented similar scores in hedonism as measured by the Physical Anhedonia Scale	Participants performed two tasks: – an aesthetic task(a series of 56 pictures of paintings from Cattaneo et al., 2014, and Cela-Conde et al., 2004, 2009, after which participant should evaluate the amount of <u>pleasure</u> (on a scale from 1- "I found it unpleasant" to 7- "I liked it a lot," where 4 was "I neither liked nor disliked it"), <u>arousal</u> (on a scale from 1 to 5), and <u>familiarity</u> (on a scale from 1 to 5) experienced with that painting – an emotional sounds task (30 different sounds, selected from the International Affective Digitized Sounds, IADS-2, Bradley and Lang, 2007), after which participant should rate the degree of pleasure and arousal experienced. During both tasks skin conductance response (SCR) was recorded using two AgAgCl electrodes using a BrainVision BrainAmp device. The electrodes were attached to the forefinger and the ring finger of the left hand The level of SCR was the mean SCR amplitude after stimulus or response onset with respect to baseline (500 ms). SCR amplitude was determined in the 0-15s windows after the presentation of a painting or an emotional sound	Specific musical anhedonics showed similar hedonic reactions, both behaviorally and physiologically, as the HDN control group in both tasks Post hoc analysis revealed that HHDN individual reported higher liking rates than the ANH (P = 0.002) and the HDN group (P = 0.038) but no differences were found between the ANH and the HDN (P = 0.46) Pleasant paintings evoked more SCR amplitude among all participants and that this effect was independent of their music reward sensitivity In the emotional sound task, there were no statistically significant differences among group means as determined by one-way ANOVA, neither in liking, nor in arousal rating These findings suggest that music hedonic sensitivity might be distinct from other human abstract reward processing and from an individual's ability to experience emotion from emotional sounds

The results shown in tables highlight an important fact: that the brain areas involved in musical anhedonia, whether we talk about healthy individuals, whether we consider subjects with brain damage, are also widely involved in the elaboration of emotions and reward in connection with more specific auditory circuits (superior temporal gyrus in Loui's)¹⁴. In addition to the musical anhedonia, a behavioral response of reduced reactivity (emotional arousal) is also associated, given concordance with the reduced function of

the brain circuits that elaborate emotions. These areas are roughly located in the medial brain and include the medial temporal lobes, the temporal poles, the orbitofrontal cortex, the cingulate cortex, the insula, the nucleus accumbens and certain basal ganglia (e.g. striatum in Zatorre's)²⁹.

Discussion

Results show that musical anhedonia is related to dif-

TABLE II. *Characteristics of 5 case reports of patients with MA.*

Article	Age, gender, handedness, musical history	Diagnosis	Site of lesion	Clinical features of MA	Patient's characteristics and abilities
Mazzoni et al., 1993	24, M, Ambidextrous, Amateur guitarist	Haemorrhage due to an arterio-venous malformation	Right temporo-parietal, including the plica curva and supramarginal gyrus	Loss of aesthetic pleasure from listening to music ("music is flat, it's no longer 3-dimensional, it's only on two planes")	Neurological examination, tonal audiometry, neuropsychological and neuromusicological examinations were normal
Griffiths et al., 2004	52, M, R, np	Infarction	Left insula, partly extending into the left frontal region and left amygdala	Loss of pleasure from listening to particular pieces of classical music	No anhedonia in different domains. No depression. Neuromusicological assessment was normal
Satoh et al., 2011	71, male, R, np	Infarction	Cortical and subcortical regions of the right inferior parietal lobule, including both the angular and supramarginal gyrus	Unable to experience emotion in listening to music. He described music as dull and lacking freshness	Neuropsychological assessments were normal. Speech audiometry and recognition of environmental sounds were within normal limits. Neuromusicological assessment revealed no abnormality in the perception of elementary components of music, expression and emotional perception of music. Psychiatric assessment was normal
Hirel et al., 2014	43, male, R, amateur	Infarction	Right ischemic lesion affecting the superior temporal cortex, in particular lateral Heschl Gyrus and the posterior part of the Superior Temporal Gyrus (Brodmann areas 21 and 22)	Loss of interest for music and lack of emotion in listening to music, associated with amusia	Hamilton Depression Scale was normal. No anhedonia in different domains than music. Mild auditory impairment for high frequencies (> 2000 Hz) Montreal Battery for the Evaluation of Amusia: total score = 21.3/30, with pathological score in tonality, pause, and prosody. Montreal Evaluation of communication was normal. Evaluation of emotion perception (for faces and music) showed a severe impairment of musical emotion



TABLE I. *continue*

Article	Age, gender, handedness, musical history	Diagnosis	Site of lesion	Clinical features of MA	Patient's characteristics and abilities
Satoh et al., 2016	63, M, R, professional chorus conductor	Putaminal hemorrhage	Subcortical region of right temporal lobe. Subcortical fiber degeneration between the superior temporal gyrus and the posterior two-thirds of the right insula. Decreased regional cerebral blood flow in the right insula and temporal lobe	Unable to have any emotional experience while listening to music. Sound was described as dull and lacking freshness	No hearing deficit No anhedonia in different domains Neuropsychological examination was normal Normal speech audiometry and environmental sound recognition Normal perception and expression of music Impairment of judgment of "musical sense" Inability to discriminate the sound of chords in pure versus equal temperament Impairment listening to the inner vocal parts, such as alto and tenor, while conducting a chorus, and when experiencing the cocktail party effect during conversation Intact response to visual and other auditory stimuli and sensory modalities
Loui et al., 2017	53, M, R, np but 4 years of musical training started from the age of 13; versus 46 controls (17 F), 20.5 age, R, 7.3 y of musical training	None specific lesion reported	Decreased white matter but higher Fractional Anisotropy (FA) between auditory and reward areas, in detail: – lower tract volume between left Superior Temporal Gyrus (STG) and left Nucleo Accumbens (NAcc); left Anterior Insula and left NAcc – Mean FA was greater between left STG and left AIns	A self-reported, socially debilitating lack of reward experience from music (intact reward responses to visual art) BMRQ (Music Reward overall score)-9, 5.89 standard deviation below controls	PAS (Physical Anhedonia Scale): – Not anhedonic except for items that pertain to sounds – Montreal Battery for Evaluation of Amusia and the nonverbal measure of the Shipley Institute of Living Scale were used to rule out any differences due to amusia or general intellectual impairment, respectively (results similar to controls) No other information about Neuropsychological or Psychiatric assessment

ferent patterns of connectivity from auditory to emotion and reward centers of the brain. This auditory access to the reward system informs the evolutionary basis of music: perhaps music evolved as a direct auditory pathway toward social and emotional reward centers in the

brain. Building on to Patel's Transformative Technology of the Mind (TTM) theory, the Mixed Origins of Music (MOM) theory posits that music transforms the brain through an affective signaling system common to many social animals^{38,39}.

Music can effectively elicit highly pleasurable emotional responses⁴⁰. Neuroimaging and noninvasive brain stimulation studies identify activation of brain emotion and reward circuits during pleasurable music listening^{12,13,41-46}. The “liking” and “wanting” components²⁶ that are lacking in anhedonia^{47,48} may result from dysfunctions in limbic reward system (MRS) and its associated pathways⁴⁹. The main brain areas of the reward system are the nucleus accumbens (NAc), septum, and the ventral tegmental area/substantia nigra (VTA/SN)^{50,51}, which are interconnected by the medial forebrain bundle (MFB). In VTA, the mesolimbic dopamine neuron cell bodies reside and project to the NAc, and dopamine release in VTA is crucial for reward processing⁵². The MFB connects the VTA to the NAc as well as to other basal forebrain (eg, septum) and frontal lobe regions involved in reward and motivation⁵³. Mesolimbic and mesocortical pathways involving the VTA, NAc, amygdala, septum, orbitofrontal cortex and medial prefrontal cortex are involved in reward processing, anticipation and learning⁵⁴⁻⁵⁶.

According to Zatorre²⁹ perhaps musical reward is different, given its complex and abstract nature, and given its important dependence on cultural factors and learning. As such, music reward may depend to a greater extent on cortical mechanisms than other more basic ones. Musical reward may be mediated via cortical mechanisms in interaction with subcortical system, so that music reward value increases as a function of enhanced functional interactions between the striatum and a temporofrontal cortical network²⁹.

There are marked individual differences in the reward value of music and some individuals find music more pleasing than others¹⁹. These differences extend to both spectral ends: excessive pleasure from music (“musicophilia”) and on lack of pleasure from music (“musical anhedonia”). Congenital musical anhedonia occurs in approximately 5% of healthy adults^{19,20,33}. These individuals derive no pleasure from music, both in self-reported ratings and physiological responses²⁰. Acquired anhedonia for specific stimuli or behaviors occurs in rare patients with neurological damage (eg, anhedonia for smoking)⁵⁷. Music-specific anhedonia is especially rare. While the types of music that are considered pleasurable vary considerably within and between cultures, the vast majority of people enjoy some forms of music some of the time. People with musical anhedonia show diminished emotional arousal on autonomic measures such as skin conductance response (SCR) and heart rate measurements compared with people with average or high sensitivity to music. Individuals with musical anhedonia show normal responses to other types of reward¹². This condition was termed specific musical anhedonia since the patients are hedonically responsive to other rewards, suggesting a

specific deficit in musical reward pathways¹³. Those individuals are not necessarily affected by psychiatric conditions (eg, depression or generalized anhedonia), have normal musical perception capacities, and have normal recognition of emotions depicted in music.

Do different types of aesthetically related stimuli activate the same neuronal circuits? Yes, similar to music, emotional responses to pleasant paintings activate regions implicated in reward processing such as the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC), and the striatum⁵⁸⁻⁶⁰. Pleasant visual art and music engage overlapping structures, including the OFC, the ACC, and the striatum, which are also involved in the processing of primary and secondary rewards⁵⁹⁻⁶¹. What differs is probably the route to access a common reward circuit. In music, the processing of time and sound is critical: listening to music engages high-order cortical structures including the auditory cortex^{62,63} as well as the frontal regions to which it connects, such as the inferior frontal gyrus, crucial for working memory and predictive coding⁶⁴⁻⁶⁶. It is still unclear whether a uniform abstract aesthetic reward network, including musical and visual aesthetics, exists; and if so, if musical anhedonia reflects a dysfunction of this network. The network implicated in the experience of musical perception and reward is posited as the nucleus accumbens (NAc), involved in reward and affective processing, the superior temporal gyrus, crucial for music perception¹² and their interconnections and connections with other reward system areas, such as ventral striatum, caudate, dorsal striatum, and limbic areas (eg, amygdala and anterior insula)^{44,45}. Individual differences in the tendency to derive chills, i.e., measurable psychophysiological responses, from music are associated with structural connections from auditory association areas in the superior temporal gyrus to the anterior insula (AIns)¹⁴, which is consistently activated when experiencing strong emotions, and the medial prefrontal cortex (mPFC), important for computing social value. Furthermore, this association is modulated by connectivity through the NAc, a hub in the dopaminergic reward system⁶⁷.

Patterns of white matter connectivity in the auditory and reward systems reflect individual differences in the tendency to perceive reward from music. In Loui's article¹⁴, the Music Reward score, among the controls, was significantly predicted by the volume of tracts between LSTG (left superior temporal gyrus) and LAIns (left anterior insula).

Moreover auditory–reward connectivity differences are observed in the extreme case of musical anhedonia¹⁴. Fractional anisotropy, the main outcome variable in Diffusion Tensor Imaging (DTI), is an index of white matter integrity, which includes myelination and coherence of axonal bundles. The pattern of simultaneously increased white matter integrity and decreased volume may suggest increased myelination and/or decreased

crossing fibers in the MA subjects' anatomical connections between LSTG and left nucleus accumbens (LNAcc), which could result in increased inhibition from LSTG to LNAcc. Functionally, the increased inhibition from LSTG could lead to a down-regulation of the activity of LNAcc, resulting in deactivation of the NAacc as observed in recent functional MRI work in musical anhedonics^{12,14}. Control subjects' data in Loui et al. article¹⁴, can predict the MA subject tract volumes but not his behavioral scores, as if he would lie at the low end of a normal distribution, as a very rare condition.

This is consistent with the observation that across patients of many types of brain damage, few report musical anhedonia³³.

Something more specific must be said on the lateralization of music and emotion, which are both complex, variable among individuals, and bilaterally represented. Having said that, there is evidence from the data we reviewed, both fMRI in normal individuals and the Belfi paper³³ that show a greater predominance of right sided activation with musical appreciation/right hemisphere decreased activity with musical anhedonia, as well as greater predominance of right hemisphere lesions above in musical anhedonia cases.

In Loui et al.¹⁴, it is noteworthy that only tracts from left or right superior temporal gyrus (the only auditory regions in Loui's model) emerged as significant predictors, sug-

gesting that individual differences in music reward do pertain to auditory-specific access to the reward system and that auditory access to the mesolimbic pathway is hemispherically asymmetric, with normal variations in reward sensitivity occurring on the right but abnormal lack of reward on the left.

In this paper we attempted to briefly synthesise the small and heterogeneous literature on musical anhedonia, a rare but interesting condition with considerable relevance for neuropsychiatry. Several limitations deserve mention in this discussion. Surely, a major limitation lies in the fact that only PubMed electronic database was used for searching, suggesting the possibility of some missing papers; however, check of reference lists from selected articles was performed to identify articles missed by the initial search. Another limitation of this study is the moderate amount of heterogeneity (e.g., in study design, sample characteristics, screening instruments, diagnostic techniques) between the studies included in this review, so that conclusions should be interpreted cautiously, and future research is needed to further investigate the musical hedonia network. Whether music is found to be pleasurable or not (anhedonia) is associated with the reward system and structural connection development and integrity. Much remains to be learned, but it is conceivable that altered white matter connectivity may primarily or even exclusively impact the appreciation of music.

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