# An Overview on Anhedonia

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**Abstract:**

Anhedonia refers to the reduced ability to experience pleasure, and has been studied in different neuropsychiatrie disorders. Anhedonia is nevertheless considered as a core feature of major depressive disorder, according to DSM-IV criteria for major depression and the definition of melancholic subtype, and regarding its capacity to predict antidepressant response. Behavioral, electrophysiological, hemodynamic, and interview-based measures and selfreports have been used to assess anhedonia, but the most interesting findings concern neuropharmacological and neuroanatomical studies. The analyses of anhedonic nonclinical subjects, nonanhedonic depressed patients, and depressed patients with various levels of anhedonia seem to favor the hypothesis that the severity of anhedonia is associated with a deficit of activity of the ventral striatum (including the nucleus accumbens) and an excess of activity of ventral region of the prefrontal cortex (including the ventromedial prefrontal cortex and the orbitofrontal cortex), with a pivotal, but not exclusive, role of dopamine.

**Keywords:** Anhedonia, depression, psychic.

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**Introduction:**

In 1896 the French psychologist Théodule Ribot coined the term “l’anhédonie” (the disappearance of pleasure) in analogy with “l’analgésie” (the absence of pain). He refers to the total loss of pleasure both physical and psychic in melancholia. (**1**)

Two case reports are provided showing loss of pleasure, affective response, emotional reactivity, and interest. Similar descriptions of anhedonic symptoms were made by Georges Dumas ( a French physician/psychologist ) in his doctoral thesis on sadness and joy.
He used “moral anaesthesia” (not anhedonia) as an umbrella term. (**1**)

Anhedonia survived, moral anaesthesia did not. American psychologist. He adopted anhedonia in his textbook on the varieties of religious experience. He distinguishes anhedonia as one of the many kinds of pathological depression, joining “passive joylessness and dreariness, discouragement, dejection, lack of taste and zest,” “incapacity for joyous feeling,” “passive loss of appetite for all life’s values.” (**1, 2**)

In 1922, the American psychiatrist Abraham Myerson devoted an entire lecture during the annual meeting of the American Psychiatric Association to the topic of anhedonia **(3)**. He referred to Ribot and James but took a more psychobiological view. He described anhedonia as a symptom complex that occurs in many mental diseases and different psychoneuroses: "akind of organic anaesthesia," "a dropping out from consciousness of desire and satisfaction." Besides these latter 2 components, Myerson added disappearance of the feeling of energy and feelings of unreality. He also suggested a practical therapeutic approach: restoration of appetite, sleep, energy feeling, and preventive measures. In contrast with this early conception of anhedonia, there was a general falling away of interest during the twentieth century. (**1**)

In a bibliometric search (PubMed search for "depression AND anhedonia"; last search performed on December 5, 2018), a first citation only appears in 1959. **(4)** Publication activity remained few (a maximum of 7 citations/year) until the beginning of the 1990s. From then on, an increase is found reaching 271 citations in 2018. (**1**)

According to **Snaith (5)** the falling away of interest was influenced by the increasing focus on depressed mood. The resurgence of interest is then attributed to the publication of DSM-III which positioned anhedonia as a core depressive symptom.

**Anhedonia: The Behaviour**

In the DSM-III diagnostic criteria of MDD anhedonia was described as "loss of interest or pleasure in all or almost all usual activities and
pastimes" (6).

A similar description is given in the current DSM-5 diagnostic criteria: "markedly diminished interest or pleasure in all or almost all activities most of the day nearly every day (as indicated by either subjective account or observation)" (7).

In the text on diagnostic features this criterion is made more explicit: "Feeling less interested in hobbies, not caring anymore, not feeling any enjoyment in activities that were previously considered pleasurable, reduction from previous levels of sexual interest of desire. Family members may notice social withdrawal or neglect of pleasurable avocations."

**Anhedonia: The Concept**

Different concepts of anhedonia have been described for example low hedonic capacity as a predisposing factor for both schizophrenia and depression, and impairment of appetitive and consummatory pleasure as a hallmark of endogenomorphic depression (8).

More recent and popular concepts pertain to the pleasure cycle and positive affectivity. Both concepts partially overlap and offer a link between psychological categories (e.g., pleasure or anhedonia) and their neurobiological substrates. However, they differ in their origin
and perspective.

The pleasure cycle concept is grounded in the affective neurosciences and narrowly focused on reward. Part of its success has been the scientific strategy of dividing the concept of pleasure into the affective reaction (objective behavioural, physiological, and neural reactions) and its subjective affective experience (9).

The study of reward processing has found substantial evidence for distinct phases within a pleasure cycle, each phase having its own brain circuitry: an appetitive phase (dominated by wanting), a consummatory phase (dominated by liking), and a satiety phase (dominated by

learning). Wanting is defined as the motivation for or the incentive salience of a reward, liking as the actual pleasure or hedonic impact of a reward, learning as associations, representations, and predictions about future rewards based on past experience. Wanting, liking, and learning constantly interact, wax and wane during the different phases of the pleasure cycle. They all have both conscious and unconscious components (10).

Anhedonia is then defined as "the impaired ability to pursue, experience, and/or learn about pleasure, which is often, but not always accessible to conscious awareness". This model is further elaborated by De Berardis (11), who describe the reward process as initially building a stimulus reward association which then leads to interest/desire (wanting a reward), anticipation (state of readiness for a reward), motivation (initial energy expenditure to attain a reward), effort (sustained energy expenditure to attain reward), hedonic response (e.g., enjoyment of reward), and feedback integration (updating reward presence and values). In this model rewards can be primary/fundamental (e.g., food, sex, social interaction) or secondary/higher order (e.g., monetary, artistic, altruistic, and transcendental); their involved brain mechanisms are supposed to generally overlap and to be distinct from the mediation of other features of the same event (e.g.,sensory, cognitive).

The actual experience of pleasure is different from a mere sensation and/or a thought, it is an additional "hedonic gloss" generated by the pleasure networks of the human brain. Although historically the liking part of anhedonia in depression has been emphasized, recent findings point at a greater importance of both wanting and learning that is a reduction in reward anticipation, the willingness to exert effort in order to get a reward, and the ability to modify behavior as a function of reward (12).

This concept of (an)hedonia is largely reflected in the positive valence systems of the Research Domain Criteria (NIMH): reward valuation (reward, delay, effort), reward responsiveness (reward anticipation, initial response to reward, reward satiation), and learning (probabilistic and reinforcement learning, reward prediction error, habit) (13).

The **positive affectivity concept** is grounded in a more general theory of affective psychology. Given their popular use (in which clinical anhedonia is often equated with deficits in reward processing or positive affectivity)

In addition to anhedonia as a specific dysfunction of the pleasure cycle, anhedonia may also be described within more general, dimensional models of affect. Based on studies of the intercorrelations among emotional experiences (subjective reports of words, faces, and experiences) these models organize our affective space in 2 (or more) higher order dimensions (the circumplex models of affect): for example, valence and arousal, positive and negative affect (PA and NA). Affective states are then construed as linear combinations of these 2 dimensions. In these models a distinction can be made between "core affect" (object-free, flee-floating neuro physiological state consciously accessible as a simple, non-reflective feeling) and emotional episodes. These latter are changes in core affect elicited by and attributed to an object. Emotional episodes are accompanied by instrumental action, physiological, and expressive changes (as part of the changes in core affect and as part of the instrumental action), perceptual cognitive appraisal of the object (for example, expectations for the future, relevance for one's goals, causal antecedents), and other conscious, subjective experiences. The subjective experience of a specific

emotion (or emotional meta-experience; e.g., a person perceiving himself as being happy) finally results from a cognitive interpretation/categorisation of the neurophysiological changes that are elicited by the object: these changes being organised in relation to their object, behavioral responses, past experiences, and semantic knowledge. The modelling of the affective space into PA and NA seems of particular interest for anhedonia in depression. PA and NA pertain to the general and evolutionary adaptive systems of approach and withdrawal. PA represents the extent to which a person avows a zest for life, and NA the extent to which a person reports feeling upset or unpleasantly aroused. PA and NA are not therefore opposites, but uncorrelated and independent dimensions (14).
In particular, PA feelings (feelings of energy, power, enthusiasm, confidence) serve as a motivating source and affective reward of goal-directed behavior. Anhedonia may then be defined as low PA. Defined as such, anhedonia appears to be a relatively specific feature of depression: more specific than high NA (15).

**Anhedonia: A Psychopathological Perspective**
Anhedonia may be deconstructed according to different principles (16).
1. Inherent in its current use is the difference between consummatory (lack of actual pleasure, experiential enjoying, liking) and appetitive (lack of interest, looking forward and wanting) anhedonia. Thereby, the form (in a Jaspersian tradition) of anhedonia is complex: phenomena pertaining to both feeling and affective states, and urge, drive, and will (17).

2. A difference has to be made between anhedonic symptoms (patients' subjective complaints; for example, loss of interest and enjoyment) and signs (behavior deemed pathological by a clinician; e.g., lack of positive emotions or mood observed/elicited during a psychiatric interview). Theoretically, anhedonic symptoms should be differentiated from an impaired ability to express (in words or behaviour) the feeling of pleasure, that is, a kind of "anhedonic alexithymia." (18).

3. Anhedonia may be a trait or a state. A historical example of the former is low hedonic capacity as a risk factor for schizophrenia (19). An example of the latter is anhedonia as defined in current DSM classifications
of MDD.

4. Anhedonia may be pervasive or selective. Like pleasure, anhedonia may then be divided according to its object. Pleasures like food, sex, and social interaction are said to be fundamental (or primary, instinctual) the reward is inherent. They contrast with higher order (or secondary, non-instinctual) pleasures (like music, art, money, intellectual and altruistic activities) the reward is not inherent and has to be learned (20). These rewards may belong to the past (remembered), present (actually experienced), or future (anticipated).

5. Although anhedonia suggests a categorical all or nothing phenomenon, anhedonia (or hedonic functioning) has to be seen within a dimensional perspective.

6. Finally, anhedonia may exist on its own or may be part of a more general flattening of emotions and affect (e.g., general paralysis of feeling, blunted affect, derealisation).

## Neurobiology of Anhedonia

Neural basis of normal positive emotion perception

Feeling a normal emotion requires the identification of the emotional significance of a stimulus (appraisal), then the production of affective state (production), which can be regulated at different levels (regulation).

These three steps can be considered as being organized through two different systems with a reciprocal functional relationship.

A **ventral system** (including the amygdala, insula, ventral striatum, and ventral regions of the anterior cingulate gyrus and prefrontal cortex), could be more specifically involved in the identification of the emotional significance of environmental stimuli, and the production of affective states. This system could also be in charge of automatic regulation and mediation of autonomic responses to emotive stimuli and contexts accompanying the production of affective states.

A **dorsal system** (including the hippocampus and dorsal regions of the anterior cingulate gyrus and prefrontal cortex), on the other hand, could be more important for effortful rather than automatic regulation of affective states, probably through executive functions, including selective attention and planning.

The basis of hedonic feelings has been more specifically studied through different paradigms. Euphoric response to dextroamphetamine, cocaine-induced euphoria, monetary reward, and even pleasurable responses to music, pictures, and attractive faces, have been associated with activity within the nucleus accumbens, ventral caudate, and ventral putamen, and, in studies devoted to the neurobiology of pleasure, with dopamine release in the ventral caudate and putamen. The ventral striatum, and particularly the nucleus accum-bens, may indeed have a priority role according to studies in both animals and humans, in behavioral responses to, anticipation of, and/or monitoring of errors in the pre-diction of reward. The nucleus accumbens appears to respond to the emotional intensity and self-relatedness of a variety of stimuli, independent of their valence, with both positive and negative valences possibly processed along a rostrocaudal gradient. The nucleus accumbens receives projections from midbrain regions (such as the ventral tegmental area), from regions involved in emotion (such as the amygdala, orbitofrontal cortex, and medial prefrontal cortex), from motor regions (such as the dorsal caudate and globus pallidus), and from regions involved in memory (such as the hippocampus). The accumbens also indirectly projects to cortical regions including the cingular and medial prefrontal cortex, the ventral pallidum, the thalamus, the amygdala, and the hypothalamus. Many of these regions are also implicated in emotion processing, suggesting a network of tightly anatomically and functionally connected regions. The orbitofrontal cortex is a nexus for sensory integration, the modulation of autonomic reactions, and anticipation in learning, prediction and decision making for emotional and reward related behaviours. Neuroimaging studies have found that the reward value, and the expected reward value, and even the subjective pleasantness of food and other reinforcers are represented in the orbitofrontal cortex. The orbitofrontal cortex receives input from the five classic sensory modalities: gustatory, olfactory, somatosensory, auditory, and visual, and also receives visceral sensory information.

This large variety of inputs makes the orbitofrontal cortex one of the most polymodal regions in the entire cortical mantle. The orbito frontal cortex has direct reciprocal connections with other brain structures, including the amygdala, cingulate cortex, insula/operculum, hypothalamus, hippocampus, striatum, periaqueductal grey, and dorsolateral prefrontal cortex. Hence, the orbitofrontal cortex may have an important role for representing incentive salience, hedonic impact, and subjective hedonic experience, ie constituting the link between reward and hedonic experience. It has been shown that the human amygdala is a key structure for extracting the affective significance from external stimuli, responds preferentially to emotionally valenced faces, for fearful but also for happy faces, and rapidly habituates to them. According to discrepant findings, the amygdala could be considered as reacting more intensively for negative stimuli, explaining its major function in fear and anxiety. The anterior cingular cortex was not activated by transient happiness induced by recalling positive life events and looking at happy human faces. On the other hand individual differences in the ability to accurately detect emotional signals, interoceptively or exteroceptively, maybe at least in part a function of the degree to which the anterior cingulate cortex participates in the experiential processing and response to emotion cues (21).

The ventromedial prefrontal cortex (VMPFC) has been implicated in the generation of an abstract representation of the rewarding value of a stimulus by attending to its context, and the learning of contingencies based on the outcome of a rewarding situation. By contrast lateral areas of the ventral prefrontal cortex may be less involved in hedonic emotions, responding to aversive rather than rewarding stimuli. Some other regions might have a more obvious role in negative and/or distressing emotions rather than hedonic experiences, such as the insula. Recall generated sadness was associated with significantly greater increases in activity in the vicinity of the anterior insular cortex, suggesting that this region participates in the emotional response to potentially distressing cognitive or interoceptive sensory stimuli (22).

Anhedonia in Depression and Schizophrenia: Brain Reward and Aversion Circuits

Anhedonia, which is characterized by a loss of interest or pleasure, reflects deficits in hedonic capacity and is closely related to the constructs of reward valuation, decision making, anticipation, and motivation. Anhedonia is considered a transdiagnostic symptom that is associated with deficits in reward and aversion processing and is especially present in patients with major depressive disorder (MDD) and schizophrenia. In addition, anhedonia is linked to greater severity of clinical symptoms, poorer treatment response, and poorer clinical outcomes in patients with these two disorders. Anhedonia is a multidimensional construct that includes anticipatory anhedonia (inability to anticipate rewards), consummatory anhedonia (impairments in hedonic response to rewards), and motivational anhedonia (diminished motivation to pursue rewards). The constructs of anhedonia have common and dissociable neural underpinnings (23).

Anhedonia is a core feature of MDD. Patients with MDD have deficits in motivation for rewards owing to low anticipatory pleasure and reduced ability to modulate behavior in response to intermittent rewards. In contrast, anhedonia in patients with schizophrenia is one of the cardinal negative symptoms and is independent of positive, disorganized, and depressive dimensions. As defined in the “Schizophrenia Spectrum Anhedonia Paradox”, hedonic capacity is impaired in individuals with schizotypy and youth at clinical high-risk, whereas it appears intact in patients

with schizophrenia. Moreover, a higher frequency of anhedonia is detected during the chronic phase of schizophrenia than during the early phase of illness. Anhedonia in schizophrenia may stem from deficits in integrating and maintaining representations of hedonic values, which results in impairments in anticipatory pleasure and goal-directed behavior (24).

Previous findings suggest that a common neural basis and genetic factors underlie anhedonia, which transcends the disorder categories of depression and schizophrenia. Consistent with the Research Domain Criteria initiative focused on transdiagnostic dimensions of psychopathology, there is a crucial need for a more detailed approach to investigate specific properties at the symptom level. A better understanding of the precise psychopathological and neurobiological underpinnings that are highly relevant to anhedonia is a necessary step to develop more effective treatment plans for psychiatric disorders. The transnosographic method is a promising approach for revealing the overall neurobiological framework that contributes to clinical symptomology and may help improve targeted treatment strategies. Notably, neuroimaging can be a powerful tool for investigating the neurobiological mechanisms of anhedonia. Numerous studies have provided evidence for the neurobiological reward and aversion systems underlying anhedonia. Investigating the reward and aversion pathways of the brain may help improve our understanding of the neurological substrates underlying the clinical transdiagnostic symptomatology of anhedonia. In this context, developing interventions to treat anhedonia across different psychiatric disorders could be targeted according to the shared neural abnormalities of critical brain circuits (25).

Anhedonia is a prominent symptom in patients with MDD and schizophrenia. The characteristics of anhedonia across these two disorders, as well as anhedonia-related reward and aversion neural circuits, have not been extensively explored from a transdiagnostic perspective. Therefore, this review aimed to summarize the neurobiological mechanisms under lying anhedonia based on the reward and aversion neural pathways in depression and schizophrenia. Furthermore, we highlight recent findings of aversion circuits associated with anhedonia in these two disorders.

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