

Anhedonia and Reward System: Psychobiology, Evaluation, and Clinical Features

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ABSTRACT

Anhedonia can be defined as a condition in which the hedonic capacity is totally or partially lost. From a psychobiological perspective, several researchers proposed that anhedonia has a putative neural substrate, the dopaminergic mesolimbic and mesocortical reward circuit, which involves the ventral tegmental area, the ventral striatum and part of the prefrontal cortex. Anhedonia is, besides depressed mood, one of the two core symptoms of depression; furthermore it is one of the most important negative symptom in schizophrenia. Anhedonia is also present in substance use disorders as part of the abstinence symptomatology, and interrelations between hedonic capability, craving and protracted withdrawal have been found, particularly in opiate-dependent subjects. Although anhedonia is regarded as an important symptom in psychopathology, so far it has received relatively little attention. In general, two main approaches have been utilized to investigate and assess anhedonia or hedonic capacity: laboratory-based measures and questionnaires. Among measurement scales, the most commonly used are the Snaith-Hamilton Pleasure Scale (SHAPS), the Fawcett-Clark Pleasure Scale (FCPS), and the Revised Chapman Physical Anhedonia Scale (CPAS). Nevertheless, other measurement scales, particularly used within broader psychopathological dimensions, are the Anhedonia-Asociality subscale (SANSanh) of the Scale for the Assessment of Negative Symptoms (SANS) and the Bech-Rafaelsen Melancholia Scale (BRMS). In this paper we analyze these different scales, individuating their strengths and limits and their current clinical applications.

Keywords: Anhedonia; Pleasure; Dopaminergic Reward System; Substance Dependence; SHAPS; CPAS; SAS; FCPS; SANS; BRMES; VAS; TEPS

1. Introduction

The word anhedonia comes from ancient Greek: *ἀν-* an-, “without” + *ἡδονή* *hēdonē*, “pleasure”, and it was introduced in Psychiatry by Théodule-Armand Ribot in 1896 [1]. He defined anhedonia as the inability to experience pleasure, and it refers to both a state symptom in various psychiatric disorders and a personality trait [2]. The DSM-IV-TR defines anhedonia as diminished interest or pleasure in response to stimuli that were previously perceived as rewarding during a premorbid state [3].

Anhedonia has been considered crucial for the diagnosis of depression [4-7], and schizophrenia [8-11]. It is, besides depressed mood, one of the two core symptoms of depression [3]; moreover lack of reactivity and anhedonia are key diagnostic criteria for the DSM-IV-TR

melancholic subtype of major depression [3]. Anhedonia is also one of the most important negative symptoms frequently observed in schizophrenia [12,13]. For example, Blanchard and Cohen [14], in a review published in 2006, suggested that anhedonia is, together with diminished expression, one of the two key features involved in the negative symptom complex of schizophrenia; however, other studies [15], indicate that patients with schizophrenia maintain dynamics in their affect.

Even though anhedonia plays a very significant role in depression and schizophrenia, it is not just limited to them. In fact, it was linked to anxiety and adjustment disorders [16], suicidal ideation [17] and successful suicide [18]. In the model proposed by Loas [19], a genetically determined low hedonic capacity was regarded as a specific character trait, which, together with aspects like

pessimism, passivity, introversion and obsessive-compulsivity could represent a risk factor, which could lead, under stress conditions, to unipolar depression.

Anhedonia is also present in individuals suffering from a substance use disorder, as part of the abstinence symptomatology [20]. Several authors suggested that anhedonia is an important factor involved in relapse [21,22], as well as in the transition from recreational use to excessive drug intake [23]. Anhedonia was found to be a frequent feature in alcoholics and addicted patients during acute and chronic withdrawal [24], as well as in cocaine, stimulant, cannabis [25-27], and polysubstance abusers [28]. In particular, Heinz *et al.* [24] found that, together with avolition and dysphoria, anhedonia, is a common symptom of schizophrenic, depressive, and alcohol-dependent patients during withdrawal. According to the authors and as supported by PET and SPECT findings, these symptoms could be caused by a functional deficit of dopaminergic transmission in the dopaminergic reward system.

Anhedonia and craving, along with typical withdrawal symptoms, may arise independently during the phase of abstinence from rewarding psychoactive substances, but their intensity, temporal pattern and responsivity to treatment appear not to overlap. In the so-called protracted withdrawal, the syndrome that is usually described as depression could be better interpreted as anhedonia, and it cannot be merely attributed to the psychological effects of abstinence [29].

Interesting findings about the presence and correlation of anhedonia in substance related disorders have been found by Janiri *et al.* [30], who found interrelations between hedonic capability, craving and protracted withdrawal, particularly in opiate-dependent subjects, in a study published in 2005, in which were enrolled 70 alcohol-, opiate- or multiple substance-dependent subjects. These data were confirmed and enriched by following studies made by Martinotti *et al.* [31], who found that the positive correlation between the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) score and anhedonia scales was consistent with the hypothesis that the clinical dimension of anhedonia cannot be separated from the other behavioural symptoms of withdrawal and should be considered as part of the same process. According to Martinotti *et al.* [31], the strong correlation of specific withdrawal symptoms like "nausea" and "headache, fullness in head" with anhedonia scales leads to assume that they may represent physical correlates of anhedonia. The findings describing that in alcohol addicts somatoform disorders are possible [32], and the study describing gastrointestinal discomfort and headache as two of the most common pain complaints in depressive disorders [33] are in alignment with this hypothesis.

In another study, Martinotti *et al.* [34] investigated the relationships between anhedonia, craving and temperament and character dimensions in a sample of patients with alcohol and opiate dependence. The authors found that the temperament dimension of Novelty Seeking (NS) [35] was positively correlated to both anhedonia and craving, with a higher score of Novelty Seeking among anhedonic subjects with respect to both non-anhedonic and control subjects. In this study, the possibility that difficulty in experiencing pleasure in psychiatric disorders can lead to the use of psychoactive substances in an attempt to decrease anhedonia, is extended to subjects without psychiatric disorders, who may try substances to counterbalance a tonic state of anhedonia.

A study by Pozzi *et al.* (2008) [36], conducted on 70 patients affected by alcohol-, opiates- or multiple drugs-dependence, investigated the influence of recent clinical and social-environmental factors on hedonic capability and related psychopathology, and showed that anhedonia is a psychopathological entity independent from other clinical and psychosocial features.

From a psychobiological perspective a relationship was found between anhedonia, craving, and dysphoric mood on one side, and the hypoactivity of the dopaminergic system on the other side, particularly in the dopamine outflow in the nucleus accumbens (NAcc) [37], confirming the relationship between the hypoactivity of the dopaminergic system and anhedonia in substance use disorders, as supported by previous studies based on animal models [29,38,39]. Notwithstanding, in clinical studies a central receptor dopamine dysfunction was shown to occur as a correlate of affective blunting rather than anhedonia [37].

In a study made by Diana *et al.* [40] anhedonia was associated with craving and dysphoric mood in an animal model of alcohol dependence with abrupt ethanol discontinuation. This study indicates that physiological symptoms of ethanol withdrawal syndrome (*i.e.*, tremors, motor impairment, and reduced seizure threshold) and the decline in dopaminergic neuronal activity responsible for anhedonia, show a different time course, with the hypoactivity of the dopaminergic system emerging later and lasting longer. The same association was outlined by Robertson [41] and Miller [42], who postulated an alteration of the monoaminergic transmission in cocaine and opiate abusers.

Imaging studies provided evidence of reduced and altered sensitivity to natural reinforcers in the reward circuits of drug addicted subjects, which could represent the mechanism underlying dysphoria and anhedonia experienced during withdrawal [22,43]. The same decreased striatal dopaminergic responsiveness was found in detoxified cocaine dependent subjects with craving and a reduced "high" experienced in specific pleasant situa-

tions [44].

Moreover anhedonia is present in other disorders and dysfunctional behaviours as well, such as Parkinson's disease [45], over-eating [46] and risky behaviours in general [47].

As previously mentioned, the term anhedonia was introduced in 1897 by Ribot, who accused psychologists of paying little attention to the study of the experience of pleasure [1]. However, in the late nineteenth century the loss of the pleasure response was already recognised as an early and preeminent symptom of depression [48-50]. Anhedonia played an important role in psychopathology theories at the beginning of the 20th century [51-53]. In particular, Kraepelin [51] described anhedonia as a state of individual suffering which was part of the dementia praecox. Kraepelin described his patients as if they could not feel any real joy in life; according to him, the characteristic indifference of patients towards social interactions, the extinction of affection for family and friends and the loss of satisfaction in their works and occupations, in recreation and pleasure, was rather often the first symptom to manifest, marking the onset of the disease.

Bleuler [52], with regard to the indifference that some patients exhibited towards their acquaintances, colleagues, friends and familiars, and at last life itself, defined anhedonia as a basic feature of their disease, "an external signal of their pathological condition."

What emerges by reading works by Kraepelin and Bleuler is that they fundamentally interpreted the loss of the pleasure experience as only one facet of the deterioration of patient's emotional life.

Nevertheless, after the turn of the century, psychiatric interest in anhedonia faded, and Jaspers in his "*Allgemeine Psychopathologie. Ein Leitfadens für Studierende, Ärzte und Psychologen*" mention it only as an aspect of the more severe and pervasive loss of all emotional responses [54]. Attention focused then on depressed mood as the pathognomonic feature of depressive illness. The *International Classification of Diseases, 9th revision (ICD-9)* does not mention anhedonia in its definition of the depressive phase of manic-depressive psychosis, but defines the disorder in terms of a "widespread depressed mood of gloom and wretchedness with some degree of anxiety" [55].

In the 1960s, Rado [56,57] assigned a more central role to anhedonia in the development of schizophrenia. He suggested that anhedonia is a central, genetically transmitted defect both in overt schizophrenia and in compensated schizotypes, not actually experiencing a psychotic breakdown. According to Rado, this defect reduces enthusiasm for life, weakens the feelings of joy, affection, love, pride, and self-respect, impairs the ability to relate with other people, and prevents the development of normal healthy sexual functioning.

Meehl [58,59] integrated Rado's theory into a theory of neurological dysfunction in schizophrenia. He asserted that low hedonic capacity, or joylessness, is a heritable trait predisposing to the development of schizophrenia and depression. Moreover, like Rado, Meehl suggested that the lack of pleasure in relationships with other people leads to social withdrawal, inappropriate behaviour, and even deviant logic.

The *Diagnostic and Statistical Manual of Mental Disorders* recognised anhedonia in its third edition, in which the concept of anhedonia was promoted to the position of one of the two pathognomonic features of major depressive disorder. Klein's definition "a sharp, unreactive, pervasive impairment of the capacity to experience pleasure, or to respond affectively, to the anticipation of pleasure" was slightly turned into "a loss of interest or pleasure in all or almost all usual activities and pastimes" [60]. Moreover, for the melancholic subtype of major depression the anhedonic experience became essential to the definition.

With recent scientific advances in elucidating the genetic basis of psychopathology by identifying endophenotypes, anhedonia gradually gained renewed research attention. Endophenotypes are subclinical traits associated with the expression of an illness, and represent the genetic liability of the disorder in non-affected individuals [61]. A study by Hasler *et al.* [62], published in 2004 demonstrated that anhedonia, together with increased stress reactivity, is the most important candidate for psychopathological endophenotype of major depression.

2. The Dopaminergic Reward System and Its Alteration in Anhedonic Patients

Several researchers have proposed that anhedonia has a putative neural substrate, the dopaminergic mesolimbic and mesocortical reward circuit, which involves the ventral tegmental area, the ventral striatum and part of the prefrontal cortex [24,45,63,64].

The reward system is a mass of brain structures which role consist in regulating and controlling behaviour by inducing pleasurable effects. A psychological reward is a process that reinforces behaviour, or something that, when offered, induce a behaviour to increase in intensity. Reward is an operational concept to describe the positive value that a person attribute to an object, behaviour or internal physical state. Natural rewards include those necessary for the survival of the species, such as eating, drinking, sex, and fighting. Secondary rewards derive their value from the primary reward, and include shelter, money, pleasant touch, beauty, music, etc. Rewards are generally considered more effective than punishment in enforcing positive behaviour and they induce learning, approach behaviour and feelings of positive emotions.

The major neurochemical pathway of the reward system in the brain involves the mesolimbic and mesocortical pathway. Between these pathways, the mesolimbic pathway plays the most important role, and it projects from the ventral tegmental area (VTA), via the medial forebrain bundle, to the ventral striatum, including the nucleus accumbens (NAcc), to the amygdala and to the hippocampus; the mesolimbic pathway is chiefly related to reward motivation, associative learning and reinforcement. Indeed, the mesocortical pathway projects to cortical regions, including the medial prefrontal cortex (mPFC), the orbital frontal cortex (OFC), the anterior cingulate cortex (ACC), and the insula; this pathway is mainly related to attention, working memory, and inhibitory control (**Figure 1**).

Dopamine acts on one out of five post-synaptic receptors, called D₁, D₂, D₃, D₄ and D₅ [65]. These receptors are arranged into two families, defined D₁-like, which includes D₁ and D₅ receptors, and D₂-like, which includes D₂, D₃ and D₄ receptors. The stimulation of D₁-like receptors increases the responsiveness of medium spiny neurons, generating “up-states” [66], whereas the stimulation of D₂-like receptors decreases the responsiveness of medium spiny neurons, generating “down-states” [67].

As previously mentioned, central dopaminergic dysfunction has been broadly proposed as a common neurobiological correlate of the psychopathological expression of anhedonia. Some studies on depressive disorders sup-

ported the hypothesis of a dysfunction of dopamine turnover as reflected by levels of homovanillic acid in cerebrospinal fluid and by assessment of dopamine receptors and neuroendocrine function through neuroimaging, genetic or postmortem techniques. Further evidence came from several studies on the effectiveness of dopamine agonists and antagonists in the treatment of depressive disorders, especially from the recognition that drugs that enhance dopamine transmission present antidepressant activity [68-71]. It has been widely recognized that rewarding events, irrespective of their modality, share the common property of activating the mesolimbic and the mesocortical dopamine system. On the contrary, as suggested by evidence coming from intracranial stimulation, dopaminergic antagonism of neuroleptic drugs, and from studies on the mechanism of action of substances of abuse [72], the inactivation of dopamine function leads to anhedonia [73].

Additional findings on altered dopamine function in anhedonia come from single photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging of the dopamine transporter (DAT) [74-77]. The ligand [123I]N-fluoropropyl-carbomethoxy-3β-(4-iodophenyl)tropane (DATSCAN) was developed as a high-affinity SPECT radiotracer of the DAT, and it is considered to be a pre-synaptic marker of dopaminergic neurons, which is able to provide a sensitive measure of changes in the transporter density. The DAT has been implicated in several neuropsychiatric disorders either as a possible component of polygenetic disorder or as a marker of dopaminergic neurotransmission, that could reflect compensation mechanism in response to a central dopaminergic dysfunction [78]. Worth mentioning is a study conducted by Sarchiapone *et al.* [79], and conducted at the University Hospital A. Gemelli of the Catholic University of the Sacred Heart in Rome, Italy, on a total of 11 depressed outpatients with anhedonia and 9 healthy comparison subjects, recruited from the Day Hospital of Clinical Psychiatry. All patients included in the study had a Snaith-Hamilton Pleasure Scale (SHAPS) [80] total score > 7 and a Hamilton Depression Rating Scale (HAM-D) [81] score > 18. SPECT with the radiotracer DATSCAN was used to evaluate DAT binding. Significantly lower specific/non-specific DAT binding ratios were found in the putamen and caudate individually and in the whole striatum bilaterally of depressed patients with anhedonia compared with control subjects. In that case, the reduced DAT binding ratio may be explained by a reduced number of transporters per neuron rather than by a reduced number of dopaminergic synapses and neurons, because the examined patients did not show any sign of dopaminergic neuron degeneration, such as symptoms of Parkinson's disease. Furthermore a reduced number of reuptake sites per neuron may be ex-

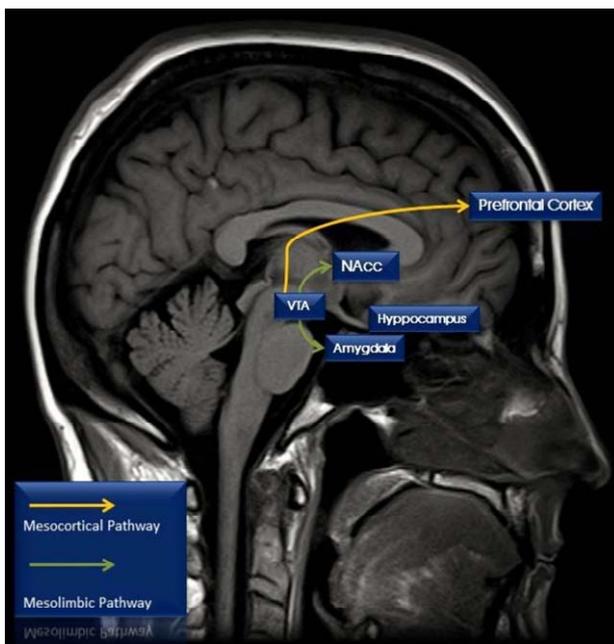


Figure 1. Schematic illustration of mesocortical and mesolimbic pathway. VTA: Ventral Tegmental Area; NAcc: Nucleus Accumbens. The localization of labels referring to the structures involved in reward system is approximate.

plained as a down-regulation secondary to lower dopamine concentrations in the synaptic cleft, and to an impairment of dopaminergic transmission. However it is worth noting that it may also be a primary defect leading to a predisposition to develop anhedonia or depression.

In addition to dopamine, primarily involved in hedonic experience are endogenous opioids. Endogenous opioids include different families of neuropeptides, like enkephalins, dynorphins, endorphins, and orphanin FG, which act on μ , δ , κ and ORL1 receptor subtypes [65], which are broadly expressed in the ventral striatum. The stimulation of these receptors is believed to play a role in the hedonic responses to natural rewards [82]. The most relevant causal centres of affective pleasure responses are supposed to be the shell of the nucleus accumbens (NAcc) [83] and the ventral pallidum (VP) [84]. Other important cerebral regions involved in the hedonic response are the orbital frontal cortex (OFC) [85,86], the anterior cingulate cortex (ACC) [87-90], and the amygdala [91-93].

In a recent review, Treadway and Zald [94] from the Vanderbilt University of Nashville, United States, according to theoretical models of anticipatory and consummatory pleasure [5,95,96], proposed a distinction between deficits in the motivation to pursue rewards (reward “wanting”), which leads to motivational anhedonia, and deficits in the hedonic response to them (reward “liking”), which leads to consummatory anhedonia. Reward “wanting” and, subsequently, motivational anhedonia would be linked to dopamine and basal ganglia, whereas reward “liking” and consummatory anhedonia would be linked to opioids, ventromedial prefrontal cortex and amygdala. Given substantial preclinical evidence that dopamine is primarily involved in motivational aspects of reward, they suggested that a refined definition of anhedonia, able to distinguish between deficits in pleasure and motivation, is essential for the purpose of identifying its neurobiological substrates. Furthermore, bridging the gap between preclinical and clinical models of anhedonia, may require to overcome the conceptualization of anhedonia as a steady-state, mood-like phenomenon. Consequently, they proposed to introduce the term “decisional anhedonia” to address the influence of anhedonia on reward decision-making.

3. Diagnosing Anhedonia

Although anhedonia is esteemed an important symptom in psychopathology [97,98], up to this point it has received relatively little attention. This could be the result of the lacking availability of well-validated, short, and easy to use evaluation instruments [99].

In general, two main approaches have been used to assess hedonic capacity and anhedonia: laboratory-based measures and questionnaires.

3.1. Laboratory-Based Measures of Anhedonia

The first approach uses laboratory-based measures of anhedonia, including physiologic measures, signal-detection methods, and subjective hedonic response to pleasant stimuli [9,100-104]. These studies showed that individuals with higher scores on self-report measures of anhedonia report lower hedonic responses respectively to sucrose solutions [101], emotion-eliciting pictures on slides [102], and positive emotional scripts [103]. In particular, Berlin *et al.* [101] assessed hedonic responses to sucrose solutions and sweet taste perception threshold in patients with major depression and schizophrenia in comparison with healthy subjects; they then compared these responses to evaluations made by the Physical Anhedonia Scale (PAS) [105,106] and Social Anhedonia Scale (SAS) [105] of Chapman and the Fawcett-Clark Pleasure Scale (FCPS) [107]; as a result hedonic response to sucrose solutions was similar in patients with major depression, schizophrenia, and healthy controls, whereas sweet taste perception threshold was significantly higher in depressive patients than in controls. Therefore they assessed that hedonic responses to sucrose solutions and sweet taste perception threshold may be used as complementary evaluation to quantify anhedonia. Similar results were found in previous and following studies [108-110].

According to Jamesian theory [111], Ferguson and Katkin [102] asserted that individuals who are more aware of their visceral activity should demonstrate greater affective response to emotion-eliciting stimuli than individuals who are not viscerally perceptive. Therefore certain groups of “unemotional” subjects, such as anhedonics, may report fewer or less intense emotional experiences due to an attenuation or lack of autonomic feedback. Results from their study reported that people who reported a high score on self-report measures of anhedonia demonstrate hyporesponsiveness on measures of facial expressions and heart rate in response to emotion-eliciting pictures as compared to those with lower self-reported anhedonia.

Besides these behavioural measures, anhedonia can also be evaluated using electrophysiological [112-114] and hemodynamic [115-117] measures. Particularly interesting and worth mentioning is a study by Mitterschiffthaler *et al.* [117], which aim was to investigate the neural correlates of affect processing in depressed patients with anhedonia and healthy controls. In this study, whole brain functional magnetic resonance (fMRI) imaging scans were obtained from seven females with a diagnosis of chronic unipolar major depression and high levels of anhedonia, and seven healthy females, while they were presented with neutral and positive valence images. Compared to controls, patients showed decreas-

ed activation in medial frontal cortex, and increased activation in inferior frontal cortex, anterior cingulate, thalamus, putamen and insula. Reduced activation in medial frontal cortex may underlie abnormal positive affect processing in patients, whereas increases in neural activation in putamen and thalamus, previously found in transient sadness, and anterior cingulate, could point to an involvement of these structures in anhedonia.

3.2. Self-Report and Interview-Based Questionnaires to Measure Anhedonia

A secondary approach to the diagnosis of anhedonia involves the use of questionnaires. Many different scales have been elaborated in order to assess anhedonia or hedonic capacity (see **Table 1**). Specific scales for the measurement of anhedonia are the Revised Chapman Physical Anhedonia Scale (CPAS) and Social Anhedonia Scale (SAS) [105,106]; the Fawcett-Clark Pleasure Scale (FCPS) [107]; and the Snaith-Hamilton Pleasure Scale (SHAPS) [80]. Other rating scales can be employed to evaluate anhedonia within broader psychopathological dimensions, such as those of depression and negative symptoms of schizophrenia. The Scale for the Assessment of Negative Symptoms (SANS) [118] and particularly the Subscale for Anhedonia (SANSanh) has been used in patients affected by schizophrenia with [119] or without [120,121] cannabis abuse. The Bech-Rafaelsen Melancholia Scale (BRMS) [122,123] has been administered to both melancholic and acute schizophrenic patients, in order to rate the latent dimension of depressive and negative symptomatology and it shows a positive correlation with SANS [124]. Furthermore it is worth mentioning the 10-cm VAS [125,126] for pleasure and the Temporal Experience of Pleasure Scale (TEPS) [127], which was developed to assess anticipatory and consummatory pleasure.

The three most broadly used scales in the measurement of anhedonia are the Snaith-Hamilton Pleasure Scale (SHAPS), the Fawcett-Clark Pleasure Scale (FCPS), and the Revised Chapman Physical Anhedonia Scale (CPAS). Although each of these instruments is intended to evaluate a common construct of hedonic capacity, there are some differences in the content, format, and psychometric characteristics of these scales.

The Snaith-Hamilton Pleasure Scale (SHAPS) [80] is a brief 14-item self-report questionnaire that intends to measure hedonic tone and its absence, anhedonia. These 14 items cover four domains of hedonic experience: interest/pastimes (item 1, 4 and 9), social interaction (2, 7, 8, 13 and 14), sensory experience (item 5, 6, 11 and 12), and food/drink (3 and 10). The SHAPS instructs participants to agree or disagree with statements of hedonic response in pleasurable situations, which are likely to be

encountered by most people (e.g., “I would enjoy my favourite television or radio programme”; “I would enjoy being with family or close friends”; “I would be able to enjoy my favourite meal”, etc.). Four responses are possible: Strongly disagree, Disagree, Agree, or Strongly agree. If the subject answers “Strongly agree” or “Agree” to an item, it is assigned a score of zero, while if it says “Disagree” or “Strongly disagree” it is assigned a score of 1. A total score can be derived by summing the answers to each item, therefore going from 0 (absence of anhedonia) to 14 (complete anhedonia); thus higher SHAPS total scores indicate greater anhedonia, and a score of 3 or higher indicates a significant reduction in the hedonic capacity and seems to discriminate between healthy and clinically depressed patients. Participants completing the SHAPS are instructed to respond based on their ability to experience pleasure “in the last few days.” The scale was constructed in such a way that cultural, gender and age biases were kept to a minimum.

The SHAPS has shown adequate overall psychometric properties in clinical and student samples [80,128,129]. In particular, in a work conducted by Franken *et al.* [99] and published in 2007, various aspects of the reliability and validity of the SHAPS were examined in three separate studies. First, they assessed the internal consistency, convergent and discriminative validity of the SHAPS in a non-clinical sample. Second, they investigated in another sample the test-retest reliability of the SHAPS. In the third study, they tested the internal consistency, convergent and discriminative validity of the SHAPS by administering the scale in three clinical samples of psychiatric inpatients. At last, the SHAPS was found to be highly reliable in terms of internal consistency and test-retest stability. Furthermore the SHAPS correlated in a theoretically meaningful way with other measures of affect and personality. Patients with depression, psychosis or substance dependence scored significantly higher on the SHAPS than non-patient controls, while patients with depression displayed the highest SHAPS-score. Thus the study by Franken *et al.* shows that the SHAPS is a reliable and valid questionnaire to assess hedonic tone in patient and non-patient populations. Since it is a brief scale, it seems to be a very useful instrument for measuring anhedonia in clinical and research settings.

The SHAPS convergent validity has been also supported by its correlations with Montgomery Asberg Depression Rating Scale (MADRS) [130] Hedonic Tone item, the Mood and Anxiety Symptom Questionnaire Anhedonic Depression subscale, and Positive and Negative Affect Schedule-Positive Affect subscale [80,128]. Its discriminant validity has been supported by its lack of association with MADRS Depressed Mood and Anxiety items [80].

The Fawcett-Clark Pleasure Scale (FCPS) [107] is a

Table 1. Self-report and interview-based questionnaires to measure anhedonia.

Scale	Type	Number of items	Domains investigated	Score	Anhedonia	References
SHAPS	Self-report	14	Interest/pastimes Social interaction Sensory experience Food/drink	Binomial score Item: 0 - 1 Total: 0 - 14	≥ 3	Franken, <i>et al.</i> , 2007
FCPS	Interview-based	36	Social activities Sensory experiences Sense of mastery of difficult tasks	Likert scale Item: 1 - 5 Total: 36 - 180	Lower score	Fawcett, <i>et al.</i> , 1983 Clark, <i>et al.</i> , 1984 Loas, <i>et al.</i> , 1994 Loas, <i>et al.</i> , 1996 Berlin, <i>et al.</i> , 1998
CPAS	Interview-based	61	Interest in activities and hobbies Sensory experiences Pastimes Social interactions Food/drink	Binomial score Item: 0 - 1 Total: 0 - 61	Higher score	Berenbaum, <i>et al.</i> , 1987 Loas, <i>et al.</i> , 1994 Fiorito, <i>et al.</i> , 1994 Loas, <i>et al.</i> , 1996 Ferguson, <i>et al.</i> , 1996 Berlin, <i>et al.</i> , 1998 Germans, <i>et al.</i> , 2000
SAS	Interview-based	40	Talking, socializing, exchanging expressions of feelings	Binomial score Item: 0 - 1 Total: 0 - 40	Higher score	Leak, <i>et al.</i> , 1991 D'Haeren, <i>et al.</i> , 1996
10-cm VAS	Self-report	/	Pleasure	Visual	Lower score	Aitken, <i>et al.</i> , 1969 Mottola, <i>et al.</i> , 1993
SANSanh	Interview-based	4	Recreational interests and activities Sexual interests and activities Ability to feel intimacy and closeness Relationship with friends and peers	Likert scale Item: 0 - 5	Higher score	Andreasen, <i>et al.</i> , 1982 Lewine, <i>et al.</i> , 1990 Schuldberg, <i>et al.</i> , 1990 Mueser, <i>et al.</i> , 1994 Norman, <i>et al.</i> , 1996 Peralta, <i>et al.</i> , 1999 Horan, <i>et al.</i> , 2006
BRMS	Interview-based	11	Mood Verbal activity Social contact and activities Motor activity Sleep Guilt feelings Tiredness Suicidal thoughts Concentration Anxiety	Likert scale Item: 0 - 4 Total: 0 - 44	Higher score	Bech, <i>et al.</i> , 2002
TEPS	Interview-based	18	Sensory experiences Anticipatory pleasure Consummatory pleasure	Likert scale Item: 1 - 6	Lower score	Gard, <i>et al.</i> , 2006

36-item questionnaire in which participants are asked to rate imagined hedonic reactions to hypothetical pleasurable situations (e.g., "You sit watching a beautiful sunset in an isolated, untouched part of the world"). Unlike the SHAPS, which instructs participants to base their answers on their pleasure experience in the last few days, participants completing the FCPS are asked to respond based on their current state. Responses are made on a 5-point Likert scale, going from 1 "No pleasure at all" to 5 "Extreme and lasting pleasure". Each item on the FCPS is worded so that higher scores indicate greater pleasure capacity. A total score can be derived by summing the responses to each item. Higher FCPS total scores indicate

greater pleasure capacity. Items cover several domains of hedonic experience, including sensory experiences, social activities, and sense of dominance of difficult tasks. The decision to refer to hypothetical, not current, situations, is designed to encourage the patient to answer freely, unencumbered from its present symptomatology which, in some cases, could induce him to deny any form of present pleasure.

The psychometric properties of the FCPS have received a considerable degree of attention from depression researchers. This measure was shown to discriminate depressed and non-depressed participants [11,101,131], distinguish depressed from schizophrenic patients [101],

associate with melancholic symptomatology within a depressed sample [132], correlate with hedonic responses to sucrose solutions [101], and demonstrate good overall psychometric properties in clinical and nonclinical samples [133]. One study demonstrated that manifest items from the FCPS tap a single latent dimension, suggesting that loss of pleasure capacity as measured by this scale influenced all itemized experiences (physical and social) in a relatively uniform way [107].

The Revised Chapman Physical Anhedonia Scale (CPAS) [105,106] is a 61-item questionnaire, in which participants are asked to respond true or false to self-statements about their typical feelings about normally pleasurable stimuli and activities; it includes items concerning the experience of pleasure related to taste, sight, touch, sex, and smell (e.g., “The beauty of sunsets is greatly overrated” [keyed True]; “I like playing with and petting soft little kittens or puppies” [keyed False]; “I have usually found love making to be intensely pleasurable” [keyed False]). Like SHAPS and FCPS, the CPAS measures several domains of the pleasure experience, including sensory experiences, food/drink, interest in activities and hobbies, pastimes, and social interaction. The CPAS is different from the FCPS and SHAPS in several ways. First, it uses a true-false response format. Second, it contains some items for which responding true indicates greater pleasure capacity (e.g., “The taste of food has always been important to me”) and others for which responding true indicates lower pleasure capacity (e.g., “Dancing, or the idea of it, has always seemed dull to me”). Items for which a true response indicates greater pleasure capacity are reversed scored so that higher total scale scores indicate lower pleasure capacity (*i.e.*, greater anhedonia). Third, items on this scale are formulated so that they cover hedonic characteristics throughout the lifetime, rather than focusing on recent experience like SHAPS and FCPS. Fourth, some items assess hedonic reactions to activities (e.g., “The sound of rustling leaves has never much pleased me”), which is congruent with the format SHAPS and FCPS. However, other CPAS items assess interest in activities (e.g., “I have had very little desire to try new kinds of foods”). Psychometrically, there has been some disagreement regarding this scale’s construct validity [134]. This disagreement centres around discrepant findings of studies comparing high and low scorers on the CPAS on emotional responses to affective stimuli. Some studies showed that low scorers report less positive emotion in response to emotion-eliciting pictures [102] and imagery of positive emotional scripts [103]. However, other studies found no differences between high and low scorers in reported experience of pleasure in response to pleasant pictures [100, 134]. In a clinical context, the CPAS was shown to differentiate depressed versus non-depressed individuals,

distinguish melancholic versus non-melancholic depression, and correlate with FCPS scores [101,131,132]. At the same time, the CPAS may have poor discriminant validity, evidenced by its association with non-affective forms of psychopathology, such as personality and psychotic disorders [135-137].

The Chapman Revised Social Anhedonia Scale (SAS) [105,106] is an instrument related to the CPAS; it is a 40-item questionnaire that assesses deficits in the ability to experience pleasure from non physical stimuli such as talking, socializing, exchanging expressions of feelings, and being with people in other ways (e.g., “A car ride is much more enjoyable if someone is with me” [keyed False]; “writing letters to friends is more trouble than it’s worth” [keyed True]; “I could be happy living all alone in a cabin in the woods or mountains” [keyed True]; “I have often enjoyed long discussions with other people” [keyed False]; “getting together with old friends has been one of my greatest pleasure” [keyed False], etc.). As the CPAS, the SAS uses a true-false response format; it contains some items for which responding true indicates greater hedonic capacity and others for which responding true indicates lower hedonic capacity. Moreover items on this scale are worded so that they cover hedonic characteristics throughout the lifetime, rather than just the present time. The SAS has revealed to have problems with respect to divergent and convergent validity [138,139] and seems to be more related to social anxiety and rigidity rather than anhedonia.

The 10-cm VAS [125,126] for pleasure is part of the great family of the Visual Analogue Scale, originally designed by Aitken [125], and which structure is suitable to be used in any context simply by changing the question, although the author has originally proposed it for the assessment of depression. In the VAS the evaluator is called to put a sign on a segment measuring 100 mm in length, that way indicating the severity of patients’ disease, disorder or symptom, considering that the left end corresponds to the absence of disease and the right to its maximum severity; therefore the severity of the disease is expressed by mm lying between the left end (normal) and the point of the segment in which the patient has been placed. In the case of the 10-cm VAS for pleasure, the hedonic capability, *i.e.* the subjects’ capacity to experience pleasure in everyday life, is directly assessed as emerges from a complex of types of pleasure explored by asking them about food, sexual behaviour and meeting friends; and the left end corresponds to the absence of pleasure, whereas the right to extreme pleasure.

The Anhedonia-Asociality subscale (SANSanh) of the Scale for the Assessment of Negative Symptoms (SANS) [8,118] was designed to assess either difficulties or reduction in experiencing interest or pleasure, which may be expressed as a loss of interest in pleasurable activities,

an inability to experience pleasure when participating in activities normally considered pleasurable, or a lack of involvement in social relationships. The subscale consists of 4 items that cover recreational interests and activities, sexual interest and activities, ability to feel intimacy and closeness, and relationships with friends and peers. These 4 items, as well as a global summary score, are rated on a Likert scale going from 0 "Not at all" to 5 "Extreme". In rating this subscale, there is a considerable variability across studies in the sources of information (e.g., patient interview alone versus additional information from family members, medical records, etc.) and in the covered period of time (ranging from 1 week to several months). The SANS Anhedonia-Asociality subscale shows several strengths in the assessment of anhedonia. Patients are queried not only about how frequently they engage in social and recreational activities, but also how much they enjoy and are interested in those activities. The assessment time frame can be adjusted to cover relatively brief periods (e.g., 1 month), thus capturing patients' characteristic experiences.

Considerable evidence documents the good psychometric properties and clinical relevance of this subscale [8,140-145]. Nevertheless, some conceptual and psychometric features of this subscale may limit its ability to validly assess the construct of anhedonia. The main limitation is that a single item may actually reflect several conceptually distinct processes or domains, *i.e.* an item rating may reflect either frequency of engagement or pleasure derived from or interest in various types of activities. However, it is not clear that anhedonia, interest, and asociality should be considered in a unitary rating, as these constructs do not necessarily measure the same thing. As a consequence, patients may receive high ratings on the items that comprise this subscale for reasons that have little or no relationship with anhedonia. For example, limited engagement and/or interest in recreational, sexual, or social activities will almost inevitably result in increased ratings on the Anhedonia-Asociality subscale items, whereas they may also result from a variety of emotional, motivational, and social factors other than a decreased ability to experience pleasure. Thus, by conflating assessment of anhedonia with actual performance of and interest in recreational and social activities, SANS Anhedonia-Asociality ratings may often reflect a social "performance" deficit more than a fundamental hedonic "capacity" deficit [140].

Anhedonia-Asociality ratings are strongly related to other negative symptoms and are distinguishable from psychotic, disorganized, and mood symptoms, as well as from neurocognitive deficits. It is worth noting that, although SANS Anhedonia-Asociality ratings tend to be relatively stable, several studies [120,146-148] have reported that these ratings demonstrate sensitivity to treat-

ment effects, suggesting that an interview format may be useful for detecting relatively short-term changes in anhedonia.

The Bech-Rafaelsen Melancholia Scale (BRMS) [122, 123] (also referred to as MES or BRMES) can be employed to evaluate anhedonia within depression, even though it was administered not only to melancholic patients, but also to acute schizophrenic subjects, in order to rate the latent dimension of depressive and negative symptomatology, and it shows a positive correlation with SANS [118].

The BRMS is an 11-item clinician-rated scale that assesses the severity of depressive symptoms over the previous three days (or other specified period of time). Items are scored on a 0 to 4 basis, yielding a total score range going from 0 to 44, with higher score indicating greater severity of depression. The scale developers suggest that scores in the range of 0 - 5 indicate "No depression"; 6 - 9 "Doubtful depression"; 10 - 14 "Minor depression"; 15 - 20 "Mild depression"; 21 - 28 "Moderate depression"; 29 - 44 "Severe (psychotic) depression". In the BRMS information must be collected through a free interview, during which the patient should be left free to express his situation in its own words; if necessary, to ensure a more complete assessment, information provided by relatives or caregivers can be used. To avoid the influence of diurnal variation of symptoms on the assessment, the evaluation should always be done in the morning and (more or less) at the same time (from 8 to 9:30). The BRMS has not properly diagnostic purposes, but it simply evaluates the current clinical situation. Even when applied repeatedly (e.g., every week), any assessment must be regarded as a separate thing, without reference to the previous assessments and without inquiring any changes in the meantime.

The BRMS is based on the core items of depression as identified by Bech *et al.* [149] when making the first validation study of the Hamilton Rating Scale for Depression (HAM-D). The results showed that this global assessment was statistically associated with only six of the 17 items included in the HAM-D [149]. Therefore the authors developed BRMS using the 6 most significant item of the HAM-D to which they added 5 items derived from the Cronholm-Ottosson Depression Scale [150], which explores the motor, verbal, emotional and intellectual components of depressive slowdown. The choice of the number of items [11] is related to the fact that the same authors had previously developed a scale for the assessment of mania, the Bech-Rafaelsen Mania Scale (BRMAS) [151], consisting of 11 items and, in their intentions, both scales would have been used jointly for the study of the bipolar disorder.

The BRMS appears to show reasonable psychometric properties; in particular it fulfils the basic psychometric

criteria of internal validity, reliability, and external validity [123]. The BRMS covers approximately the DSM-IV checklist of major symptoms of depression, and it is one-dimensional, *i.e.* the total score is a sufficient statistic to assess severity of illness, as confirmed by different methodological approaches including Rasch analysis. The interobserver reliability was found to be acceptable in various settings. The external validity of the BRMS was tested both in regard to sensitivity and responsiveness. The sensitivity was demonstrated in trials on the relapse prevention of depressive episodes in which a high BRMS discrimination was shown between active therapy and placebo when compared with other depression scales. Furthermore, the responsiveness of the BRMS was found high in short-term-trials in which the BRMS discrimination between TCAs and SSRIs was of statistical significance [123]. Moreover, the scale is able to discriminate major depression with melancholic features as opposed to depression without melancholia.

The Temporal Experience of Pleasure Scale (TEPS) [127] was designed by Gard *et al.* to assess both anticipatory and consummatory experiences of pleasure, which should be differentiated, as emerged from accumulated evidence across disciplines, such as neuroscience studies [95,96,152], psychopathology research⁵ and social psychology [153]. This scale is composed of a 10-item anticipatory pleasure scale (TEPS-ANT) and an 8-item consummatory pleasure scale (TEPS-CON). Items assessing anticipatory pleasure reflect the pleasure experienced in anticipation of a positive or pleasurable stimulus, while items assessing consummatory pleasure reflect the online, *hic et nunc* pleasure in response to a stimulus. Items covered both specific (e.g., “I appreciate the beauty of a fresh snowfall.”) and general (e.g., “I look forward to a lot of things in my life.”) situations, including all five sensory modalities. In order to have a relatively homogenous set of items measuring one construct [154], items of the TEPS focus on physical pleasure, rather than on pleasure related to social, intellectual, and achievement domains; furthermore items that could be specific to any cultural or socioeconomic group are not included.

The TEPS shows good internal consistency and good test-retest reliability [127]; the anticipatory pleasure scale and the consummatory pleasure scale are moderately, positively correlated with each other. Examination of convergent and discriminant validity indicated that the two scales measure distinct and specific constructs. In particular the anticipatory scale is related to responsiveness to reward, imagery ability, some aspects of approach, and positive affect, while the consummatory scale is related to openness to different experiences, and appreciation of pleasurable stimuli in a variety of sensory domains. Both scales are related to other pleasure scales as well as aspects of approach, positive affect, extraversion,

and openness, but are not redundant with measures of these other constructs.

4. Conclusions

In our review we have taken anhedonia into consideration. As originally formulated by Ribot [1], anhedonia consists of the inability to experience pleasure, and it refers to both a state symptom in various psychiatric disorders and a personality trait. Anhedonia can be found in many psychiatric disorders, such as major depression and mood disorders in general, schizophrenia, as well as in Parkinson’s disease, over-eating and risky behaviours.

As highlighted by many studies, anhedonia is also a common feature in substance use disorders; it is part of the abstinence symptomatology [20], and several authors suggested that it is an important factor involved in relapse [21,22], as well as in the transition from recreational use to excessive drug intake [23]. In particular, anhedonia has been found to be a frequent feature in alcoholics and addicted patients during acute and chronic withdrawal [24], as well as in cocaine, stimulant and cannabis abusers [25-27]. As previously mentioned, interesting findings about the presence and correlation of anhedonia in substance related disorders have been found by Janiri *et al.* [30], who found interrelations between hedonic capability, craving and protracted withdrawal, especially in opiate-dependent subjects; in particular from this study emerged that craving was positively associated with anhedonia levels and negatively with hedonic capability. These data were confirmed and enriched by following studies made by Martinotti *et al.* [31], who found that the positive correlation between the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) score and anhedonia scales was in line with the hypothesis that the clinical dimension of anhedonia cannot be separated from the other behavioural symptoms of withdrawal and should be considered as part of the same process. In another study, Martinotti *et al.* [34] found that the temperament dimension of Novelty Seeking (NS) was positively correlated to both craving and anhedonia. Thus these findings suggest that difficulty in experiencing pleasure in psychiatric disorders can lead to the use of psychoactive substances in an attempt to decrease anhedonia, as well as subjects without psychiatric disorders may try substances to counterbalance a tonic state of anhedonia.

What emerges from the cited studies is the idea that anhedonia could have important treatment implication; in fact, treating anhedonia in detoxified dependent subjects, could be critical in terms of relapse prevention strategies, given its strong relationship with craving, since the higher the craving scores the higher the level of anhedonia.

We have then observed that, although anhedonia is regarded as an important symptom in psychopathology, diagnostically it has so far received relatively little attention. In general, two main approaches have been employed to investigate and assess anhedonia or hedonic capacity: laboratory-based measures and questionnaires. Among measurement scales, the most commonly used are the Snaith-Hamilton Pleasure Scale (SHAPS) [80], the Fawcett-Clark Pleasure Scale (FCPS) [107], and the Revised Chapman Physical Anhedonia Scale (CPAS) [105,106]. Nevertheless, other measurement scales, particularly used within broader psychopathological dimensions, are the Anhedonia-Asociality subscale (SANSanh) of the Scale for the Assessment of Negative Symptoms (SANS) [118] and the Bech-Rafaelsen Melancholia Scale (BRMS) [122,123].

In the end we believe that the importance of anhedonia as a symptom is fundamental and should be strongly stressed, because of its implication in the pathogenesis of several psychiatric disorders, of which it represents one of the major symptoms. Furthermore, it should be underlined because of its possible treatment implications, as highlighted and confirmed by very recent works [155-157]; in point of fact treating anhedonia, of which the neuropsychobiology has been deeply investigated, could mean treating the underlying pathology. In the attempt to do that it is easy to understand how having appropriate and reliable diagnostic instruments to assess the presence and severity of anhedonia is mandatory.

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