Anhedonia in schizophrenia and major depression: state or trait? Review of the literature

L'anedonia nella schizofrenia e nella depressione maggiore: stato o tratto? Rassegna della letteratura

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Summary

Objectives
Anhedonia, a term proposed by Ribot in 1896, is an inability to feel pleasure in situations or activities that are normally pleasing. In this review, the authors describe the psychopathological features of anhedonia in schizophrenia and major depression.

Methods
Exhaustive review of the international literature (in Medline, PubMed, PsychINFO) on anhedonia in schizophrenia and major depression.

Results
In both schizophrenia and major depression, anhedonia is considered both as a state (symptom) and a personological trait (Figs. 1-4).

Conclusions
Anhedonia cannot be considered as a specific psychopathological feature of major depression (Table I), but appears to be a problematic psychological condition that is difficult to interpret due to its nosographical transversality.

Key words
Anhedonia • Schizophrenia • Major depression

Introduction

… I'm like the king of a rain-soaked country, rich but impotent, young in senility, who despises his tutors' servile features, as bored with his dogs as with other creatures. His favourite fool's most grotesque antic won't calm this brow so cruelly sick. (Baudelaire, Spleen [The Flowers of Evil], 1857) [1]

The term "anhedonia" traditionally refers to a specific psychopathological condition characterized by a deficit in the ability to experience pleasure in activities and situations usually considered gratifying [2]. The condition can present as diffuse (and therefore relative to all aspects of existence) or can be limited to some areas, such as interpersonal relations (social anhedonia), food, sexuality or somatosensorial experiences in general (physical anhedonia) [3]. The word "anhedonia" was introduced by the French psychologist Ribot [4] to describe a "pathological insensibility to pleasure" seen in several severe psychiatric diseases. "The state of anhedonia", he wrote, "if I may coin a new word to pair off with analgesia, has been very little studied, but it exists. I need not say that the employment of anaesthetics suppresses at the same time pain and its contrary, […] and there are, undoubtedly, clinical cases characterized by the isolated lack of pleasure, that render these patients absolutely unable to find gratification from any sexual activity, food, relation or affection". The main difficulty in understanding and defining anhedonic behaviour is primarily related to its peculiar characteristic of nosographic transversality [2], as it can involve a number of widely-different psychiatric disturbances in a non-specific manner. Along these lines, in fact, Silverstone [5] observed that substantial anhedonia was present in more than 50% of patients with a generic diagnosis of mental disease. In particular, the inability to experience pleasure is a complex symptom of both major depression and psychopathological syndromes belonging to the schizophrenic spectrum [6]. Manna et al. [7], Koob and Le Moal [8], moreover, attributed a relevant role to anhedonia in the pathogenesis of eating and substance abuse disorders, which according to these authors, is based on hedonic homeostatic dysregulation with a dopaminergic origin. Bermanzhon and Siris [9] argue that it may also be part of the constellation of symptoms of Parkinson's disease (and thereby predominantly neurologic), hypothesizing the existence of a specific extrapyramidal neuropsychiatric syndrome

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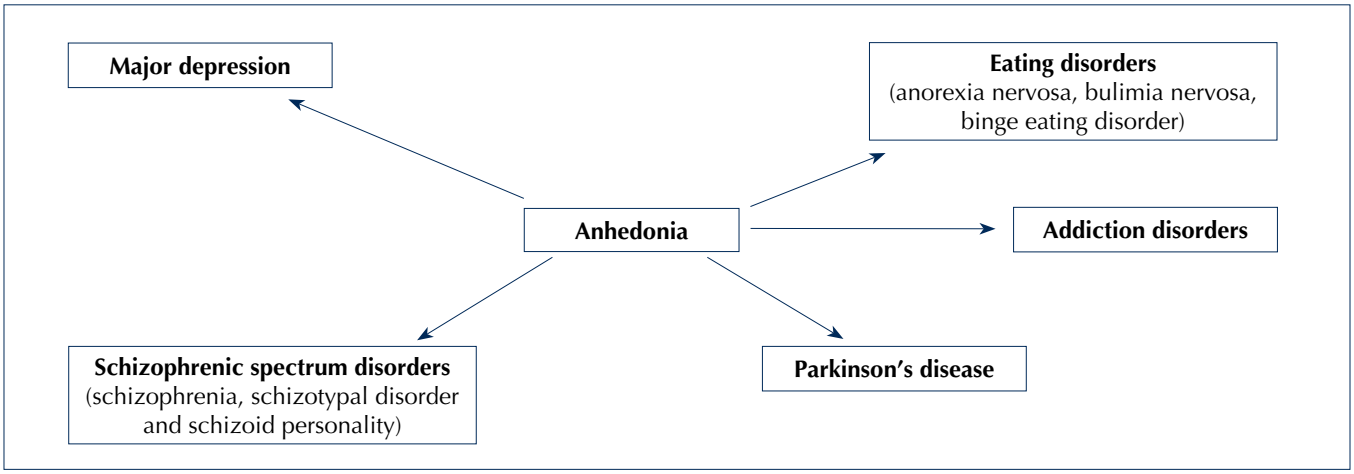

FIGURE 1.
Anhedonia and mental disorders. *Anedonia e disturbi mentali.*

(characterized by hedonic inability, akinesia and cognitive deficits) due to decreased turnover of dopamine in basal ganglia (Fig. 1).

According to Polese et al. [10], specifying what hypohedonic patients experience could help to better define and understand the nosographic transversality of anhedonia: "… the loss of intense pleasure as the lack of satisfaction of desire, due to the absence of desire itself". In other words, anhedonic subjects are not able to find gratification as they are unable to find desire. Manna et al. [7] also underlined the need to overcome use of the term "anhedonia" (which refers only to the absence of pleasure); more suitable terms such as "dyshedonia" might be used, which would allow better definition of the spectrum of symptoms, and the severity of transitory, para-physiological symptoms from clinically chronic and invalidating conditions. This would also include all possible qualitative and quantitative variations of the capacity for gratification, including the absence of desire itself.

In this review, the clinical characteristics of anhedonia in schizophrenia and major depression will be presented along with the principal psychopathological hypotheses that have considered hedonic inability as a premorbid trait or as a pathologic state (symptom) of schizophrenia and major depression.

Anhedonia and schizophrenia

Scientific interest for anhedonia in schizophrenia began around the beginning of the 20th century when Bleuler [11], having observed the apparent indifference that certain psychotic subjects exhibited with regard to friends, family, preferences and ordinary interests, considered the inability to experience pleasure a fundamental symptoms of schizophrenia and an outward manifestation of their pathologic state. A few years later, Kraepelin [12] included hedonic incapacity among the salient psychopathological characteristics of "amotivational syndrome" (as part of "dementia praecox"). He highlighted how a singular apathy towards interpersonal relationships, the extinction of affection for family and friends, the loss of satisfaction in the workplace, in vocations and in worldly pleasures were often the first symptoms of the onset of psychosis. Despite the important contributions of Bleuler and Kraepelin, modern psychiatry is still divided about the psychopathological significance of anhedonia in schizophrenia. Some authors, in fact, consider anhedonia to be an important marker for schizophrenic status, especially from a diagnostic standpoint [13 14], while others give it little or no consideration [15 16]. Yet another group retains that hedonic incapacity is not a symptom of psychosis, but rather a premorbid personality trait that predisposes subjects to development of overt schizophrenic disease [17 18].

a) Anhedonia as a symptom

Crow [19] was one of the first to sustain the concept that anhedonia is a symptom of the schizophrenic state. Refining the dichotomic clinical approach ("positive *vs.* negative symptoms") proposed by Hughlings-Jackson [20] in neurology, Crow hypothesized the existence of two forms of schizophrenia: type I ("positive"), characterized by predominance of psychotic phenomena (e.g. delusions, hallucinations), and type II ("negative"), dominated by defect symptoms, the most salient of which were emotional flattening and social withdrawal. Some years later, Andreasen [13], with the intent to create valid psychometric instruments to measure schizophrenic psychopathology, introduced hedonic inability in the anhedonia/asociality subscale of the SANS (Scale for the Assessment of Negative Symptoms), which was defined as: a) loss of interest

and gratification from activities and situations normally considered pleasuring and/or; b) lack of intimacy and emotional involvement in a variety of social and sexual relations.

Successively, Carpenter [14], when clinically redefining symptoms of psychotic defects, placed anhedonia among the primary and enduring negative symptoms of what he defined "Deficit Syndrome" of schizophrenia. In the SDS (Schedule for "Deficit Syndrome") [21], specifically created for diagnosis of this subtype of schizophrenia, hedonic inability was present in at least 3 of the 6 items proposed ([A2] diminished emotional range (incapacity to experience pleasure and/or anger), [A4] curbing of interests and [A6] diminished social drive).

The results of recent investigations seem to confirm the theory that anhedonia is indeed a genuine symptom of schizophrenic status. In particular, Loas et al. [22], Blanchard et al. [23] and Kontaxakis et al. [24] observed higher levels of hedonic inability in patients with schizophrenia (both acute and chronic) compared to non-psychiatric sibjects. Those studies also showed that in psychotic patients, even if there was significant positive correlation with other negative symptoms (emotional flattening, alogia, abulia/apathy, asociality), anhedonia was independent from positive, disorganized and depressive dimensions. In longitudinal study of 127 individuals with chronic schizophrenia (follow-up of 10 years), Herbener and Harrow [25] hypothesized that anhedonia, being typical of the chronic phase of psychosis, can be viewed as a negative component of the stable course of schizophrenia and as a direct expression of progressive functional impairment.

In recent decades, some investigators have promoted the idea that the negative symptoms of schizophrenia (including hedonic inability) are due to a deficiency in dopamine (DA) in areas of mesocortical projections of cerebral dopaminergic circuits starting from the ventral tegmental area of the midbrain, especially those that project in the prefrontal dorsolateral cortex [26-28]. According to this hypothesis, the behavioural deficit associated with defect symptoms of schizophrenia implies functional hypoactivity of these ascending dopaminergic fibres or structural impairment of their neuronal systems. In particular, deficiency in functioning of dopaminergic fibres may be due to:

1. a primary deficit in DA related to local hyperactivity ("excitotoxicity") of mesencephalic glutamatergic circuits, with consequently abnormal activation (R_{NMDA}-mediated) of apoptotic mechanisms involving dopaminergic neurons of the ventral tegmental area ("neurodegenerative" hypothesis of schizophrenia) [29]. This neuronal excitotoxicity would be associated with an unusual "individual diathesis to stress", for which, in a subject predisposed to develop biological vulnerability (overexpression of genes that regulate cerebral glutamatergic neurotransmission), would disproportionately operate under the influence of several environmental stressors (e.g. toxins, drugs, infective agents, elevated emotionality in a family environment) [28];
2. a secondary deficit in DA linked to: a) inhibition of synaptic release due to excess serotonin at the mesencephalic level; or b) blockage of prefrontal D_2 receptors associated with the administration of typical antypsychotics (e.g. haloperidol) [27]. The first of these mechanisms could help in better understanding the efficacy of atypical antipsychotics (e.g. clozapine) in reducing the negative symptoms of schizophrenia (selective antagonism of 5-HT_{2A} receptors in the mesencephalon) [30].

b) Anhedonia as a trait

At the beginning of the last century, Myerson [31] refuted the hypothesis of anhedonia as a defect symptom of schizophrenia, and forwarded the idea that it was a prodromic and/or premorbid characteristic of schizophrenia. It was further affirmed that, frequently, the long-term loss of pleasure (in activities and situations normally considered gratifying) could lead to the onset of psychosis. Several decades later, Rado [32] further elaborated this concept and proposed that anhedonia was an innate trait that predisposed individuals to schizophrenia, which manifested long before the onset of clinical symptoms (such as social withdrawal, eccentric behaviour and speech, little control over impulses). In this regard, the author coined the term "schizotypal" to indicate the phenotypic expression (behavioural) of a schizophrenic genotype responsible for organization of personality characterized by two fundamental defects: a) insufficient integration of various pleasurable experiences; and b) pathologic distortion of proprioceptive awareness of one's physical self. In order to compensate for this double deficiency in the functioning of ego, the schizotypal subject engages specific reactive mechanisms, which, if adequate, lead to an adaptation that is compensated to reality (schizotypal personality). If insufficient, however, it gives rise to uncompensated disadaptation (pseudoneurotic schizophrenia), disintegrated (hebephrenic schizophrenia) or deteriorated states (defect schizophrenia) [33]. In other words, the future schizophrenic inherits, according to Rado, a brain that is constitutionally endowed with a reduced capacity to express pleasure, which over time develops excessive fears, uncontrolled anger, diminished social relations and progressive withdrawal from interpersonal relationships [34].

A decade later, Meehl [17] included anhedonia among the fundamental schizotypal traits of preschizophrenia (together with emotional ambivalence, avoiding social relations and cognitive-perceptive distortions), hypothesiz-

ing that there was an underlying, integrated functional defect (hereditary) of the CNS (defined as "schizotaxia"). For this reason, overt schizophrenia would develop only in the presence of unusual constitutional aspects and/or unfavourable environmental conditions. According to Meehl, all "schizotaxic" individuals become "schizotypal" in their personality organization, although many remain compensated. "… Only in a minority of cases, in fact", wrote Meehl, "due to innate biological insufficiencies or to the influence of schizophrenogenic mothers, are the overt symptoms of schizophrenia manifested" [17].

Recent data supporting the theory of trait-anhedonia are mainly derived from: a) transversal clinical research by Horan et al. [35] on patients with personality disorders belonging to the schizophrenic spectrum [in which there is a highly significant positive correlation between hedonic inability and psychopathologic phenomenon of schizotypal disorder (e.g. emotional flattering, cognitive distortions of self-perceived stress, socio-relational breakdown)], and b) a longitudinal study (follow-up of 10 years) by Chapman et al. [18] on 500 university students in the US (from which a clear relation to predict levels of subjective inability to experience pleasure emerged [measured with the "Physical Anhedonia Scale" (PAS) and the "Social Anhedonia Scale" (SAS)] [3] on the risk of developing acute psychotic episodes over time). According to these authors, this provides unequivocal evidence for the role of anhedonia as a primary schizotypal marker for the biological vulnerability to develop pathologies of the schizophrenic spectrum.

Other researchers, however, have not accepted the hypothesis of Meehl [17] that anhedonia is linked to schizophrenia by a aetiopathogenetic bond; in contrast, they sustain that a hedonic deficit affects only a small subgroup of psychotic patients, with a reported frequency from 20-35% ("negative" or "deficit" subtype of schizophrenia) [36]. In particular, Schurhoff et al. [37] considered that this minority of anhedonic individuals were affected by a specific subcategory of schizophrenia characterized by an elevated familiarity for "hypohedonia" (confirmed by the presence of high psychometric levels in hedonic inability in non-psychotic first-degree relatives of carriers of the disease). According to these authors, the limited ability to experience pleasure is not a psychopathological forerunner (necessary and sufficient) of vulnerability to psychosis, but a character "non-taxonomic" trait able to enhance the clinical expression of the disorder. This then would behave as a negative personological modulator of stress perceived by the hypohedonic individual that would activate dysadaptive coping mechanisms favouring the overt development of the deficit symptoms of schizophrenia.

In a study on 60 patients with chronic schizophrenia, Pelizza [38] also revealed the existence of a clear predictive

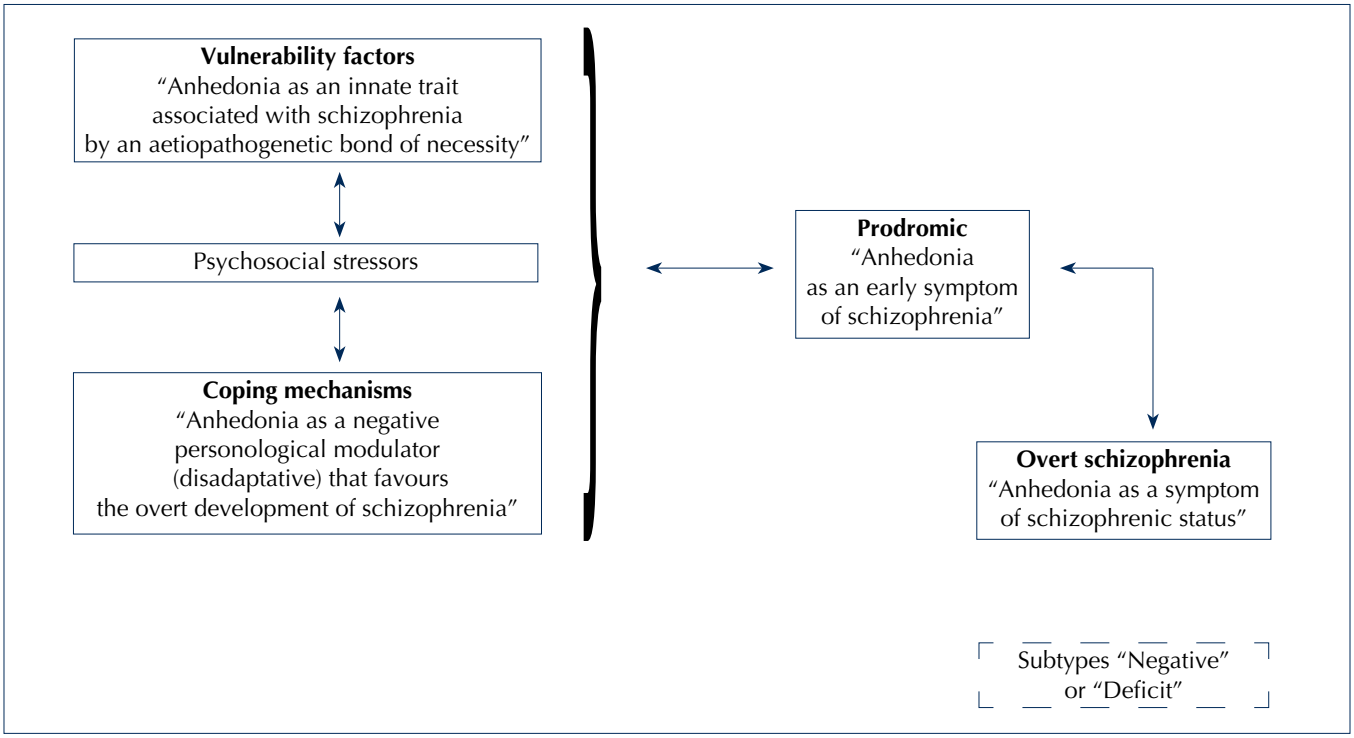

FIGURE 2.
Possible positions of anhedonia in the "Vulnerability-Stress-Coping Model" of schizophrenia [39]. *Possibili collocazioni dell'anedonia nel "Vulnerability-Stress-Coping Model" della schizofrenia* [39].

relationship between anhedonia [measured with the self-evaluation scales of Chapman et al. (PAS and SAS) [3]] (independent variable) and the negative symptoms of schizophrenia (measured with the SANS [13]) (dependent variable). In this investigation, it was hypothesized that the limited ability to experience pleasure [subjectively evaluated in psychotic individuals (subjective anhedonia)] might precede some diagnostic components (objectively detectable) of psychosis (e.g. emotional flattening, alogia, aboulia/apathy, asociality/anhedonia – objectively measured – of the SANS). In other words, hedonic deficit, even if confounded (for its "subtractive" effects) with the negative symptoms of schizophrenia, does not seem to be related to these, but rather constitutes a 'psychopathologic precursor'. Nonetheless, it remains to be clarified if this represents a prodromic and/or early phenomenon of schizophrenia or if it is an innate character trait (taxonomic or other) of a preschizophrenic personality (Fig. 2) [39].

Along these lines, in a study of 80 individuals with chronic schizophrenia, Maggini et al. [40] observed a statistically significant correlation between anhedonia and some psychopathological features of "alexithymia" (with particular reference to the difficulty in identifying and describing emotions), postulating the fundamental role of alexithymic impairment of language in determining negative and/or deficit forms of schizophrenia. In fact, these authors sustain, that the productive and deficit symptoms of the psychosis may have the same aetiology, but different pathoplastic mechanisms (related to the individual characteristics of personological features). In other words, linguistic alterations underlying a subjective condition of alexithymia would bring about an inability to elaborate the positive phenomena of schizophrenia (e.g. delusions, hallucinations) beginning with affective autopsychic tension ("Wahnstimmung") in the prodromic and/or preparatory phases of the disease. In such a situation, in contrast, the clinical expression of the disturbance would remain exclusively the negative symptoms (the "mute side") of the psychosis, which would merely be a psychopathological artefact due to the inability to communicate in these constitutionally alexithymic individuals [41].

Among Axis II disorders in the DSM-IV-TR [42] belonging to the schizophrenic spectrum (cluster A), anhedonia has a prominent position in the definition of "schizoid personality disorder", where it contributes to at least 3 of the 7 proposed diagnostic criteria [(A1) does not desire nor experience pleasure in close relationships, including familial, (A3) shows little or no interest for sexual relations with others and (A4) finds little or no pleasure in any activity]. In this nosographic manual of the American Psychiatric Association (APA), the traditional concept of "schizoid" underwent a major structural revision. In particular, it was depleted of its historical cognitive-perceptual peculiarities (now attributed to schizotypal personality disorder), and complex emotional descriptions [part of which (affective hyperaesthesia) is now considered related to avoidant personality disorder], becoming a diagnostic category that is descriptively ineffectual, of infrequent clinical relevance, and dominated exclusively by affective anaesthesia, the anhedonic construct of which is a fundamental psychopathological cornerstone [43].

Anhedonia and depression

Clouston was the first to assign a central role to depressive symptoms in anhedonia [44], which included, among the most frequent symptoms at onset of depressive illness, loss of sense of well-being and lack of pleasure for anything, which the author described as a "paralysis of emotion." A few years later, Bevan-Lewis [45] highlighted that 'simple pathological depression' was often preceded by a growing indifference to usual pleasures, as subjects became tiresome and quickly lost interests. The surrounding environment no longer evoked pleasing sensations and the patient became progressively filled with constant existential sadness. In the VIII edition of his "Lehrbuch", Kraepelin [12], analyzing in detail the clinical variability of depression, observed how a melancholic subject gradually became unsatisfied and emotionally indifferent towards close friends and relatives: nothing was able to stir his interests, and nothing caused him joy.

a) Anhedonia as a symptom

Following the observations of Clouston, Bevan-Lewis and Kraepelin, the interest in anhedonia as symptom of depressive illness gradually diminished, but later grew when Van Praag [46], considering "Vital Depression", included 'hypoesthesia' among diagnostic criteria. This was clinically comparable to that of hedonic inability, with particular reference to the difficulties of the individual to appreciate food, leisure activities, the beauty of nature and interpersonal relations with family and friends. A decade later, Klein [47] proposed the term "endogenomorphic" to describe a particular subtype of major depressive disorder characterized by the lack of reactivity to hedonic stimuli and/or lack of an appropriate affective response to anticipation of pleasure. Such a functional deficit involving mechanisms of cerebral gratification, according to the author, involved both appetitive and consummatory behaviours, leading the patient to experience a widespread lack of interest about the surrounding environment. This was also associated with a profound inability to appreciate food, sexuality and normal pleasures. For Klein, endogenomorphic depression constituted a distinct subgroup of melancholy characterized by severe and diffuse anhedonia.

Successively, Fawcett et al. [48] experimentally confirmed Klein's hypothesis, showing how over time the empirical

data in the literature provided justification for a Kleinian form among the anhedonic subtypes of major depression and a depressive subgroup with a normal ability to experience pleasure. Moreover, having revealed that patients with endogenomorphic depression presented severe hypohedonia even after clinical remission of a melancholic episode, these authors suggested that hedonic deficit might be considered as a post-depressive 'scar' or sequelae.

In agreement with the hypothesis of Klein, the APA decided to consider anhedonia as a core symptom of depression, giving it a central role in the diagnostic definitions of the DSM-IV-TR [42] for 'Major Depressive Episode' and for its specification of 'Melancholic Features' (Table I). Similarly, in the ICD-10 [49], the World Health Organization (WHO) included the loss of gratification for food and sexual activity, reduction in interests and loss of pleasurable feeling among the somatic symptoms of major depression.

Several recent investigations provide support for the hypothesis that anhedonia is a specific symptom of depressive status. In particular, Joiner et al. [50] showed that compared to patients with schizophrenia and non-psychiatric control subjects, individuals with major depressive disorder had a significantly higher score for anhedonic items of the BDI (Beck Depression Inventory) [51]. This highlights how hedonic inability, even if confused with affective flattening in schizophrenia, represents a psychopathologic aspect that is specific for depression, and is frequently correlated with the presence of psychomotor delay [52], suicidal ideation [53] and a high probability of attempted suicide [54].

Pelizza [55], in contrast, after observing that the average levels of anhedonia were significantly higher in patients with schizophrenia compared to depressed patients, affirmed that considering hedonic inability among the exclusive diagnostic symptoms of major depression (as in the DSM-IV-TR and ICD-10) did not correspond to clinical reality. In fact, in agreement with other investigators[46-48], it seemed that hedonic inability applied to only a minority of patients with major depression [those characterized by higher total scores in the HDRS (Hamilton Depression Rating Scale) [56]]; its prevalence in various patient cohorts ranges from 15% to 30% ("endogenomorphic" or "vital" depressive subtype). According to these authors, moreover, a predictive relationship was found in a cohort of 60 depressed subjects between anhedonia [measured with the self-rating scales by Chapman et al. (PAS and SAS) [3]]

TABLE I.
DSM-IV-TR diagnostic criteria for Major Depressive Episode [42]. *Criteri diagnostici del DSM-IV-TR (2000) per l'episodio depressivo maggiore* [42].

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.	
1	Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents can be irritable mood
2	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 made by others)
3	Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains
4	Insomnia or hypersomnia nearly every day
5	Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6	Fatigue or loss of energy nearly every day
7	Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8	Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9	Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
Note: specify if with melancholic features. A) If one of the following symptoms is present during the period of greatest severity of the current depressive episode: 1) loss of pleasure for all or almost all activities; 2) loss of reactivity to normally pleasurable stimuli (the subject does not feel better, even momentarily, when something good happens). B) Three (or more) of the following symptoms: 1) a particular quality of mood (i.e., depressed mood is distinctly different from the type of sentiment felt after the death of a loved one); 2) depression that is habitually worse in the morning; 3) waking up early in the morning (at least 2 hours before the usual time); 4) marked psychomotor retardation or agitation; 5) significant anorexia or weight loss; 6) excessive or inappropriate guilt.	

(independent variable) and the severity of clinical depression (measured with the HDRS) (dependent variable). This led to the hypothesis that anhedonia (experienced subjectively) could precede or objectively anticipate overt depressive symptoms. It could thus be considered as a prodromic symptom and/or early melancholic sign, or alternatively, as a premorbid trait of pre-depressive personality (Fig. 3).

According to modern neurobiological hypotheses of major depression, anhedonia seems to be due to a functional deficit in cerebral dopaminergic neurotransmission, and in particular, to malfunctioning of the mesolimbic and mesocortical pathways of DA. This would affect several areas including the ventral tegmental area of the mesencephalon and several specific zones of the limbic system (e.g. nucleus accumbens, amygdala, anterior cingulate cortex, orbitaria and entorhinal cortex), basal ganglia (e.g. globus pallidus, caudate nucleus) and frontal lobes (e.g. prefrontal dorsolateral cortex) [57]. The empirical evidence for this derives from both clinical observations (by the fact that some antihypertensive agents that cause extensive synaptic depletion of dopamine – e.g. reserpine – frequently induce psychopathologically severe forms of depressive anhedonia) [28], and laboratory experiments (where it has been demonstrated that the administration of 6-hydroxy-dopamine – 6-OH-DA – in the nucleo accumbens of rats disrupts mesolimbic circuits and leads to hypohedonia, aphagia and adipsia, even if animals still have motor capacity to eat and drink) [58].

The latency to onset of therapeutic effect of antidepressant drugs (about 3 weeks after initiation of treatment) has led to increased interest in synaptic neurotransmission ("neurotransmitter hypothesis" of depression) and intracellular signal transduction events that regulate gene expression in neurons ("gene hypothesis" of depression) [59]. In particular, some investigators have developed the idea that anhedonic depression can be caused by a "pseudo-deficit" of DA, related to defects in functioning of postsynaptic systems. Such defects could be in second messengers that control the activity of specific sites in neuronal DNA (e.g. the gene for brain-derived neurotrophic factor (BDNF), whose reduced expression might give rise to the apoptosis and cellular atrophy seen in limbic areas in depressed and anhedonic subjects such as the hippocampus and caudate nucleus) [27].

b) Anhedonia as a trait

Myerson [60] was one of the first psychiatrists to consider anhedonia as a premorbid trait of pre-depressive personality. In particular, he hypothesized the existence of individuals who were hypohedonic by nature, with a genetic constitution that could be affected by diverse stress fac-

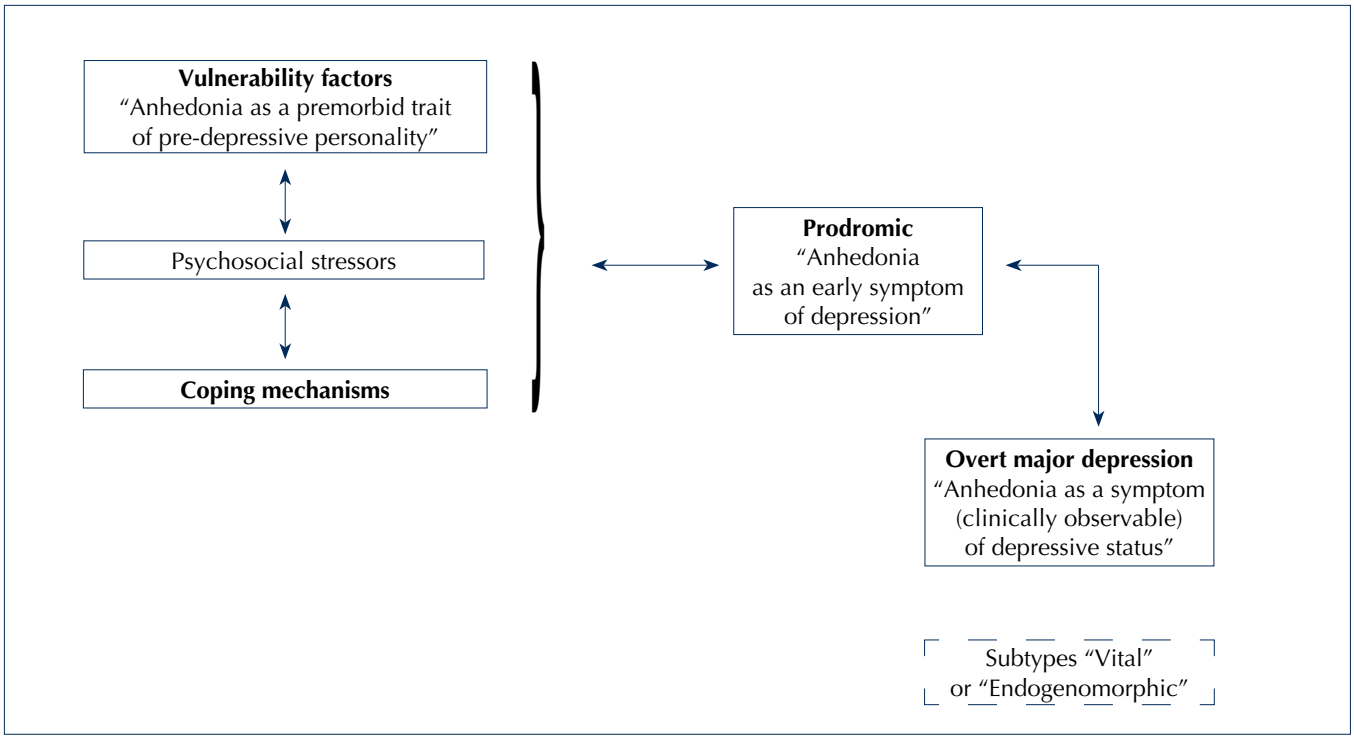

FIGURE 3.
Possible positions of anhedonia in the "Biopsychosocial Model" of major depression [55]. *Possibili collocazioni dell'anedonia nel "Modello Biopsicosociale" della depressione maggiore* [55].

tors (organic brain damage, infant trauma or unfavourable environmental modifications) until the emergence of overt depression. According to Myerson, this "constitutional anhedonia" creates a mild and chronic form of depression that predisposes to the development of more severe clinical symptoms of melancholy. Several decades later, Meehl [61] used the term "hedonic capacity" to describe a positive psychological attribute of personality that presented a normal distribution in the general population. In anhedonic subjects, therefore, the loss of the ability to feel pleasure was an innate and hereditary character trait (comparable to a chronic, mild mood disorder), which following stress, could evolve to an overt form of unipolar depression, thus constituting a predisposing psychopathological precursor.

The results of recent investigations appear to partially confirm the hypothesis that hedonic inability is a constitutive personological trait (normally distributed) correlated with the risk of developing major depression. In particular, Kendler [62] showed that, for depressive anhedonia, there is good concordance with the disorder in monozygotic twins compared to dizygotic twins. Furthermore, Akiskal and Weise [63] suggested that the inability to experience pleasure was a fundamental psychological characteristic of "depressive temperament" (together with sadness, pessimism, disesteem, distrust in the future, passivity and introversion). The identification of depressive temperament, alongside nosographically-defined melancholic features, and within a single psychopathological depressive spectrum (the "depressive

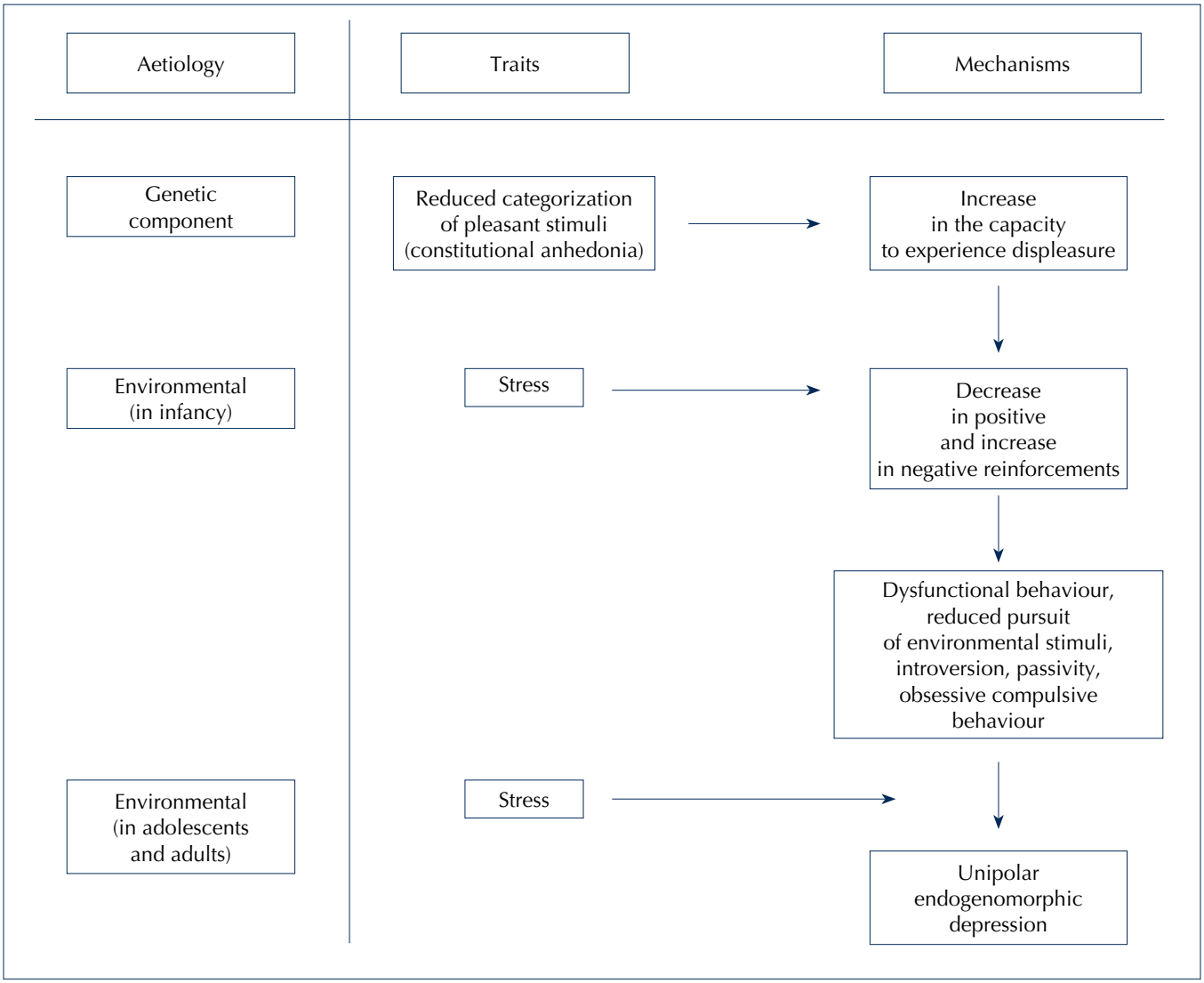

FIGURE 4.
The "Vulnerability to depression model centred on anhedonia" [68]. *Modello di vulnerabilità alla depressione centrato sull'anedonia* [68].

spectrum", according to De Palma and Pancheri [64] includes dysthymic disorder and major depression as described in the DSM-IV-TR [42]), would be justified by the fact that some depressed individuals often experience melancholic symptoms that are so severe and constant that they appear to be personological traits rather than a transient clinical state [65]. In Klein's [66] opinion, such a depressive constitution would merely be an early expression of the same genetic susceptibility (vulnerability) to depression, which would predispose the subject to the risk of developing a future dysthymic disturbance and/or major depressive episode.

In reality, temperamental depressive aspects had already been observed at the beginning of the last century by Kraepelin [12] (depressive variant of "cyclothymia disposition"), Kretschmer [67] ("melancholic cyclothymia") and Schneider [15] ("hypothymic personality"). All these authors agreed to emphasize that a characterizing feature of constitutionally-depressed individuals was persistent sadness, from a decrease in self-esteem to self-contempt, with features of introversion and the tendency to deliberate, accompanied by feelings of guilt, pessimism, insecurity, anhedonia and affective depersonalization. In the DSM-IV-TR [42], the clinical observations formulated by classic psychiatric tradition are partially confirmed in the nosographic definition of "depressive personality disorder", which the APA included among Axis II 'supplementary' personological disorders that require additional research to validate diagnostic criteria. According to the US manual, in fact, the normal mood of these subjects is dominated by flattening, melancholy, lack of joy, delight and happiness. These individuals lack enthusiasm and a sense of humour, appear constantly sad, oppressed, pessimistic and incapable of experiencing enjoyment, and experience pervasive feelings of guilt, inadequacy and interpersonal exclusion.

A few years ago, Loas [68] proposed a model of vulnerability to depression centred around anhedonia, which should be considered as an innate, premorbid trait that is genetically determined (Fig. 4). According to this hypothesis, the interaction between a reduced constitutional hedonic capacity and unfavourable environmental circumstances during infancy would lead to high levels of displeasure and introversion, dysfunctional behaviour, passivity, pessimism and obsessive-compulsive features. Due to this and other environmental stressors, unipolar endogenomorphic depression can develop during adolescence and adulthood.

Conclusions

Anhedonia is a psychological condition that is difficult to interpret clinically given its nosographic transversality [2]. In fact, anhedonia can have a number of different features: a) a personality trait that predisposes to abuse/dependence of mood-altering substances [7 8], development of depressive disorder [60 61 63 68] or schizophrenia [17 31 32]; b) an early prodrome of several severe and complex psychiatric pathologies (schizophrenia [38], major depression [55] and eating disorders [7]); or c) a core symptom of melancholy [46-48] or other psychopathologic disorders of the schizophrenic spectrum [13 14 19 22].

According to Polese et al. [10], however, if anhedonia is described in broader terms as the inability to desire gratification, it is easy to understand why it exists in a large proportion of psychiatric patients in a nonspecific manner. These subjects would all share the way in which they deal with their environment. Anhedonia would manifest differently, with a tendency towards isolation of major depression or with thought disorders and affectivity that is typical of schizophrenics. As described by Manna [69], this altered capacity to relate to the external world is correlated with the absence of self-integrity, which does not allow either desire or of pleasure itself (in the absence of satisfaction). In this sense, therefore, anhedonia involves not only functional alterations in the ability to experience pleasure, but also the anomalies in the ability to desire pleasing stimuli. This would implicate a dimensional approach of psychopathological spectrum that would include, on the one hand, the paraphysiological and transitory levels of anhedonia. On the other, it would comprise some chronic and disabling psychiatric conditions, such as major depression, schizophrenia, substance abuse/dependence, eating disorder, Parkinson's disease, impulses control disorders and borderline personality disorder [7].

However, the aetiopathogenetic mechanisms of anhedonia remain to be clarified, even if it is clear that dopaminergic pathways are not the only cerebral circuits involved [70]. According to most investigators, there are many different and interactive causal factors (genetic, environmental, cultural, social) that determine the psychopathological complexity of the inability to experience desire and pleasure [2].

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