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# Anhedonia and major depression: The role of agomelatine

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**Abstract**

Anhedonia is a condition in which the capacity to experience pleasure is totally or partially lost. Although anhedonia is a feature of major depressive disorder according to DSM IV criteria for major depression diagnosis, so far it has received relatively little attention. The scale that is most commonly used in the measurement of anhedonia is the Snaith-Hamilton Pleasure Scale (SHAPS), a brief 14-item self-report questionnaire designed to measure hedonic tone and its absence. Two studies have described the efficacy of agomelatine in the treatment of anhedonia: an open-label study and a comparative trial versus the antidepressant venlafaxine XR. In both studies agomelatine significantly reduced anhedonia, as indicated using the SHAPS. This reduction was observed after the first week of treatment ($P < 0.05$) and at different times until the end of the trial. Moreover, in the comparative trial, a significant difference between groups was observed in favor of agomelatine, after 1 ($P < 0.05$), 2 ($P < 0.01$), and 8 weeks ($P < 0.01$). The possible effect of agomelatine on anhedonia may represent a novel area of interest among antidepressant agents and deserves further investigation, with larger samples and double-blind placebo-controlled designs.

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## 1. Introduction

The word anhedonia comes from the Greek: áν- *an-*, "*without*" + ηδονή *hēdonē*, "*pleasure*", and was introduced in psychiatry by Théodule-Armand Ribot in 1896 (Ribot, 1896). 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 (Loas and Pierson, 1989). 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 (American Psychiatric Association, 2000). Anhedonia is a "core" symptom of major depression, whose severity could be influenced by it (Loas, 1996).

Anhedonia played an important role in psychopathology theories at the beginning of the 20th century (Myerson, 1923). In particular, Kraepelin (1919) spoke of anhedonia as a core symptom of a state of individual suffering which was part of dementia praecox. Kraepelin described his patients as if they did not feel any real joy in life; according to him, the characteristic indifference of patients towards social

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interactions, which previously used to elicit emotion, the extinction of affection for family and friends, and the loss of satisfaction in their work and vocation, in recreation and pleasure, were rather often the first symptoms to manifest, marking the onset of the disease.

Bleuler (1911), noting the indifference that some patients exhibited towards their friends, acquaintances, colleagues, and towards 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 the patient's emotional life.

Nevertheless, after the turn of the century, psychiatric interest in anhedonia faded, and Jaspers in his "*Allgemeine Psychopathologie. Ein Leitfaden für Studierende, Ärzte und Psychologen*" does not mention it except as an aspect of the more severe and pervasive loss of all emotional responses (Jaspers, 1913). Attention then focused on depressed mood as the pathognomonic feature of depressive illness.

For most psychiatrists it was Klein's concept of endogenomorphic depression that revived interest in the notion of anhedonia (Klein, 1984). 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 modified to "a loss of interest or pleasure in all or almost all usual activities and pastimes" (Snaith, 1992). Furthermore, for the subtype of major depression, for which the term melancholia was resurrected, the anhedonic experience became essential to the definition.

Anhedonia has been considered crucial for the diagnosis of depression (Klein, 1984; Schrader, 1997). It is, besides depressed mood, one of the two core symptoms of depression (Loas and Pierson, 1989). Moreover, lack of reactivity and anhedonia are key diagnostic criteria for the DSM-IV-TR melancholic subtype of major depression (Klein, 1984), and anhedonia is also one of the most important negative symptoms frequently observed in schizophrenia (Mason et al., 2004), although the differences between the anhedonic symptoms observed in mood disorders and schizophrenia is profound from both the clinical and neurobiological points of view.

Although anhedonia plays a very important role in depression and schizophrenia, it is not limited to them. In fact, anhedonia has been linked to anxiety and adjustment disorders (Silverstone, 1991), suicidal ideation (Oei et al., 1990), successful suicide (Fawcett, 1993), alcohol and substance abuse (Martinotti et al., 2009; Janiri et al., 2005). On the other hand, in the model proposed by Loas (1996), a genetically determined low hedonic capacity was regarded as a specific character trait, which, together with aspects like introversion, obsessive-compulsivity, pessimism, and passivity, could represent a risk factor which could lead, under stress conditions, to unipolar endogenomorphic depression. Moreover, anhedonia is also present in other disorders and dysfunctional behaviors, such as Parkinson's disease (Isella et al., 2003), overeating (Davis and Woodside, 2002), and risky behaviors in general (Franken et al., 2006).

## 2.  Diagnosing anhedonia

Although anhedonia is regarded as an important symptom in psychopathology, so far it has received relatively little attention. This limited attention could be the result of the low availability of short, well-validated, and easy-to-use instruments (Snaith, 1993).

In general, two main approaches have been utilized to investigate and assess anhedonia (or hedonic capacity): laboratory-based measures and questionnaires. The first approach utilizes laboratory-based measures of anhedonia, involving signal-detection methodology, physiologic measures, and subjective hedonic response to pleasant stimuli (Berlin et al., 1998). Besides these behavioral measures, anhedonia can also be evaluated using hemodynamic (Keedwell et al., 2005) and electrophysiological (Franken et al., 2006) measures. The second approach to the diagnosis of anhedonia involves the use of questionnaires. Several scales have been developed to assess anhedonia or hedonic capacity. Specific scales for the measurement of anhedonia are the Revised Chapman Physical Anhedonia Scale (CPAS) and Social Anhedonia Scale (SAS) (Chapman et al., 1976), the Fawcett-Clark Pleasure Scale (FCPS) (Fawcett et al., 1983), and the Snaith-Hamilton Pleasure Scale (SHAPS) (Snaith et al., 1995). Other rating instruments can be employed to evaluate anhedonia within broader psychopathological dimensions, such as those of depression, with the Bech-Rafaelsen Melancholia Scale (BRMS) (Bech, 2002), and negative symptoms of schizophrenia, with the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1989) and particularly the Subscale for Anhedonia (SANSanh). Furthermore, it is worth mentioning the 10-cm VAS (Mottola, 1993) for pleasure and the Temporal Experience of Pleasure Scale (TEPS) (Gard et al., 2006), which was developed to assess anticipatory and consummatory pleasure.

The scale most commonly used in the measurement of anhedonia is the SHAPS (Snaith et al., 1995), a brief 14-item self-report questionnaire designed to measure hedonic tone and its absence, anhedonia. These 14 items cover four domains of hedonic experience: interest/pastimes (items 1, 4, and 9), social interaction (items 2, 7, 8, 13, and 14), sensory experience (items 5, 6, 11, and 12), and food/drink (items 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", the item is assigned a score of zero, while for "Disagree" or "Strongly disagree" the score is 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 more indicates a significant reduction in 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 SHAPS has shown adequate overall psychometric properties in clinical and student samples (Snaith et al.,