Behavioral Anhedonia in Major Depressive Disorder (MDD)

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Abstract---*Introduction: Depression is a major public health problem, with existing pharmacological and non-pharmacological treatments not equally effective in all patients. The complex etiology and pathogenesis of depression pose a challenge that requires different approach strategies to effectively alleviate this mental symptom. Anhedonia, or loss of interest and pleasure in commonly enjoyed activities, is one of the main diagnostic criteria for depressive disorders in the psychiatric diagnostic systems of the Diagnostic Statistical Manual (DSM) and International Statistical Classification of Diseases (ICD). Major depressive disorder indicates a depressive condition that does not solely rely on reports of sad mood but the presence of anhedonia behavior. The review of these studies aims to determine changes in anhedonia behavior in depressive disorders. Methods: This research review was prepared using the literature review method by collecting valid scientific literature, namely Google Scholar, PubMed and Scientific Direct. Discussion: Anhedonia behavior is related to several factors, including social interaction is the most complex and ambiguous human environment. Hence the existence of rules that are fraught with misunderstandings. It requires complex examination to determine exactly what the rewarding components of social interaction are. Social interactions are highly dynamic, complex states that seem more likely to produce anxiety than lead to reward given their ambiguity. For those with social anhedonia, whose sensitivity to the positive benefits of social interactions may be limited, it is easy to see why relationships are best avoided. Individuals with social anhedonia may require greater perceived gains before they engage in social approach behaviors. As such, individuals may experience less pleasure in response to certain stimuli, while responses to other stimuli remain intact. There are three types of stimuli, namely social stimuli, sensory stimuli, and drugs/substances. Conclusion: Behavioral social anhedonia, physical anhedonia and substance anhedonia are criteria for major depressive disorder. They may refer to a decreased ability to experience pleasure from all (or at least some) positive stimuli.*
Keywords---*Anhedonia, major depression disorder, psychiatry, social reward.*

Introduction

The World Health Organization's Global Burden Disease study found high prevalence, comorbidity and costs of depression, making depression a high burden disorder worldwide (Ferrari et al., 2013; Hamilton et al., 2012). There is no single underlying cause of depression. Depression is a common condition that everyone can experience due to different causes and triggers, with the highest lifetime prevalence (17%) of all psychiatric disorders (American Psychiatric Association, 2000; Sadock et al., 2017). The biopsychosocial model explains that depression occurs due to the interconnection and interdependence of biological, psychological and social factors (Kusumawardhani, 2013). Social anhedonia or reduced social interaction, especially in the form of reduced capacity to feel pleasure through social interaction, is one of the prominent symptoms in depression (Rizvi et al., 2016; Winer et al., 2017). This symptom is often used in behavioral tests in rats that represent animal models of depression, assessed by the sucrose preference test (SPT).

Anhedonia behavior in depressed patients has important implications for understanding the pathophysiology as it suggests alterations in neurobiological mechanisms involved in motivation and reward (Pelletier-Baldelli et al., 2020;

Mowet al., 2020). This could be useful for finding biomarkers in depression. The search for biomarkers could be a pioneer in the development of novel treatments in depression prevention, given that one-third of patients' do not respond to current standard pharmacological and psychological therapies (Ritsner, 2014).

Methods

The methodology used was a literature review. The review sources consisted of relevant journals from several databases Google Scholar, PubMed and Scientific Direct. The authors searched with keywords and synonyms that fit the topic. The search was limited to the year of publication to ensure the articles used were up-to-date. All relevant articles were screened and analyzed for inclusion or exclusion from the literature review based on quality and relevance to the review topic, questions and objectives of the literature review.

Discussion

Depressive disorder, also known as major depressive disorder, is characterized by episodes of at least 2 weeks' duration (although most episodes last much longer), involving marked changes in affect, cognition, and neurovegetative function and interepisode remission (Sugiharta et al., 2022). Depression is characterized by three main symptoms and seven additional symptoms (American Psychiatric Association, 2000; Sadock et al., 2017; Elvira & Hadisukanto, 2017).

Anhedonia, or loss of interest and pleasure in commonly enjoyed activities, is one of the main diagnostic criteria for depressive disorders in the psychiatric diagnostic systems of the Diagnostic Statistical Manual (DSM) and International Statistical Classification of Diseases (ICD) (Ritsner, 2014). Often depressed patients present not with complaints of sadness or dysphoric feelings, but complain of loss of interest and pleasure in various things (De Fruyt et al., 2020).

Social interaction is a complex and often ambiguous human environment. There are many explicit and implicit "rules" about what is appropriate and what can be expected in an interaction. Highly dynamic, complex and ambiguous, social interactions tend to produce anxiety rather than lead to reward. Individuals with social anhedonia experience a limited sense of positive benefits from social interactions, which may be the reason why they choose to avoid social interactions. They need to feel a great sense of reward before they will engage in social interactions (Barkus & Badcock, 2019).

Anhedonia can refer to a decreased ability to experience pleasure from all (or at least some) positive stimuli, or it can refer to specific stimuli. There are three types of stimuli, namely social stimuli, sensory stimuli, and drugs/substances (Ritsner, 2014).

1. Social Anhedonia
   Most individuals derive pleasure as a result of their social interactions with others through chatting, sharing experiences, doing activities together, expressing feelings, loving, and even competing with others. In social anhedonia there is significantly reduced or even no pleasure derived from these social situations.
2. Sensory Anhedonia
   Individuals can also derive pleasure from a wide variety of sensory stimuli through the five senses. Individuals with physical anhedonia, derive less pleasure from physical sensations. The most commonly studied physical stimuli are sexual and gustatory stimuli. Sexual anhedonia, although often associated with major depression, has also been studied in the context of sexual dysfunction. Whereas gustatory anhedonia is often used in animal models of depression.
3. Anhedonia and Substance Use
   Anhedonia can be associated with several aspects of substance use. Some addiction theories suggest that drugs/substances act on the mesocorticolimbic dopamine system, which mediates intense feelings of pleasure when the addictive drug is administered and anhedonia during withdrawal. In addition, it is possible that physiological and psychological tolerance to addictive substances is related to anhedonia, i.e. when taken regularly, the same amount of a particular addictive substance elicits less pleasure than when the individual first started using the substance.

Anhedonia is one of the main symptoms in depression and in some cases can be a marker of major depression (Ritsner, 2014). Studies have found that anhedonia is difficult to treat and a predictor of poor therapeutic response (Carpinelli et al., 2018). A significant association was found between anhedonia and suicidal ideation in depressed patients. Suicidal ideation becomes a maladaptive coping strategy to avoid unpleasant emotions (Ducasse et al., 2018).

Anhedonia is one of the most frequently treatment-resistant aspects of depression, which is related to our lack of understanding of the etiology and neurobiology underlying its symptoms. In anhedonia there are deficits in the hedonic experience of reward and motivation to obtain reward (Borsini et al., 2020). Reward networks are described in the dopaminergic/dopaminergic mesolimbic pathways that originate in the ventral tegmental area (VTA) and spread to the nucleus accumbens (NAc) located in the ventral striatum (VS), nucleus of the base of the stria terminalis, amygdala, and hippocampus (Höflich et al., 2019). Studies have revealed biological mechanisms by which psychological stress is converted into inflammatory signals in the brain and periphery, and inflammation impacts neurotransmitters and neural circuits that contribute to behavioral symptoms of anhedonia. It is also associated with increased inflammatory biomarkers such as C-reactive protein (CRP) and cytokines, and shown to impact corticostriatal reward circuitry and improve anhedonia-related symptoms (Mehta et al., 2022).

Behavioral mechanisms of anhedonia in animals

Various mehods have been used to assess physical anhedonia, including sucrose or saccharin preference tests, in animal models (Chiba et al., 2023). Animal studies have provided evidence of a connection between depression and the neurobiological processes underlying the reward system. Research investigating monetary rewards as a pleasurable response to music has been associated with increased neural activity within the ventral striatum and ventromedial prefrontal cortex (vmPFC) (Sacher et al., 2012; Arnold, 2008). This is consistent with animal studies showing that dopaminergic activity in the ventral striatum is important in mediating positive reinforcement effects. In comparison, the vmPFC seems to integrate sensory experiences from various modalities and contribute to the subjective experience of stimulus reinforcement (Ritsner, 2014).

Various aspects of anhedonia, can be studied in humans and experimental animals. Rodents are still the most commonly used species. Food is a frequently used stimulus because it is moderately easy to manipulate; confounding variables can be identified and controlled. Consumption of palatable food, including sucrose, increases extraneuronal dopamine levels in the NAc. Pontine parabrachial nuclei, play a central role in controlling nucleus accumbens dopamine levels through their extensive connections to the ventral forebrain. Although the role of dopamine in reward remains controversial, dopaminergic activity, especially in the mesolimbic system, increases when regularly preferred stimuli are encountered. Thus, the increase in extraneuronal dopamine in the NAc serves as an index of the reward value of the sucrose stimulus (Scheggi et al., 2018).

The sucrose preference test (SPT) is a reward-based test used as a sign of anhedonia in laboratory rats. Adolescent rats that experience chronic early-life adversity/stress (CES) show a decline in SPT results. There is an aberrant interaction between stress and reward networks after CES, and there is a role for amygdala neurons that express corticotropin-releasing hormone (CRH) in emotional deficits that signal neuropsychiatric disorders (Bolton et al., 2018). In assessing anhedonia behavior in experimental animals, weight loss can also be used as a result of reduced motivation to obtain rewards, one of which is food. Antidepressant administration showed a significant increase in body weight in depressed rats (Ju et al., 2021).

Sucrose preference is based on an animal's natural preference for sweet foods, assuming that this preference is proportional to the pleasure the animal experiences when consuming them. In general, the test measures the amount of sweet solution an animal ingests over a given period. Since the animal does not need effort to gain access to the sweet solution, this test is thought to reflect the animal's capacity to experience the hedonic pleasure elicited by the sweet solution (Guessoum et al., 2020; Bzdok & Meyer-Lindenberg, 2018). The usual two-bottle testing paradigm is used, where one drinking bottle contains a sucrose solution and the other contains plain water. The sucrose concentration typically used is around 0.5-2% (Du Hoffmann & Nicola, 2016).

Conclusion

Depressive disorder, also known as major depressive disorder, characterized by three main symptoms and seven additional symptoms. Anhedonia, or loss of interest and inability to feel pleasure in hobbies, is one of the main diagnostic criteria for depressive disorder. Individuals with social anhedonia are unable to experience the positive benefits of social interactions and thus choose to avoid social interactions. Anhedonia in some cases can be a marker

of major depression and a predictor of poor therapeutic response. There is a significant association between anhedonia and suicidal ideation in depressed patients, indicating it as a maladaptive coping strategy. Various methods have been used to assess physical anhedonia, including sucrose or saccharin preference tests in animal models. The Sucrose Preference Test (SPT) is a reward-based test used as an indicator of anhedonia in laboratory. Adolescent rats subjected to stress manifest a decreased in SPT results.

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