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Review article

Olfactory and gustatory functions in bipolar disorders: A systematic review

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ABSTRACT

Olfactory and gustatory dysfunctions have been described in different psychiatric disorders. Several studies have found gustatory and olfactory function change in bipolar disorders with various results. The aim of this study is to have a systematic review of studies evaluating gustatory and olfactory function in bipolar disorders. After a systematic search, 15 studies on olfaction and 5 studies on taste were included in this review. The UPSIT (University of Pennsylvania Smell Identification Test) and Sniffin' Sticks were the most widely used tests to evaluate smell. Some studies on olfaction described dysfunctions in smell identification as potential markers for bipolar disorders. Moreover, olfactory acuity was associated with psychosocial and cognitive performances. For taste, only few studies used standardized tests to evaluate gustation. These studies showed that patients with Bipolar disorders had more gustatory dysfunction compared to controls, and to non-bipolar depressed patients.

1. Introduction

Bipolar disorder (BPD) is characterized by the recurrence of mood episodes, either depressive or manic. Patients suffering from bipolar disorders go through phases of acute mood episodes and phases of remission, usually free of clinical symptoms (Samalin et al., 2014). Some bipolar patients may also exhibit psychotic symptoms with delusions or hallucinations during their acute episodes (APA, 2000). Depressive episodes with common clinical symptoms are seen in Major depressive disorders (MDD), and in bipolar disorders. Bipolar and unipolar episodes of depression can be distinguished clinically at some level (Mitchell et al., 2008). However, we still do not have early biomarkers to distinguish between unipolar and bipolar depression. Moreover, given the close anatomical links between the olfactory system and the brain circuits involved in memory (Savic et al., 2000) and emotion (Anderson et al., 2003), the study of olfaction in this disease may have potential clinical implications.

1.1. Olfactory dysfunctions in psychiatric disorders

Unipolar depression has been associated with olfactory and gustatory dysfunctions (Naudin and Atanasova, 2014; Swiecicki et al., 2009). Some studies have reviewed olfactory dysfunctions in both unipolar and bipolar depression (Schablitzky and Pause, 2014). Major depressive episodes are associated with negative biases in olfactory alliesthesia, olfactory anhedonia, and facial emotion expression recognition (Naudin and Atanasova, 2014). Olfactory deficits and biases were considered as potential markers for depression and other psychiatric disorders (Naudin and Atanasova, 2014; Atanasova et al., 2008). Olfactory dysfunction may also be a potential vulnerability marker for psychosis (Turetsky et al., 2009; Kamath et al., 2012). Most studies evaluating these sensory functions in depression included patients with unipolar depression. Fewer studies have evaluated patients with bipolar disorders (Schablitzky and Pause, 2014).

Bipolar disorder (BPD) has been associated with sensorimotor abnormalities (motor deficit, steadiness and movement velocity deficit, and emotion perception deficits after visual and auditory stimuli) (Lohr and Caligiuri, 2006). These abnormalities were described in euthymic bipolar patients suggesting that these can be trait related deficits (Neves Mde et al., 2014). Studied sensory deficits in bipolar disorder were mainly auditory or visual (Thaler et al., 2013). While some studies have reported the absence of olfactory dysfunction in BPD (Burón and Bulbena, 2012), several others found significant perceptual and sensorimotor abnormalities (olfactory, identification, sensitivity, intensity, discrimination, and hedonic rating) (Schablitzky and Pause, 2014). Several studies have found a relation between the olfactory function in BPD and affective state (Cumming et al., 2011; Hardy et al., 2012), psychotic symptoms (Striebel et al., 1999), and social functioning

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(Hardy et al., 2012; Lahera et al., 2016). These relations could be explained by neuroanatomical connections between olfactory, emotional, and cognitive functions (Takahashi et al., 2014; Soudry et al., 2011). Moreover, some pharmacological treatments used in BPD can have an impact on smell or taste perception. It was shown that treatment with Lithium salts (Li) or Valproic Acid (VPA) can prevent secondary olfactory discrimination deficits (Castro et al., 2012). Some reports identified taste changes associated with Li treatment (Terao et al., 2011).

1.2. Measures of smell and taste

Smell and taste can be measured and altered at different levels. The odor and the taste thresholds are the minimum concentration at which an odor or a taste are perceived. The capacity to identify and discriminate an odor or a taste can also be measured and evaluated (Wrobel and Leopold, 2004). Recognition memory, where an individual is able to recognize an odor or a taste previously presented is also a characteristic that can be evaluated in normal and pathological situations. Finally, the pleasantness, the familiarity, and the intensity of an odor and a taste can be measured to evaluate possible changes or deficits in different psychiatric disorders. Various tests can be used clinically for the evaluation of different olfactory and gustatory characteristics (Atanasova et al., 2011; Wrobel and Leopold, 2004).

1.3. Brain regions involved in bipolar disorder

Bipolar disorder is associated with structural brain abnormalities in prefrontal cortical areas, striatum, and amygdala early in the course of the illness. It also involves dysfunctions within subcortical-prefrontal networks and the associated limbic regions (Strakowski et al., 2005). Neurochemical abnormalities are found in bipolar depression mainly in the prefrontal cortex (Patel et al., 2008). Neurophysiological dysfunctions seen in BPD depression are similar in many ways to those seen in unipolar MDD. These include inhibition of the dorsolateral prefrontal cortex (DLPFC), of the amygdalar complex, and an activation of the ventromedial prefrontal cortex (VMPFC), leading to a top-down inhibition of posterior perceptual regions (Shahaf, 2016). Cerullo et al. (2014) did not find differences in brain activation of the cortico-limbic regions between bipolar and unipolar patients during depressive episodes.

1.4. Brain regions involved in olfaction and taste

Brain anatomic regions involved in olfaction and taste are often involved in the physiopathology of depression and BPD.

- The orbitofrontal cortex (OFC) is an important region of convergence of gustatory and olfactory inputs, implicated in the representation of taste and smell. The lateral part of the OFC includes the secondary taste cortex, while the medial OFC has an olfactory area with direct connections from the primary olfactory cortex (pyriform cortex). Some single neurons of the OFC respond to both gustatory and olfactory stimuli (Rolls, 2000). Therefore, an alteration in olfactory function can lead to impaired gustatory representations (Rolls, 2000; Rolls and Baylis, 1994). The OFC and the anterior cingulate gyrus in the frontal cortex are involved in the processes of olfaction and taste (Fulbright et al., 1998; Rolls, 2000). In depression, overactivation and hypoactivation of the anterior and posterior parts of the OFC respectively contribute to anxiety, pain sensitivity, apathy, psychomotor, memory, and attention deficits (Naudin and Atanasova, 2014; Rogers et al., 2004).
- The OFC receives strong inputs from the amygdala and the thalamus, and projects back to the temporal areas, to the hippocampus, and to the cingulate cortex. It also projects to the preoptic region and lateral hypothalamus, to the ventral tegmental area (VTA), and to the head of the caudate nucleus (Rolls, 2000).
- The olfactory bulb is the first relay of olfactory information to the brain. Studies have shown decreased volume of olfactory bulb in depressed patients, suggesting an association between depression and neurogenesis in this region of the brain (Negoias et al., 2010).
- The amygdala is a part of the limbic system and plays an important role in the processing of emotions. Amygdala is involved in the processing of the hedonic judgment of taste (Rolls, 2000). It is also involved in the perception, memory, and hedonic judgment of olfactory stimuli (Pouliot and Jones-Gotman, 2008; Anderson et al., 2003). Studies have reported dysfunctions in amygdalar activity and volume in depression (Kronenberg et al., 2009; Van Eijndhoven et al., 2009; Hamilton et al., 2008).
- The hippocampus is also part of the limbic system. It is involved in the processing of memory and emotion. The hippocampus is associated with the memorization of gustatory and olfactory stimuli (Kesner et al., 2002; Lathe, 2001). It is partly responsible for conditioned taste aversion (Lathe, 2001). Studies reported a decrease of hippocampal volume in depression (Campbell et al., 2004).

Therefore, BPD and olfactory and gustatory functions share common anatomical regions, explaining some of the perceptual alterations described in BPD. But those alterations in olfactory and gustatory functions in BPD are various and even contradictory in some cases. The objective of this study was to provide a systematic review of studies evaluating olfactory or gustatory functions in bipolar disorders in order to have a comprehensive view of these perceptual alterations in taste and smell commonly seen in this disorder.

2. Methods

A Systematic Literature Review was conducted in January 2017. This systematic review was reported using PRISMA guidelines. To capture all the relevant studies, we searched the abstract, title, and keyword fields in the MEDLINE electronic database, to identify studies evaluating taste and olfaction in bipolar disorders. We performed two separate searches: the first regarding olfactory function in BPD, and the second concerning gustatory function. We used the following keywords for our first search: ((olfactory$) OR (olfaction$) OR (smell$) OR (sensory$) OR (sensorial$) OR (odor$)) AND ((mood$) OR (psychosis$) OR (depression$) OR (bipolar$) OR (mania$) OR (affective$)). We used the following keywords for our second search: ((gustation$) OR (gustatory$) OR (taste$) OR (sensory$) OR (sensorial$)) AND ((mood $) OR (psychosis$) OR (depression$) OR (bipolar$) OR (mania$) OR (affective$)).

Searches were limited to English and French languages studies with human participants without any date restriction.

Any papers describing research on olfactory or gustatory function in BPD that was deemed relevant to one or more of the theories in this area were included. All studies describing research on patients with bipolar disorder (total or partial sample), and assessing any component of olfactory or gustatory process (perception, anatomy, physiology, pathophysiology) were included. Studies evaluating the impact of bipolar disorder treatments on either olfaction or taste were also included. Relevant theoretical papers, review articles, and books were consulted to supplement our knowledge of the area. We excluded all review articles as well as the studies evaluating olfaction or taste in samples of patients with either affective or psychotic disorder, but not having any BPD patients in the sample. We also excluded epidemiological studies, single case studies, and case report studies. Following removal of duplicates and citations from non-English or non-French language journals, paper titles were scrutinized by FK, those evidently outside the scope of the review were rejected (Figs. 1 and 2).

Several descriptor variables were coded for each study: 1) Number of patients, sex, and diagnosis; 2) Age; 3) Depression severity scores; 4) Procedures employed to evaluate for bipolar disorder; 5) Outcome on