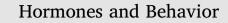
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Review article

Revisiting the wandering womb: Oxytocin in endometriosis and bipolar disorder



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ABSTRACT

Hippocrates attributed women's high emotionality - hysteria - to a 'wandering womb'. Although hysteria diagnoses were abandoned along with the notion that displaced wombs cause emotional disturbance, recent research suggests that elevated levels of oxytocin occur in both bipolar disorder and endometriosis, a gynecological condition involving migration of endometrial tissue beyond the uterus. We propose and evaluate the hypothesis that elevated oxytocinergic system activity jointly contributes to bipolar disorder and endometriosis. First, we provide relevant background on endometriosis and bipolar disorder, and then we examine evidence for comorbidity between these conditions. We next: (1) review oxytocin's associations with personality traits, especially extraversion and openness, and how they overlap with bipolar spectrum traits; (2) describe evidence for higher oxytocinergic activity in both endometriosis and bipolar disorder; (3) examine altered hypothalamicpituitary-gonadal axis functioning in both conditions; (4) describe data showing that medications that treat one condition can improve symptoms of the other; (5) discuss fitness-related impacts of endometriosis and bipolar disorder; and (6) review a pair of conditions, polycystic ovary syndrome and autism, that show evidence of involving reduced oxytocinergic activity, in direct contrast to endometriosis and bipolar disorder. Considered together, the bipolar spectrum and endometriosis appear to involve dysregulated high extremes of normally adaptive pleiotropy in the female oxytocin system, whereby elevated levels of oxytocinergic activity coordinate outgoing sociality with heightened fertility, apparently characterizing, overall, a faster life history. These findings should prompt a re-examination of how mind-body interactions, and the pleiotropic endocrine systems that underlie them, contribute to health and disease.

1. Introduction

Egyptian medical records dating back to 1990 BCE describe cases of women experiencing erratic emotions with accompanying physical manifestations including seizures, paralysis, choking, and mutism (Novais et al., 2015). Because of their female specificity, medical and gynecological practitioners and writers of antiquity such as Aretaeus, Soranus, Plato, Hippocrates, and Galen explained these symptoms as emerging from the womb (Novais et al., 2015; Tasca et al., 2012; Gilman et al., 1993). A belief held by some of these men was that the womb was a separate being or even an animalistic entity that lived within a woman and could cause health issues by wandering around her body and disturbing other organs (reviewed in Gilman et al., 1993). Hippocrates (460–377 BCE) grouped these heterogeneous symptoms under *hysteria* (from Greek *hysterikos*, meaning 'of the womb'), a term that has since been subsumed into other diagnostic labels (Fig. 1). Debate over the nature of the womb and its ability to truly wander around a woman's body continued well into the Renaissance, informing medical treatments and influencing attitudes about women (Novais et al., 2015).

In a continuation of ascribing animalistic traits to women, the 'father of psychiatry,' Emil Kraepelin, characterized hysteria as a clash between instinct and volition, intuiting later psychoanalytic developments that emphasized the role of conflicting drives in hysteria, and psychopathology more generally (Decker, 2004). Within the frameworks of the DSM, the dissociative and somatic symptoms formerly belonging to hysteria remain, and are commonly observed in mood and personality disorders, including bipolar disorder (Fig. 1). Although severe forms of bipolar disorder are equally prevalent in both sexes (Blanco et al., 2017), women tend to report higher levels of somatic, dissociative and mood symptoms (Delisle et al., 2012; Dessotte et al., 2015; Tabassum and Farooq, 2007), and overall, meet criteria for affective disorders much more frequently than men (O'Donnell et al., 2016).

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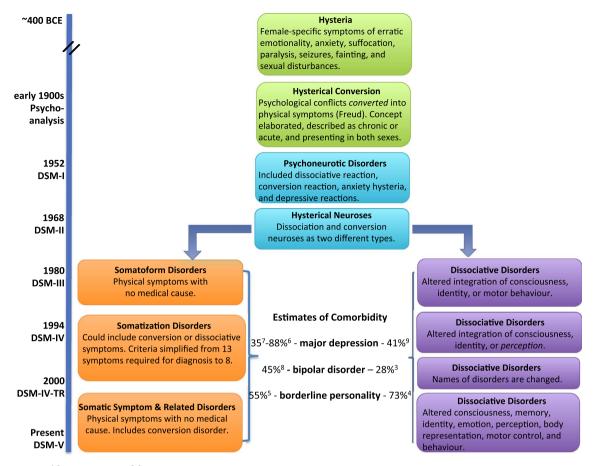


Fig. 1. Simplified timeline^{1,2} and comorbidities^{3–9} of hysteria-related, female-preponderant categories. Hysteria is no longer a diagnostic category but its heterogeneous symptoms still exist and have been subsumed by other diagnoses in modern versions of the DSM.

References: 1. North, 2015, 2. Kapfhammer, 2001, 3. Yayla et al., 2015, 4. Sar et al., 2006, 5. Rechlin et al., 1997, 6. Bowman and Markand, 1996, 7. Kuloglu et al., 2003, 8. Tavormina, 2011, 9. Sar et al., 2013.

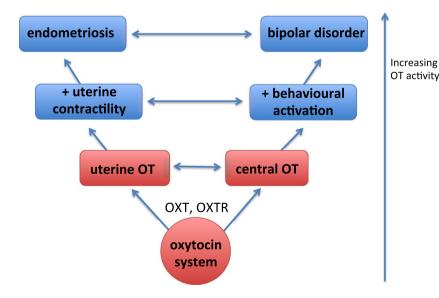


Fig. 2. Hypothesized effects of elevated oxytocin system activity on psychological and physiological traits that contribute to bipolar disorder and endometriosis. A highly simplified diagram showing how the pleiotropic genes (OXT, OXTR) that shape the oxytocin (OT) system contribute to both uterine and central OT levels and OT receptor densities. Given OT's potentiating effects on uterine contractility and social behaviour, it is hypothesized that as net OT system activity increases, through either increased OT levels or heightened OT receptor densities or both, the joint risk of endometriosis and bipolar disorder also increases. Under this model, OT-mediated physiological and psychological processes are positively associated, and jointly affected by increasing (or decreasing) oxytocin system activity.

Bipolar disorder, characterized by alternating high and low affective states, is different from hysteria, but it has long been recognized that the two phenotypes overlap, especially with respect to mood volatility (noted by Kraepelin; reviewed in Kapfhammer, 2001). Somatic symptoms, such as muscular tension and migraines, are frequently observed in people seeking treatment for bipolar disorder (Tavormina, 2011). For about half of women with bipolar disorder, shifts in menstrual cycle

phase also precede symptom onset, and menstrual cycling notably impacts symptom severity (Teatero et al., 2014), highlighting the complex interplay between the body, particularly with respect to female reproductive physiology, and psychological health (Galea et al., 2016).

The interactions of mind with body - and their joint disturbance in female-preponderant psychiatric diagnoses - thus centrally contributed to the emergence of psychiatry, and at present remain both mysterious Download English Version:

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