- Review
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Allopregnanolone as a mediator of affective switching in reproductive mood disorders

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Abstract

Rationale

Reproductive mood disorders, including premenstrual dysphoria (PMD) and postpartum depression (PPD), are characterized by affective dysregulation that occurs during specific reproductive states. The occurrence of illness onset during changes in reproductive endocrine function has generated interest in the role of gonadal steroids in the pathophysiology of reproductive mood disorders, yet the mechanisms by which the changing hormone milieu triggers depression in susceptible women remain poorly understood.

Objectives

This review focuses on one of the neurosteroid metabolites of progesterone — allopregnanolone (ALLO) — that acutely regulates neuronal function and may mediate affective dysregulation that occurs concomitant with changes in reproductive endocrine function. We describe the role of the "neuroactive" steroids estradiol and progesterone in reproductive endocrine-related mood disorders to highlight the potential mechanisms by which ALLO might contribute to their pathophysiology. Finally, using existing data, we test the hypothesis that changes in ALLO levels may trigger affective dysregulation in susceptible women.

Results

Although there is no reliable evidence that basal ALLO levels distinguish those with PMD or PPD from those without, existing animal models suggest potential mechanisms by which specific reproductive states may unmask susceptibility to affective dysregulation. Consistent with these models, initially euthymic women with PMD and those with a history of PPD show a negative association between depressive symptoms and circulating ALLO levels following progesterone administration.

Conclusions

Existing animal models and our own preliminary data suggest that ALLO may play an important role in the pathophysiology of reproductive mood disorders by triggering affective dysregulation in susceptible women.

Fig. 1

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