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Letter to the Editor: Demonstration of Elevated Cerebrospinal Fluid CRH Levels During Pregnancy Provides Support for (Not Against) the Link Between CRH and Postpartum Depression

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Issue Section: Correspondence

Zaconeta et al (1) found that cerebrospinal fluid (CSF) levels of CRH are higher among pregnant than among nonpregnant women. These results represent a substantial contribution to our understanding of pregnancy endocrinology. The authors also suggest that their study demonstrates a lack of association between the prenatal CSF CRH levels of women with vs without postpartum depression (PPD). This study, however, was not sufficiently powered to assess this secondary question. Notably,

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their analyses included only 6 women with new-onset depression postpartum, compared with 90 control women. The authors interpret the high *P* value derived from their Student *t* test of case/control data as meaningful evidence of a lack of relation between CSF CRH and new-onset PPD. We urge readers to consider the alternative view that, with only 6 cases, the *P* value does not provide meaningful insight that would justify this interpretation (2).

The authors position the importance of their findings among studies examining the association between CRH and PPD by suggesting that they are unique in distinguishing between prenatal and postnatal depression onset. In fact, they neither distinguish between these two nor would they have been unique in doing so. The authors' assessment of prenatal depression was problematic both because impending surgery would contaminate mood states and because the presence of depressive symptoms on the day of delivery is not a valid index of prenatal mood. Further, their assertion that previous studies fail to account for prenatal depressive symptoms is inaccurate (3–8). A close examination of the studies cited by the authors (3–8) reveals the opposite of their assertion: most of these studies (3 of 5) statistically adjust for prenatal depression (Ref. 8 does not test the association between placental CRH [pCRH] and PPD). Zaconeta et al (9) have raised this inaccurate concern previously. Previous studies have statistically covaried prenatal depressive symptoms, isolating the contribution of pCRH to the prediction of PPD symptoms above and beyond prenatal depressive symptoms (10). In addition, to further demonstrate the validity of this covariate approach, Glynn and Sandman (10) excluded women who exhibited PPD symptoms at any 1 of 5 prenatal assessments and reported results identical to those for the covariate approach. pCRH remained a statistically significant predictor of new-onset PPD symptoms. Summarily, covarying for prenatal depression and excluding subjects with prenatal depression are 2 equally valid methods for investigating the correlates of new-onset PPD. This logic, combined with the complementary analyses (10), supports not only the results of Glynn and Sandman (7), but also those of the other studies (5, 6) criticized by Zaconeta et al.

In sum, contrary to the assertions of Zaconeta et al, their results provide evidence in support of (not against) the notion that CRH is functionally implicated in PPD. Their demonstration of elevated CSF CRH during pregnancy is consistent with the potential that the high levels of CRH secreted from the placenta do, indeed, cross the blood-brain barrier and thereby modify neuroendocrinology. This evidence supports a

mechanistic pathway of causality through which placental CRH may play a role in PPD etiology.

Disclosure Summary: The authors have nothing to disclose.

Abbreviations

CSF cerebrospinal fluid

pCRH placental CRH

PPD postpartum depression.

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