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Biological and Psychosocial Predictors of Postpartum Depression: Systematic Review and Call for Integration
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SUPPLEMENT B: THE THYROID SYSTEM

Although not typically discussed in the context of withdrawal theories, hormonal fluctuations in the thyroid system have been implicated in PPD. These theories have emerged from observations that postpartum thyroiditis, a normally temporary dysregulation of the thyroid resulting from autoimmune inflammation affecting about 5% to 7% of women in the first year after birth overlaps with symptoms for PPD, with tiredness, lethargy, weight gain and depression reported frequently in both (Kennedy et al 2010). Several explanations have been provided to explain this potential link, including the possibility that lower postpartum thyroid hormone levels may directly impair the activity of the serotonin system (Hendrick et al 1998, Upadhyaya et al 1992) or that estrogen receptor sensitivity may be altered by changes in thyroid hormone secretion and availability during pregnancy (Sylvén et al 2013, Vasudevan et al 2002).

Pregnancy leads to substantial alterations in the thyroid system. Starting very early in pregnancy, steep increases in human chorionic gonadotropin, a glycoprotein structurally similar to thyroid-stimulating hormone (TSH), result in a transient increase of free tri-iodothyronine (T3) and free thyroxine (T4) release from the thyroid gland and a transient decrease in TSH levels. Over time, pregnancy-related increases in estrogen concentrations stimulate the production of thyroid hormone-binding globuline production, and levels of bound T3 and T4 increase. Free T3 and T4 concentrations, however, remain relatively stable until the end of pregnancy because of a compensatory increase in TSH release from the anterior pituitary (Feldt-Rasmussen & Mathiesen 2011, Moleti et al 2014). Because estrogen has these influences on the thyroid system and because of the overlap in mood changes typical to postpartum thyroiditis and PPD, some studies have tested the link between thyroid measures and PPD.

REVIEW OF THYROID STUDIES

The literature on thyroid hormones and PPD is relatively small. A total of 11 studies were identified (see Table 1; Online Supplement A) that can broadly be divided into those on thyroid antibodies, which are markers for autoimmune thyroiditis, and those testing direct or combined effects of thyroid hormones (TSH, T3, T4) with respect to PPD symptoms.

Thyroid Antibodies. Studies on PPD and thyroid antibodies have yielded mixed findings. Kuijpens et al (2001) found a link between positive antibody status and a concurrent PPD diagnosis at 4 and 12, but not at 20, 28 and 36 weeks post partum in 291 women. Similarly, two smaller studies report associations with PPD symptoms within the first postpartum days (Le Donne et al 2012) and at 4 weeks post partum (McCoy et al 2008), although in one of the studies the association disappears after controlling for thyroid hormones (Le Donne et al 2012). In another study, a prospective link between thyroid antibodies between 16 and 25 weeks' gestational age and PPD symptoms at 1 week and 6 months post partum was observed among 199 mothers (Groer & Vaughan 2013). While these findings seem to converge regarding positive antibody status and PPD symptoms through three months post partum, they stand in contrast with three studies that report no associations of antibody status with a PPD diagnosis (Albacar et al 2010) and PPD symptoms (Lambrinoudaki et al 2010, Lucas et al 2001).

Thyroid Hormones. Studies in this area have either assessed effects of individual hormones (TSH, T3, T4) or created a combined thyroid dysfunction score based on abnormal TSH and T4 levels. The two large studies testing the link between a thyroid dysfunction score and PPD symptoms yielded null findings (Kuijpens et al 2001, Lucas et al 2001). The remaining studies all tested associations with individual hormones, and two suggested a link between increased TSH and PPD symptoms. McCoy et al (2008) report higher TSH levels with concurrently assessed EPDS symptoms at 4 weeks post partum in 51 women, and in a sample of 347 Swedish women, higher TSH levels upon delivery were associated with PPD risk at 6 months, but not at 5 days or 6 weeks post partum (Sylvén et al 2013). Although results of these two studies converge, the balance of studies assessing TSH levels either in pregnancy or post partum, some with larger sample sizes, suggest the absence of a link with a PPD diagnosis or symptoms of PPD (Albacar et al 2010, Ingram et al 2003, Kuijpens et al 2001, Lambrinoudaki et al 2010, Le Donne et al 2012, Lucas et al 2001, Pedersen et al 2007).

For T3, Lambrinoudaki et al (2010) found lower T3 levels with higher concurrently assessed EPDS scores on the fifth day after delivery, but no prospective association with symptoms at 6 weeks post partum in a small sample of 57 women. However, three studies with similar sample sizes did not detect a link between T3 levels in pregnancy (Pedersen et al 2007, Wissart et al 2005) or post partum (Le Donne et al 2012) and PPD symptoms.

A similar pattern emerges for studies assessing T4 concentrations. Two studies found lower T4 with more concurrently assessed PPD symptoms in the first week post partum, but not at 6 weeks (Lambrinoudaki et al 2010, Sylvén et al 2013) or 6 months post partum (Sylvén et al 2013). Similarly, a study of 31 pregnant women reports lower average total T4 but not free T4 pregnancy levels with more PPD symptoms at two to six weeks post partum (Pedersen et al 2007).

These findings did not hold up at 8 or 24 weeks post partum. Taking a somewhat different approach, a study of 73 Jamaican pregnant women found pronounced changes in total T4 (but not in free T3) were associated with more depressive symptoms at 6 weeks post partum, suggesting that a more pronounced change is associated with more mood disturbance (Wissart et al 2005). However, these significant findings stand in contrast with another set of studies that do not report significant associations between levels of T4 and symptoms of PPD (Albacar et al 2010, McCoy et al 2008, Stuebe et al 2013).

Summary. Studies on thyroid antibodies are inconsistent regarding their associations with PPD symptoms. Some studies on individual thyroid hormones suggest links between higher TSH and lower T3 and T4 levels with PPD symptoms, as theorized, but at least as many studies yielded null findings. We propose that the role of the thyroid system in PPD will become clearer once thyroid markers are considered in interaction with closely related biological factors - most prominently perhaps estrogen - instead of studying their influence on PPD risk in isolation.

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