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SHORT COMMUNICATION

Decreased brain tryptophan availability as a partial determinant of post-partum blues

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Kynurenine;
Serotonin

Summary *Background*: The post-partum blues is a transient mood alteration affecting most women a few days after delivery. Its stereotypic pattern of symptoms and time course, peaking on post-partum day 3–5, is suggestive of biological determinants superimposed on psycho-social factors. This study was designed to evaluate the possible role of the serotonin system during this period through assessment of brain tryptophan availability.
Methods: Blood samples from 50 women were collected just before (D0) and 3 days after (D3) delivery. Based on plasma concentration of tryptophan, amino acids competing with tryptophan for transport across the blood–brain barrier and on their respective affinities for this transporter, a brain tryptophan availability index (BTAI) was calculated and its variation correlated with the intensity of post-partum blues evaluated through the Kennerley and Gath score at D3.
Results: The BTAI showed a −15% decrease between D0 and D3 ($p<0.01$, paired t-test). This decrease was not supported by a drop in plasma tryptophan since its level rather increased (+19%). There was no evidence for change in placental indoleamine-2,3-dioxygenase activity since the variation in plasma L-kynurenine (+12%) paralleled the change in tryptophan level. The decreased BTAI appeared the consequence of a dramatic increase in plasma levels of most amino acids, particularly the competitor aminoacids leucine, isoleucine, valine and tyrosine, during the early post-partum. This decrease in brain tryptophan availability was concomitant to the post-partum blues, whose intensity significantly correlated with the amplitude of BTAI variation (Pearson's coefficient −0.283, $p<0.05$).

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Conclusion: This study suggests that generalized, large amplitude metabolic and/or nutritional changes occurring in the early post-partum result in a transient decrease in brain tryptophan availability, partly accounting for the mood alteration referred to as the post-partum blues, a model for the triggering of puerperal mood disorder in vulnerable women.

1. Introduction

Most women experience a transient mood change in the early post-partum, referred to as the post-partum blues or baby blues (Robin, 1962; Yalom et al., 1968; Pitt, 1973; Kennerley and Gath, 1985; Iles et al., 1989; Glover et al., 1994; Sutter et al., 1997). Occurring during the first week and culminating between the 3rd and 5th days after delivery, this non-pathological feature is considered as a mild and brief depressive state. Its high incidence, together with the reproducibility of both its time course and symptomatic features, is suggestive of common psychological and/or biological determinants present in almost every pregnant woman (O'Hara et al., 1991; Da Costa et al., 2000). Besides the major psychological impact of child birth, a large number of biological mechanisms may account for mood or emotional disturbances.

Among biological determinants, functional alterations in the serotonin system have long been associated with mood disorders (Lucki, 1998), and also with impaired control of emotion (Mann, 1999). Brain serotonin synthesis is highly dependent on brain tryptophan availability. Tryptophan is an essential amino acid provided by food and transported into the brain through the high affinity LAT1/r4F2hc L-system transporter (Kanai et al., 1998; Prasad et al., 1999). Tryptophan availability in the brain is also dependent on the competition with large neutral amino acids occurring at the blood-brain barrier (Pardridge, 1979; Smith, 2000; Verrey, 2003). The change in tryptophan bioavailability is a rate-limiting step in brain serotonin synthesis and triggers mood alteration in animals and human. Rapid tryptophan depletion is a model for depressive symptoms (Moore et al., 2000) and tryptophan supplementation (or a reduced diet of competitor amino acids) leads to an improved mood and social status in primates (Moskowitz et al., 2001). The risk of post-partum depression is associated with a tryptophan hydroxylase gene polymorphism (Sun et al., 2004). Moreover, there is some evidence that plasma tryptophan concentrations progressively decrease during pregnancy and return to normal after delivery (Schröcksnadel et al., 1996, 2003; Maes et al., 2001). Recently, Kohl et al. (2005) showed an increase in plasma tryptophan and kynurenine after delivery, with an impaired tryptophan-to-kynurenine ratio in women experiencing baby blues.

During the post-partum period, many factors may account for possible changes in brain tryptophan availability. Among these factors, indoleamine-2,3-dioxygenase (IDO, that transforms tryptophan into L-kynurenine) activity may explain changes in level of tryptophan.

There could be at least two distinct sources of IDO activity in the post-partum context: (i) the immune system (Maes et al., 2002), where IDO transcription is induced under appropriate inflammatory cytokine stimulation (including inflammation related to delivery); and (ii) the placenta, since IDO is highly expressed in the syncytiotrophoblast (Kudo and Boyd, 2000; Santoso et al., 2002; Sedlmayr et al., 2002; Baban et al., 2004), and IDO is considered to play a local immunosuppressive role and to participate in materno-fetal tolerance (Munn et al., 1998; Mellor et al., 2002). In the latter hypothesis, abrupt removal of placenta might lead to withdrawal of IDO activity in the early post-partum. In addition, the liver enzyme tryptophan 2,3-dioxygenase (TDO), another tryptophan catabolizing pathway, may also undergo change in activity during the post-partum period, due to increased corticosteroid levels (Comings et al., 1995).

This study was therefore designed to correlate the intensity of baby blues, as assessed by the Kennerley and Gath rating scale (1989), with the intensity of metabolic changes determining brain tryptophan availability.

2. Methods

2.1. Subjects

Fifty pregnant women were enrolled in this study. Pathological pregnancies were not considered for inclusion, and obstetrical complications as well as surgical delivery were exclusion criteria. Informed consent was obtained and the study was approved by the local ethics committee. Blood samples were