

Perinatal SSRI exposure and neonatal brain plasticity: role of maternal gut microbiome?

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Peripartum mood and anxiety disorders have enduring effects on the mother and her developing offspring. As a result, selective serotonin reuptake inhibitor antidepressants (SSRIs) are frequently prescribed during pregnancy to 5-10% of women. These medications can affect foetal brain development and alter behavioural outcomes later in life. Recent findings suggest that SSRIs can also have a direct impact on the host microbiota. Transmission of altered microbiota from the mother to the neonate can, in turn, affect early life programming of brain development.

Using a rodent maternal stress paradigm as a model of peripartum mood and anxiety disorders, we sought to explore the peripartum SSRI treatment on maternal gut microbiome and brain plasticity in the mother and neonate. To do this Sprague-Dawley female rats were either left undisturbed or subjected to chronic unpredictable stress during the pregnancy (n=8-14/group). Half of dams were supplemented daily with fluoxetine (FLX) throughout the stress exposure. Microbiota composition was analysed in faecal samples of dams and measures of neonatal neurogenesis was assessed.

Administration of FLX to stressed dams had a distinct impact on maternal gut microbiota. FLX successfully counteracted some of the stress-induced changes: a reduction in *Bifidobacterium*, *Roseburia* and *Lachnospiraceae* UCG-001, and an increase in *Bacteroides* species. Furthermore, FLX exerted a stress-independent effect in stressed dams, differentially affecting the relative abundance of *Coriobacteriaceae* UCG-002, *Clostridiales* vadinBB60 group and *Erysipelotrichaceae* uncultured bacteria. In neonatal offspring at postnatal day 2, which is similar to 3rd trimester brain changes in humans, maternal FLX treatment protected against the effects of maternal stress on neurogenesis in the forebrain of male and female neonates.

These data suggest an important role for SSRI medications in altering the maternal microbiome and neonatal brain development, potentially protecting against the effects of stress. On-going work is aimed at investigating associations between the impact of perinatal exposure to SSRIs on microbial colonization of the neonatal gut and altered neuroplasticity in the neonatal brain.

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