

Weaning-induced alterations on neuropeptidergic populations of the rat hypothalamus

Citation for published version (APA):

Diniz, G. B. (2018). *Weaning-induced alterations on neuropeptidergic populations of the rat hypothalamus*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20181218gd>

Document status and date:

Published: 01/01/2018

DOI:

[10.26481/dis.20181218gd](https://doi.org/10.26481/dis.20181218gd)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

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Appendix C

Valorisation

Valorisation

The lactation period is perhaps unrivaled in terms of the extension and depth of the metabolic demands that it imposes on the female during a short period of time. This makes motherhood a very attractive field of research, as it equips researchers with a physiological model of brain plasticity in response to both internal and external cues. An often-overlooked aspect of lactation, however, is weaning, or the terminus of lactation. During weaning, the brain must undergo a new set of alterations that will reset most of its functions to their pre-pregnancy and pre-lactation levels. The inexorable growth of the pups exerts a strong pressure on the dam's body to constrain its duration and ensure a swift interruption of maternal behaviors and resuming of reproductive functions.

If examined out of context, several of the brain alterations that take place in the maternal physiology would be considered pathological at any other moment of the dam's life. Those alterations include, for example, leptin resistance, one of the hallmarks of metabolic syndrome, decreased (and therefore potentially insufficient) response to stressors, and excessive volume expansion at the cost of harshly reduced osmoregulation. It is logical, therefore, that if weaning does not proceed appropriately, the once-mother could carry unbalances for an unknown extension of time. To identify and understand the weaning alterations in the central nervous system, therefore, could provide us with the knowledge to better intervene if something goes awry during this period.

Although an underappreciated problem, motherhood can be challenging for several women and may leave long-standing consequences. Excessive weight gain during lactation is a predictor of obesity and cardiovascular risk decades after birth (Mannan et al. 2013; McClure et al. 2013). Sleep patterns are altered during pregnancy and lactation and there is no conclusive evidence about when and if the sleep patterns return to the baseline levels (Lee 1998). Postpartum depression is a crippling illness for mothers, that could be as prevalent as 30% depending on the criteria used (Brummelte and Galea 2016). All those problems have poorly-understood causes, what makes studies focused on the brain processes of lactation and weaning particularly important to start unveiling the mechanisms that underlie those conditions.

Therefore, the results of the presented dissertations should be of high interest to all professionals in the medical field that work with women's health, especially those in the obstetrics field. Our work also fulfills a broader role of highlighting particular processes that occur in the female brain, an important step to correct the chronic underrepresentation of female subjects in research (Prendergast et al. 2014). Finally, our results should be of interest to the pharmacy industry, as we have identified a group of individuals (mothers who bottle feed) as under increased risk of inefficient brain restoration of circuits controlling sleep architecture and awareness, and we identified the neurochemical group that may be targeted for pharmacological intervention to restore the normal brain function. Clinical trials could be performed comparing the efficiency of orexin antagonism-based medication (Dubey et al. 2015) against other types of medication used in the treatment of insomnia in women in the postpartum period. Those results could then be used to inform public policies about the treatment of sleep disturbances in adult women.

Regarding the innovation of the presented results, this work can be considered innovation as it tackles a poorly-explored experimental model: the weaning brain. While most works investigated the mother physiology and behavior a few days after birth, only a few works have investigated what happens

to the dam body as lactation comes to an end. This has direct market consequences, as medical products directed to the mother's health after delivery are minimal in comparison to those marketed for mothers during gestation or to the health of the babies. An example of this is the lack of any medication to target postpartum depression, the most common complication of childbearing, even though it is believed that postpartum depression shares only a part of its etiology with other depression disorders (Wisner et al. 2002).

To conclude, this dissertation is of relevance not only to the academic field, but also to the medical field of obstetrics and, particularly, of postpartum health. It may also lead to further research into the targeting of orexin for the treatment of sleep disorders in mothers, what could help inform public policies of women's health. We believe our results may have an important positive impact for society as a whole.

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