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www.elsevier.com/locate/ejphar

PII: S0014-2999(18)30345-5

DOI: https://doi.org/10.1016/j.ejphar.2018.06.013

Reference: EJP71843

To appear in: European Journal of Pharmacology

Received date: 15 September 2017

Revised date: 1 June 2018 Accepted date: 7 June 2018

Cite this article as: Manuella da L. D. Barros, Raul Manhães-de-Castro, Daniele T. Alves, Omar Guzmán Quevedo, Ana Elisa Toscano, Alexandre Bonnin and Ligia Galindo, Long term effects of neonatal exposure to fluoxetine on energy balance: a systematic review of experimental studies, *European Journal of Pharmacology*, https://doi.org/10.1016/j.ejphar.2018.06.013

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### **ACCEPTED MANUSCRIPT**

## Long term effects of neonatal exposure to fluoxetine on energy balance: a systematic review of experimental studies.

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#### **Abstract**

Serotonin exerts a modulating function on the development of the central nervous system, including hypothalamic circuits controlling feeding behavior and energy expenditure. Based on the developmental plasticity theory, early disturbances of synaptic availability of serotonin may promote phenotypic adaptations and late disorders of energy balance regulation leading to obesity and associated diseases. The aim of this systematic review is to determine the effects of pharmacological neonatal inhibition of serotonin reuptake by fluoxetine, on parameters related to feeding behavior and energy balance. Literature searches were performed in Medline/PubMed and Lilacs databases, out of which 9,726 studies were found. Using predefined protocol and registered on CAMARADES website, 23 studies were included for qualitative synthesis. The internal validity was assessed using the SYRCLE's risk of bias toll. Kappa index was also measured for analyzing the concordance between the reviewers. In addition, the PRISMA statement was used for reporting this systematic review. Most of the included studies demonstrated that neonatal serotonin reuptake inhibition is associated with long term reduced body weight, lower fat mass and higher thermogenic capacity and mitochondrial oxygen consumption in key metabolic tissues. Therefore, experimental fluoxetine exposure during neonatal development may promote long-term changes related to energy balance associated with a lean phenotype.

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