Prenatal exposure to anti-müllerian hormone reprograms the fetus and induces polycystic ovary syndrome (PCOS) in adulthood

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Abstract

Polycystic ovary syndrome (PCOS) is the main cause of female infertility worldwide with high comorbidity and economic burden. Most women with PCOS exhibit higher levels of circulating luteinizing hormone (LH), suggestive of heightened gonadotropin-releasing hormone (GnRH) release. Moreover, women with PCOS exhibit 2-3x higher levels of circulating Anti-Müllerian Hormone (AMH) as compared to healthy women and it is unclear if the elevation of AMH is a bystander effect or is driving the condition. While the exact origin of PCOS is unknown, data from clinical and animal studies suggest that it may originate in utero and those environmental factors, such as hormonal imbalances during fetal life, could be important for etiological factors of PCOS.

Here, we measured AMH in a cohort of pregnant women with PCOS and control women revealing that AMH is significantly more elevated in the former group versus the latter. We then treated pregnant mice with AMH to model our findings in the clinic and followed the neuroendocrine phenotype of their female progeny postnatally. This new preclinical PCOS model showed that fetal exposure to excess AMH impacts the hypothalamic-pituitary-gonadal axis and induces the acquisition of PCOS-like traits in the offspring. Prenatal AMH-treated (PAMH) female offspring recapitulated the major PCOS cardinal neuroendocrine reproductive features, namely hyperandrogenism, elevation in LH pulse frequency and oligo-anovulation, and a persistent rise in the GnRH neuronal firing activity in adulthood. Collectively, our results challenge the concept of PCOS originating in utero and appear to consolidate the role of AMH as a trigger of the pathogenesis and highlight a critical role for GnRH in the neuroendocrine dysfunctions of this disease, while offering a new potential therapeutic avenue to treat the condition during adulthood.

Biography:

Nour El Houda Mimouni completed her PhD in Neuroscience from the Faculty of Medicine of Lille (France) under the supervision of Dr.Paolo Giacobini and she currently conducting her research in the PCOS field as a Postdoctoral fellow Researcher in the development and Plasticity of the Neuroendocrine brain at the Lille Neuroscience and Cognition Research Center.
Nour was elected as the Young Researchers representative in the French Society of Neuroendocrinology in France (2019-2022) and is now a part of its scientific committee.
Nour recently joined the early Career SIG of the AE-PCOS society.

Speaker Publications:

1.Prenatal exposure to anti-müllerian hormone reprograms the fetus and induces polycystic ovary syndrome (PCOS) in adulthood» B.Tata*, Nour El Houda Mimouni* et al. (Nature Medicine 2018).
2. Defective Anti-Müllerian Hormone Signalling Disrupts GnRH Neuron Development and Underlies Congenital Hypogonadotropic Hypogonadism » SA. Malone, GA. Papadakis, A.Messina, NEHMimouni et al. (eLife 2019).

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