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## Session 13: Neurobehavioral disorders

### Alterations of Neurodevelopment of Children *in utero* Exposed to Synthetic Progestogens

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#### Abstract {230 words}

*In utero* exposed children to synthetic progestins present the same neuropsychiatric disorders [Schizophrenia, Bipolarity, Anxiety, Severe depression, Suicides, Suicide attempts, Eating disorders (1, 2) and Autistic Spectrum Disorders (ASD) (3)] as those who have been exposed to synthetic estrogens [Diethylstilbestrol (DES), 17  $\alpha$ -Ethinylestradiol]. These CNS alterations occur during neurodevelopment through several mechanisms such as, among other things, an epigenetic modulation. In this mechanism, some genes affecting neurodevelopment are hypermethylated such as *ADAM TS9 gene* promotor, involved in the control of reproductive organs and in the development of CNS and *ZFP57 gene*, a transcription regulator affecting many genes implicated in neurodevelopment (4). Besides, progestins are known to induce GABA\*receptor dysfunction activation before birth (5), the promotor of the Estrogen Receptor gene (ER $\beta$ ) being hypermethylated (6). Molecular receptors of ER $\beta$  are located in the brain at the level of amygdalia and play an important role in this mechanism (6). Furthermore, a multigenerational effect is strongly suspected of being induced, via an epigenetic mechanism. Several authors have described multigenerational effects after *in utero* exposure to DES both on a somatic (endometriosis) (7), psychiatric (8) and autistic levels (9). Although some progestins have been banned from the market, even recently such as 17  $\alpha$ -hydroxymethyl caproate, others are not: from our work we highlight that caution should be taken with regard to the use of these progestins during pregnancy and even outside these periods (COCs)\*\*.

1. MO Soyer-Gobillard et al. *Gynecol Endocrinol* 35 (2019), 247-250. 2. MO Soyer-Gobillard et al. *in* : P.V. Martin C., Rajendram R., (Ed.), *Factors affecting Neurodevelopment*, Academic Press, London (2021) pp. 395-408. 3. Li et al. (2018) *Frontiers in Psychiatry*, 9, 1 –12. doi:10.3389/fpsy.2018.00611. 4. F Rivollier et al., (2017) *PLoS One* 12 (4) 1-12. 5. MJ Schmidt, K Mirnics (2014) *Neuropsychopharmacology Reviews*, 1-17. 6. Zhou et al. (2017) *Molecular Autism*, 8, 1–16. 7. MA Kioumourtzoglou et al. (2018) *JAMA Pediatr.* 172(7): 670-677. 8. MO Soyer-Gobillard et al., (2021) *Int J Environ Res Public Health*, 18 (19): 9965. 9. MO Soyer-Gobillard et al., (2022) *Front Endocrinol (Lausanne)*. 13 : 1034959. \*Gamma-aminobutyric acid, a neurotransmitter. \*\*Combined Oral Contraceptives.

### **Biography: {103 words}**

Honorary Emeritus Research Director at the CNRS\*, Doctor ès Science in Cell Biology (PH.D.), she founded and directed for many years the Department of Cellular and Molecular Biology of the Observatory of Banyuls-sur-mer (Sorbonne University, Paris 6, France). Winner of several scientific awards, she has published more than 200 articles in international peer-reviewed journals. Member of the College of Clinical Project Reviewers Inserm, she is also President of the National Patient Family Association HHORAGES-France (Stop Artificial HORMones for Pregnancy), and author of numerous publications in this new area of synthetic hormones in collaboration with Endocrinology and Psychiatry Lab. of the University of Montpellier.

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### **Head Shot Photograph**

