**Identification of an orphan GPCR, GPR151, as a target of BPA exposure and a potential actor of the GnRH network**

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Bisphenol A (BPA) is a ubiquitous endocrine disruptor chemical that has been shown to alter pubertal timing. Recently, we demonstrated that an early postnatal exposure to BPA disturbed the neuroendocrine sexual maturation in female rat through altered GABAergic neurotransmission. A dose of 25 ng/kg/d induced a slowing down of GnRH secretion frequency while acceleration of GnRH secretion was measured after a dose of 5 mg/kg/d at PND 20. The results of an RNAsequencing analysis of mediobasal hypothalamus RNAs revealed that several genes were affected by these two doses of BPA (Franssen et al, 2016). Now, we show that GPR151 is the gene most affected and in an opposite way by the 2 doses since mRNA levels increase after the low dose of BPA and decrease after the high dose. We describe for the first time that this orphan GPCR sharing sequence homology with GPR54 is expressed in the fibers of GnRH neurons in the median eminence of pubertal and adult female rats. In this region, GPR151 mRNA expression increases throughout postnatal development. Because β-arrestin is responsible for GPCR internalization after GPCR activation by a ligand, we analysed the capacity of several neuropeptides (kisspeptin, galanin and RFRP3) to activate the receptor and induce the recruitment of β-arrestin 2 using a β-arrestin recruitment assay. None of these peptides induced this recruitment but we identified a high constitutive activity for GPR151.Using a GnRH cell line (GnV3 cells), that expresses GPR151, we highlight a potential role for this receptor in the mechanisms of GnRH release. The overexpression of GPR151 in GnV3 cells leads to an increase of GnRH release from these cells.  
In conclusion, early postnatal exposure to BPA altered the onset of puberty in female rats through disruption of the GnRH release. This effect could involve changes in expression of a potential new regulator of the GnRH network, GPR151.