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Effects of environment on brain sexual differentiation: role of steroids and of endocrine disruptors

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Several environmental substances (synthetic or natural) are able to impact endocrine function (endocrine disrupting chemicals, EDCs) and, therefore, they may have long-term consequences, especially if exposure occurs during embryonic development. Most of EDCs are agonists or antagonists of androgen or estrogen receptors, therefore they may interfere with brain and behavior sexual differentiation.

We present here data collected in our laboratory on two widely used animal models: the mouse and the Japanese quail. In the quail, we investigated the effect of several EDCs [diethylstilbestrol (DES), genistein or ethylene,1,1-dichloro-2,2-bis-p-chlorophenyl (DDE)] administered in eggs on the differentiation of male sexual behavior and of the parvocellular sexually dimorphic vasotocin system. In the mouse we investigated the effects of perinatal exposure to bisphenol A (BPA) or genistein on the sexual differentiation of NO producing system and of the kisspeptin system. We investigated also the organizational effects of these EDCs on sexual, social, and explorative behaviors. Our data suggest that precocious exposure to EDCs through maternal administration (in mice) or in egg deposition (in quail) may permanently alter some sexually dimorphic circuits and influence in a gender-oriented way some behaviors. In particular, the timing of exposure to EDCs is a critical factor, such that the effects of a particular EDC will vary over the lifecycle of the animal as well as across species and phyla. Therefore, exposure to the estrogenic chemicals during embryonic development has consequences beyond impaired function of the reproductive axis. This makes it very challenging to evaluate the short and long-term effects of EDCs. These compounds are therefore, in addition to gonadal steroids and neurosteroids, a third player within the nervous system for its development and differentiation. The evolutionary implications of having them in the normal food supply for certain human populations (i.e. phytoestrogen derivatives from soy), as well as for wild and farm animals should stimulate a wide discussion about their beneficial or adverse role.

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