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Ten Most Important Things to Know About Caring for Transgender Patients

To the Editor:

Chipkin and Kim[1] conducted an excellent review on issues related to transgender persons, particularly in understanding the pathophysiologic complications of cross-sex hormone therapy. Chipkin and Kim[1] stated that transgender persons who usually take cross-sex hormone therapy to optimize their gender congruence may experience some mild side effects from estrogenic or androgenic cross-hormone therapy to achieve feminine features or a muscular appearance.[1] However, the consequences of cross-hormone use in transgender persons may not be limited to phenotypic changes.

Androgen and estrogen receptors are widely distributed in the brain, indicating that sex hormones play important roles, and in interaction with neurotrophic factors, in maintaining neuronal survival, development, and synaptic plasticity.[2] For example, the number of neurons in the brainstem nuclei XI–X in the male or female frog Xenopus can be modified with exogenous sexual hormone treatment: the number increased by androgen while decreased by estrogen.[3] In healthy elderly men, sexual hormones can change not only the brain morphology[4] but also the cognitive functions,[5] supporting the notion that androgen and estrogen play different roles in the central nervous system during development and even after maturation.

In human adult transwomen (male to female), antiandrogen cyproterone plus estrogen treatment decreases brain volume, whereas androgen treatment in transmen (female to male) increases total brain and hypothalamus volume.[6] Of note, production of sex hormones is dynamically regulated via a feedback of hormones on the hypothalamus–pituitary–gonadal axis. If the feedback is interrupted or an aberrant hormone level occurs, it may alter the functional status of hormone-sensitive neurons through hormone receptor–mediated intracellular signal transductions. Administration of estrogen plus progestin to aged postmenopausal women increases their risk for dementia, despite the earlier reports of neuroprotective actions.[7] Taken together, knowledge of the effects of cross-hormone use on the central nervous system is far from being understood. Changing your sex may change your brain.[6]

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