Social behavior of male mice needs estrogen receptor activation in brain region at puberty

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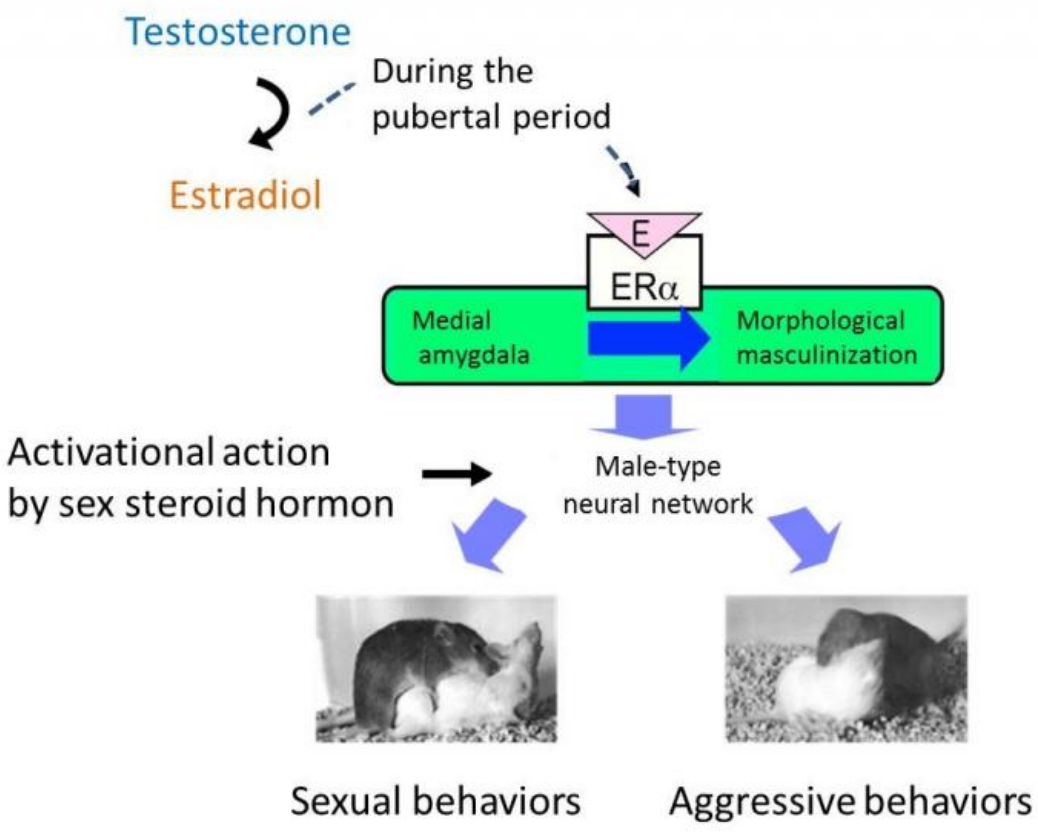

The action of medial amygdala during the pubertal period

Social behavior of male mice needs estrogen receptor activation in brain region at puberty. Credit: University of Tsukuba

A team of researchers led by Dr. Sonoko Ogawa at Tsukuba University revealed that expression of an estrogen receptor (ERα) in the medial amygdala (MeA) of the limbic system during puberty is essential for the testosterone-regulated expression of adult male social behaviors. ERα inhibition in the MeA before puberty led to a reduction in both sexual and aggressive behaviors of adult male mice. These findings further our understanding of the neural and hormonal mechanisms underlying adolescent behavioral development.

A research team led by Dr. Sonoko Ogawa at the University of Tsukuba showed that activation of an estrogen receptor in a region of the limbic system during the pubertal period is needed for adult mice to express typical male social behaviors.

Testosterone plays a major role in controlling behavior associated with masculinity in many mammals. In early development, testosterone is involved in the formation and organization of "male" neural pathways, on which it then acts to regulate various behaviors in adulthood. Testosterone binds and activates estrogen receptor alpha (ERα) after it is converted into estradiol by a process known as aromatization. ERα is known to function differently in different parts of the adult mouse brain. Inhibition of ERα in the medial preoptic area (MPOA) of the adult hypothalamus reduces sexual behavior but has no effect on aggressive behavior, while neither behavior is affected by ERα inhibition in the medial amygdala (MeA) of the adult animal. However, until now it was unclear whether ERα is involved in the organizational action of testosterone on the formation of neuronal circuitry for male social behavior during puberty. Researchers at the University of Tsukuba have shown that inhibiting ERα in the MeA before puberty in male mice reduces both sexual and aggressive behavior in adults. In contrast, the effects of ERα knockdown in the MPOA before puberty did not differ from knockdown effects in adulthood. The study was reported in *Proceedings of the National Academy of Sciences* of the United States of

America.

Behavioral responses to sexually receptive females such as mounting, and toward intruder males such as biting and attacks, were recorded in adult mice. The reduction of both sexual and aggressive behavior by ERα silencing in the MeA before puberty but not in adults suggests the importance of the receptor in this location during puberty. "ERα knockdown in the MeA may even have affected the onset of puberty itself", first author Dr. Kazuhiro Sano says. "This contrasts with the silencing of ERα in the MPOA, which reduced sexual but not aggressive behavior in mice, regardless of the time of knockdown treatment." These findings suggest that ERα gene expression in the MPOA does not control male aggression through either the organizational role of testosterone at puberty, or its regulatory role in adulthood.

To understand why ERα silencing in different areas of the brain had varying effects, the team examined MeA cells. They found that neuronal cells were greatly reduced in MeA in which ERα expression had been inhibited before puberty. "ERα in the MeA seems to be necessary for testosterone to masculinize the neural circuitry for social behavior during puberty", corresponding author Dr. Sonoko Ogawa explains. "If this masculinization is incomplete, social signals that enable adults to express male social behavior may not function correctly."

More information: Kazuhiro Sano et al. Pubertal activation of estrogen receptor α in the medial amygdala is essential for the full expression of male social behavior in mice, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1524907113

Provided by University of Tsukuba