Discovery of mechanism by which sex hormone regulates aggressive behavior

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A group led by Professor Kazuyoshi Tsutsui and Research Associate Takayoshi Ubuka, of the Waseda University Center for Advanced Biomedical Sciences, has discovered a hormonal mechanism for controlling aggressiveness in male birds.

Male aggressiveness has long been thought to depend on androgen, a male sex hormone produced in the testes. However, previous research suggested that a synthetic enzyme (aromatase) can convert androgen into female sex hormone (estrogen) in the brain and regulate male aggressiveness.

In 2000, Professor Tsutsui et al. discovered a new hypothalamic hormone (gonadotropin-inhibitory hormone, GnIH; a type of neuropeptide) in the brain which inhibits reproduction. Later, Ubuka et al. demonstrated that GnIH can inhibit aggressive behavior (*PLoS ONE* 2012).

The current research, in order to understand the mechanism of GnIH inhibiting aggressiveness, involved a series of experiments using quail, an aggressive species of bird, as a model. When GnIH was injected into a male's brain, activity of aromatase was increased, and the quantity of estrogen in the brain was greatly increased.

Next, when highly concentrated estrogen was injected, aggressiveness of the male quail was greatly decreased. Further, it became clear that neurons which synthesize estrogen have the receptor for GnIH.

This research shows that GnIH acts on the neurons which synthesize estrogen, to greatly increase production of estrogen and greatly decrease aggressiveness in male quail. Hence it is thought that when GnIH causes an extreme increase in estrogen synthesis, this creates an excess of estrogen in the brain and curbs male aggressiveness.

This research has explained a mechanism of regulating aggressiveness. Abnormally high aggressiveness is a major cause of instability in human society. This research provides a model for explaining behavior of quail, an aggressive bird species, but future work, by looking for a similar mechanism in humans, may lead to a method for regulating spikes in aggressiveness in humans, and thereby contribute to peace and order in society.

More information: "Hypothalamic inhibition of socio-sexual behaviour by increasing neuroestrogen synthesis." Takayoshi Ubuka, Shogo Haraguchi, Yasuko Tobari, Misato Narihiro, Kei Ishikawa, et al. *Nature Communications* 5, Article number: 3061 DOI: 10.1038/ncomms4061. Received 20 September 2013 Accepted 03 December 2013 Published 16 January 2014

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