

Sex hormones may play a part in autism

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Dr. Anilkumar Pillai, MCG neuroscientist and corresponding author of the study in *Molecular Autism*. Credit: Phil Jones

Higher rates of Autism Spectrum Disorders in males than females may be related to changes in the brain's estrogen signalling, according to research published in the open access journal *Molecular Autism*.

The study examined the brains of people that had Autism Spectrum Disorders compared to controls, and found that they are linked with far lower levels of a key estrogen receptor and other estrogen-related proteins. Because of the small group size, these results indicate an exciting avenue for further research, rather than confirming a role for

altered estrogen signalling in Autism Spectrum Disorders.

Anilkumar Pillai, lead author, says: "Our study is the first indicator that estrogen receptors in the brain of Autism Spectrum Disorder patients may be different to controls. Though this suggests a possible reason for the gender bias, we still need to determine what causes the reduced production of estrogen-related proteins."

Autism Spectrum Disorders are a group of disorders that affect brain development, and are commonly recognized by impaired social interaction, verbal and non-verbal communication, and restricted and repetitive behavior. The disorders appear to have a genetic basis and are around four times more common in men than in women. Autism Spectrum Disorders have been associated with higher levels of the sex hormone testosterone, but whether there is a relationship between the disorders and estrogen signalling was not known.

A group of researchers from Georgia Regents University measured the expression of proteins involved in the estrogen signalling pathway in brain tissue from 13 people that had Autism Spectrum Disorders and 13 controls. The low numbers involved in the study are because brain tissue for experimental use from individuals that had Autism spectrum Disorders is quite scarce. They looked for levels of ER β - an estrogen receptor molecule, and aromatase, an enzyme which converts testosterone to estradiol, the most potent estrogen.

They found 35% less ER β mRNA and 38% less aromatase mRNA in autistic <u>brain tissue</u> in comparison with controls. They also found much less of the mRNA of <u>estrogen receptor</u> co-factors SRC1, CBP and P/CAF - 34%, 77% and 52% respectively. The lower levels of estrogen receptors and aromatase could lead to reduced conversion of testosterone to estradiol, resulting in increased levels of testosterone.

Anilkumar Pillai says "It is worth looking at whether drugs which modulate estrogen reception, but do not cause feminization, could allow for the long-term treatment of male patients with Autism Spectrum Disorders. Current treatment involves the use of antipsychotics, which has long been a major concern as these patients are typically still in a stage of life where brain development is very rapid. However, additional studies are needed to test the <u>estrogen</u> mechanism."

More information: Dysregulation of Estrogen Receptor beta (ERbeta), Aromatase (CYP19A1) and ER Co-activators in the middle frontal gyrus of autism spectrum disorder subjects, Amanda Crider, Roshni Thakkar, Anthony o Ahmed and Anilkumar Pillai, *Molecular Autism* 2014, 5: 46. DOI: 10.1186/2040-2392-5-46

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