# Sex steroids and social behavior: From mouse to human

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Sara Karlsson

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I. **Sara Karlsson,** Kaltrina Haziri, Evelyn Hansson, Petronella Kattunen, Lars Westberg. Effects of sex and gonadectomy on social investigation and social recognition in mice. *BMC Neuroscience 16(1):83 (2015).*

II. **Sara Karlsson,** Erik Studer, Petronella Kettunen, Lars Westberg. Neural androgen receptors modulate gene expression and social recognition but not social investigation. *Frontiers Behavioral Neuroscience 10:41 (2016).*

III. Anna Zettergren, **Sara Karlsson,** Erik Studer, Anna Sarvimäki, Petronella Kettunen, Annika Torsell, Catarina Sihlbom, Lars Westberg. Proteomic analyses of limbic regions in neonatal male, female and androgen receptor knockout mice. *Submitted.*

IV. **Sara Karlsson,** Susanne Henningson, Daniel Hovey, Anna Zettergren, Lina Jonsson, Diana Sanchez Cortes, Jonas Melke, Petri Laukka, Håkan Fischer, Lars Westberg. Social memory associated with estrogen receptor polymorphisms in women. *Social Cognitive Affective Neuroscience (2016).*

V. Anna Zettergren, **Sara Karlsson,** Daniel Hovey, Lina Jonsson, Jonas Melke, Henrik Anckarsäter, Paul Lichtenstein, Sebastian Lundström, Lars Westberg. Further investigations of the relation between polymorphisms in the sex steroid related genes and autistic-like traits. *Psychoneuroendocrinology 68:1-5 (2016).*

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UNIVERSITY OF GOTHENBURG

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Sara Karlsson

Department of Pharmacology, Institute of Neuroscience and Physiology,
Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

## ABSTRACT

Social behavior is a classification of various behaviors such as sexual behavior, aggressive behavior, social memory and sociability. These behaviors are under the regulation of the brain, and the sex steroids influence important brain regions that control these behaviors in both humans and other animals. To behave and respond adequately in social situations is crucial for interacting with others in an appropriate way. Several disorders, e.g. autism spectrum disorders (ASD), display deficits in social abilities and, interestingly, show differences between females and males in prevalence and symptoms. Moreover, testosterone is hypothesized to be one of the causative factors behind the etiology of ASD. Both the androgen and estrogen receptors are of known importance for sexually dimorphic social behaviors such as sexual and aggressive behaviors. Furthermore, estrogen receptors are essential for social memory in rodents, and human studies show a female bias towards better social memory. Less is known about the role of androgen receptors.

The aims of this thesis were to elucidate if sex, sex steroids and the androgen receptor are involved in social memory and sociability in mice, if genes and proteins in brain regions regulated by sex steroids, with known importance for social behavior, show sexual dimorphisms or are regulated by androgen receptors, and if genetic variations in sex steroid-related genes are involved in social memory and/or autistic-like traits in human.

The results show that a) testosterone is not crucial for social memory or sociability but for the persistence of social investigation, b) estrogen is importance for social memory but not for sociability, c) only when the conspecifics were male did the androgen receptor appear to be involved in social memory, d) a small number of genes involved in sex steroid synthesis, were regulated by the androgen receptor but e.g. the oxytocin receptor show androgen receptor dependant sexual dimorphic expression, e) proteins expressed in postnatal day 8 old mice did not show great differences between the sexes, or between males with or without the androgen receptor, f) genetic variations in the estrogen receptors were associated with better social memory in women, and g) genetic variations in the transport protein of sex steroids were associated with language disabilities, specifically in boys.
The main findings presented in this thesis are thus that sex steroids are implicated in different manners in sociability and social memory in mice, and that genetic variation in sex steroid-related genes are associated with social abilities in humans.

**Keywords**: Social memory, sociability, androgen receptor, sex steroids, genetic variations

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