



**Karolinska  
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**Department of Women's and Children's Health**

**TESTOSTERONE AND ESTROGEN TREATMENT  
IN POSTMENOPAUSAL WOMEN –  
ASPECTS ON BEHAVIOR AND BRAIN FUNCTION**

**AKADEMISK AVHANDLING**

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# ABSTRACT

The human brain can be regarded as a target organ for sex steroid hormones. Hormones exert their influence via different pathways and sex steroid receptors are widely distributed within the brain. Several studies suggest gender differences in behavior and cognitive function and have stimulated research on the role of testosterone and estrogen. The overall aims of this thesis were to explore eventual effects of sex hormone treatment on certain aspects of behavior and brain function in postmenopausal women.

A total of two hundred naturally postmenopausal women were recruited to four weeks of treatment with either testosterone undecanoate 40 mg/day, estradiol valerate 2 mg/day or placebo in a randomized trial. At the end of treatment, all women were tested to evaluate economic behavior (altruism, reciprocal fairness, trust, trustworthiness, risk aversion, risk investment, risk assessment) and cognitive function (verbal memory, verbal fluency, spatial ability). Blood samples were collected at baseline and after four weeks and analyzed for estradiol, testosterone, androstenediol glucuronide, oxytocin, sex hormone-binding globulin and insulin-like growth factor I.

Treatment with testosterone or estrogen had no significant influence on economic behavior and cognitive function. Still, significant correlations between sex hormone levels and some aspects of cognitive function were found. High estrogen levels, a high estradiol/testosterone ratio and increasing estradiol levels during estrogen treatment were all associated with lower spatial ability. It could be that a specific balance between estrogen and testosterone is required for optimal effects on spatial- and verbal abilities. Also the estrogen/testosterone ratio and a curvilinear relationship could be important.

Ten surgically postmenopausal women were treated with estrogen alone (transdermal estradiol 100µg/day) for three months and in combination with testosterone undecanoate 40 mg/day for further three months. The influence of treatment on the serotonin transporter binding potential (5-HTT BP) in specific brain areas was studied by positron emission tomography (PET) using the special ligand [11C]MADAM. Serum levels of sex hormones, mood and cognitive abilities were measured.

Treatment with estrogen alone or in combination with testosterone significantly reduced 5-HTT BPs in several cortical and limbic regions. Furthermore, hormone treatment significantly enhanced mood and cognitive abilities like letter and category fluency. These data provide novel evidence for the influence of sex steroid hormones on the serotonergic system in the human brain.

**Key words:** cognitive function, economic behavior, estrogen, positron emission tomography, postmenopausal women, serotonin transporter, testosterone