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MEETING ABSTRACT

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Changes in progesterone levels correlate with changes in subcortical brain structures in male-to-female transgender subjects after acute high-dose cross-sex hormone administration

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Background: Sex steroid hormones exert widespread effects on the brain and the body. They are involved in sexual differentiation, development and behaviour and play a pivotal role in the development and function of the central nervous system. Transgender subjects, undergoing hormone therapy, deliver a unique model to study these effects in the living human brain. Male-to-female subjects (MtF) regularly receive high-dose estradiol and anti-androgen treatment to achieve feminization of the body. Studies are scarce, but results already point towards decreases in brain volume in MtFs after acute cross-sex hormonal treatment, which was mainly observed due to increases in the ventricular system. The aim of the investigation was to corroborate these prior findings and to test whether changes in hormonal levels are correlated with changes in brain volume in subcortical brain structures.

Methods: Fourteen MtF subjects (mean age ± SD = 26.9 ± 6.1) were measured at baseline and after a period of 4 months of high-dose estradiol and anti-androgen treatment. Blood hormonal levels were assessed at each time point. Structural MRI was carried out at 3 T (Siemens Tim Trio) using a 32-channel head coil (MPRAGE, T1; 256×240 matrix, 160 slices, voxel size 1×1×1.1 mm, TE = 4.21 ms, TR = 2,300 ms; TI = 900 ms; α = 9°). Subcortical assessment of brain structures was done with FreeSurfer [1] (version 5.1.0) using the longitudinal processing stream. Subsequently, correlations were calculated for changes in hormonal levels and significant volumetric changes in subcortical structures between pre and post treatment (TP1 *vs.* TP2). Due to missing hormonal assessment, one subject had to be excluded from the correlation analysis.

Results: Blood hormonal levels of testosterone, estradiol and progesterone changed significantly after the 4-months period of estradiol and anti-androgen treatment ($p < 0.01$). While an increase in estradiol (TP1: 29.77 ± 14.42 pg/ml; TP2: 133.54 ± 121.33 pg/ml) was observed, testosterone (TP1: 5.48 ± 2.05 ng/ml; TP2: 0.97 ± 1.84 ng/ml) and progesterone (TP1: 0.76 ± 0.28 ng/ml; TP2: 0.53 ± 0.19 ng/ml) levels decreased as expected. The structural assessment of subcortical brain regions showed significant ($p < 0.05$, uncorrected) volumetric increases in the entire ventricular system and bilateral decreases in the hippocampus, amygdala and in the right caudate and putamen after the 4-months treatment period. Furthermore, changes in hormonal blood levels and changes in subcortical regions revealed that decreasing progesterone levels were associated with increases in the left ($r = 0.65$; $p = 0.02$) and right lateral ventricle ($r = 0.55$; $p = 0.05$) and the third ventricle ($r = 0.57$; $p = 0.04$) and with decreases in the right caudate ($r = 0.65$; $p = 0.02$) and hippocampus ($r = 0.63$; $p = 0.02$).

Discussion: Acute high-dose estradiol and anti-androgen treatment in MtF subjects seems to be related to volumetric gray matter decreases in the brain. We observed increases in the ventricles and decreases in several subcortical brain regions. These results are in line with prior studies, indicating decreases in gray matter volume in MtF subjects after cross-sex hormonal treatment. Furthermore, our analysis indicate that progesterone is strongly involved in this process, as changes in progesterone levels correlated with changes in subcortical brain areas.

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Reference

1. http://surfer.nmr.mgh.harvard.edu

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