Hormonal-induced resting-state functional connectivity alterations in transgender people measured with ultra-high field 7T MRI

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Background: Recent evidence indicates modulating properties of gonadal hormones on the serotonergic system. More specifically, cross-sex hormone therapy in Male-to-Female (MtF) transsexual subjects led to a significant decrease in serotonin transporter (SERT) binding in the anterior cingulate cortex (ACC) after a continuous 4 months treatment period with estradiol and anti-androgens (Kranz et al., 2015). On the other hand, studies already demonstrated sex differences in resting-state functional connectivity (rsFC) metrics, which may be related to fluctuating hormonal levels. We assessed whether these hormonal induced changes in the ACC are accompanied by changes in rsFC between the baseline measurement and a 4 months hormonal treatment interval.

Methods: The PET analysis has already been carried out and all demographics and analysis steps can be found in Kranz et al. (2015). For the rsFC analysis, a subsample of the prior study was included and consisted of 15 MtF subjects (29±6.8 years), measured before and after a 4-months period of high-dose estradiol and anti-androgen treatment. MRI measurements were conducted at 7T using a 32-channel head coil. An echo-planar imaging sequence was used (TE/TR=23/1400ms, 32 axial slices, voxel size=1.5x1.5x2mm). Resting state fMRI was acquired over the course of 6 min. Data were corrected for slice timing effects and movement, spatially normalized and smoothed in SPM8 (http://www.fil.ion.ucl.ac.uk/spm). Potentially confounding signals were removed by linear regression (white matter, cerebrospinal fluid, movement parameters) and a bandpass filter was applied. Finally, rsFC was computed using the ACC as seed region and connectivity maps were z-transformed.

Results: Comparing rsFC changes between baseline and a 4 months treatment period using the ACC as seed region we found significant increases over time during hormonal treatment (p<0.05 corrected, t=3.4, cluster size=370). Increases were detected in superior brain regions like the postcentral gyrus, precentral gyrus, the supplementary motor area, cuneus, precuneus and the superior parietal cortex. Furthermore, connectivity increases between the ACC and the right insula were found.

Conclusions: Here we could demonstrate increased rsFC metrics in MtF subjects after 4 months of high-dose estradiol and anti-androgen treatment between the ACC and widespread regions in the brain including somatosensory and motor areas as well as the insula. Hence, decreased SERT binding in the ACC was accompanied by connectivity increases in the motor network and networks related to body representation and awareness indicating hormonal induced alterations in these faculties.