OR25-4: Modulatory Effects of Estradiol on the Resting-State Functional Connectivity in Transwomen Following Gender Affirming Surgery

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The profound incongruence between sex and gender identity leads transgender individuals to seek cross-sex hormone therapy (CSHT) and gender affirming surgery (GAS). After GAS, a transient period of hypogonadism is established. Literature suggests that sex hormones exert important effects on the brain during physiologic development and aging. Also, CSHT is known to impact brain anatomy and connectivity before the completion of GAS on transgender people. However, literature evaluating the brain impact of CSHT after GAS is still sparse. Here, we aimed to investigate the impact of CSHT on the resting-state functional connectivity (rs-FC) in transwomen (male-to-female) following GAS. Seed-based and data-driven approach were complementarily employed to explore rs-FC adaptations. To test for the effects of hypogonadism correction following CSHT, eighteen post-GAS transwomen underwent a 3T functional magnetic resonance imaging (fMRI) at two time points: 30 days after CSHT washout, and 60 days following estradiol reinstitution (CSHT). Anxiety assessment and blood sample collection were conducted at both time points. First, region-of-interest to region-of-interest (ROI-to-ROI) rs-FC was explored using Principal Component Analysis. Bilateral thalamus and right caudate were defined as seeds, while the sensorimotor cortex (SMC) was defined as target, according to previous literature.[1,2] Rs-FC was compared between time points using a paired t-test. Additionally, a whole-brain data-driven approach using multivoxel pattern analysis (MVPA) was performed to generate a seed for further whole-brain seed-to-voxel analysis. All analyses were thresholded at $p < 0.05$ (two-tailed), controlled for age and anxiety changes between time points and FDR corrected for multiple comparisons. Following estradiol therapy, we found higher rs-FC between left thalamus and the bilateral SMC (p-FDRLeft=0.0027; p-FDRRight=0.0196). MPVA analysis identified a cluster within the subcallosal cortex (SubCalC) representing the greatest variability in functional activation between time-points (p[FDRcorr]=0.0017; size=91 voxels). Lastly, whole-brain seed-to-voxel analysis using the SubCalC as seed pointed out for a rs-FC decoupling between SubCalC and a region within the middle frontal cortex (p[FDRcorr]= 0.001; size= 313 voxels). In conclusion, estradiol seems to modulate rs-FC in regions engaged in cognitive[2,3], emotional[4] and sensorimotor processes[2] in transwomen following GAS. This phenomenon highlights rs-FC adaptations due to hypogonadism correction and helps to understand cognitive and emotional regulation changes occurring during hormonal adjustment.

[1]Alloway et al.,*Front Syst Neurosci*.2017;86,187-195 [2]Kenna et al.,*Neurochem Res*. 2008;34, 234-237. [3]De Simoni et al.,*Brain*.2017;141,148-164. [4]Dunlop et al.,*Am J Psychiatry*. 2018; 174,533-545. Support: CNPq.

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