Brain morphology and resting-state functional connectivity in adult women with 47,XXX

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Background: Triple X syndrome (47,XXX) is a relatively common sex chromosomal aneuploidy characterized by the presence of a supernumerary X chromosome in females and has been associated with a variable cognitive, behavioural and psychiatric phenotype. Previous studies have shown alterations in brain structure in 47,XXX particularly in childhood and adolescence. Here, we examined both subcortical and cortical brain morphology, and resting-state functional connectivity in adult women with 47,XXX.

Methods: Twenty-one women with 47,XXX and 22 age-matched healthy controls were included in this cross-sectional study. Structural T1-weighted images and resting-state functional images were acquired using a 7-Tesla Magnetic Resonance scanner. Measures of subcortical brain volumes, cortical surface area and thickness, and cortical folding were obtained and compared between groups. Resting-state functional MRI (rs-fMRI) images were analysed using independent component analysis and dual regression. Functional connectivity was compared between groups.

Results: Adults with 47,XXX showed lower volumes of the thalamus, caudate, putamen, hippocampus, nucleus accumbens and pallidum, and larger lateral ventricle volumes. Lower surface area was found in the superior frontal gyrus and superior temporal gyrus in 47,XXX participants compared to healthy controls. Altered cortical thickness and cortical folding were not present in 47,XXX. Dual regression revealed increased connectivity between voxels located in the parietal lobe and the fronto-parietal resting-state network and decreased functional connectivity between voxels located in the left frontal lobe and the default mode network in 47,XXX.

Conclusions: Results suggest that a supernumerary X chromosome in females affects subcortical and lateral ventricle volumes, and cortical surface area in adulthood. Moreover, results suggest differences in resting-state functional connectivity between 47,XXX and

healthy controls. Further research is needed to determine potential relationships between resting-state functional connectivity and clinical characteristics in 47,XXX. 47,XXX may serve as a suitable model for studying sex chromosomal influences on structural brain morphology and resting-state functional connectivity across developmental stages in order to understand neurobiological mechanisms underlying cognitive and behavioural impairments.
Keywords: 47,XXX, brain morphology, resting-state functional connectivity