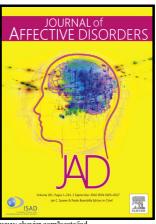
# Author's Accepted Manuscript

High levels of mitochondrial DNA are associated with adolescent brain structural hypoconnectivity and increased anxiety but not depression

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## **ACCEPTED MANUSCRIPT**

# High levels of mitochondrial DNA are associated with adolescent brain structural hypoconnectivity and increased anxiety but not depression

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\*Corresponding author: Department of Radiology & Biomedical Imaging, University of California, San Francisco, 1700 4th St., Byers Hall Suite 102, San Francisco, CA 94158. Phone: +1 415 514 4870; fax: +1 415 514 4451. Olga.Tymofiyeva@ucsf.edu Abstract

### Background:

Adolescent anxiety and depression are highly prevalent psychiatric disorders that are associated with altered molecular and neurocircuit profiles. Recently, increased mitochondrial DNA copy number (mtDNA-cn) has been found to be associated with several psychopathologies in adults, especially anxiety and depression. The associations between mtDNA-cn and anxiety and depression have not, however, been investigated in adolescents. Moreover, to date there have been no studies examining associations between mtDNA-cn and brain network alterations in mood disorders in any age group.

#### Methods:

The first aim of this study was to compare salivary mtDNA-cn between 49 depressed and/or anxious adolescents and 35 well-matched healthy controls. The second aim of this study was to identify neural correlates of mtDNA-cn derived from diffusion tensor imaging (DTI) and tractography, in the full sample of adolescents.

#### Results:

There were no diagnosis-specific alterations in mtDNA-cn. However, there was a positive correlation between mtDNA-cn and levels of anxiety, but not depression, in the full sample of adolescents. A subnetwork of connections largely corresponding to the left fronto-occipital fasciculus had significantly lower fractional anisotropy (FA) values in adolescents with higher than median mtDNA-cn.

#### **Limitations**:

Undifferentiated analysis of free and intracellular mtDNA and use of DTI-based tractography represent this study's limitations.

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