Biological Networks and the Relation Between Mitochondrial Genes and Functions with the Obsessive-Compulsive Disorder

Lemos Ribeiro, Giovanna

Obsessive-compulsive disorder (OCD) is the fourth most common psychiatric disorder. Mitochondria are organelles that exert key functions in the nervous system. This research project investigated the association between mitochondrial genes and OCD. First, a literature review was conducted. Second, two PPI (protein-protein interaction) networks were created. Both contained OCD candidate genes: the first included nuclear genes with mitochondrial functions and the second mitochondrial genes with de novo variants only in OCD patients. Network's significance was tested by randomization techniques. The genes were prioritized according to topological measures and the over-represented biological pathways identified. Until today no research has focused on investigating the role of mitochondria in OCD. In this project, both analyses resulted in a connected, significantly scale-free network. The first network presented the following over-represented pathways and central genes with mitochondrial functions: nervous system development (SDHA and TOMM70A), apoptosis (SMAC, PRODH and TRAP1), inflammation (NFKB1), oxidative stress (SMAC, PRODH and TRAP1) and glutamate metabolism (MMAA). Concerning the analysis of mitochondrial genes, only one trio was studied and RNR1, ATP6, ND4 and ND5 genes presented SNP´s only in OCD patients. This network's most expressed pathways were DNA regulation, cellular respiration and inflammation. My hypothesis is that mitochondrial functions contribute greatly to predisposition to OCD. Moreover, a disruption in the identified functions could cause a change in nervous system topology, triggering a hyper-activation of the fronto-striatal circuit and, therefore, increasing OCD risk. Future treatments should normalize those functions by focusing on mitochondria.

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