

Potential involvement of the mitochondrial unfolded protein response in depressive-like symptoms in mice

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Many evidences strongly suggest that a mitochondrial deficit is implicated in major depression. A mitochondrial deficit leads to mitochondrial stress responses, including the mitochondrial unfolded protein response (UPR_{mt}), which is associated with certain brain disorders such as spastic paraplegia and Parkinson's disease. However, there is no evidence regarding the relationship between depressive disorder and UPR_{mt}. Mice treated with chronic restraint stress showed significant depressive-like behaviors in the tail suspension and forced swim tests. In addition, the isolated brain mitochondria showed decreased oxygen consumption rate, decreased protein expressions related to oxidative phosphorylation, and increased levels of molecules associated with UPR_{mt}, such as Hspa9, Hspd1, Ubl5, Abcb10, and ClpP. The expressions of all of the UPR_{mt}-related molecules were significantly correlated with depressive-like behavior in the forced swim test. Thus, the present study is the first to reveal a relationship between the UPR_{mt} and depressive disorder, suggesting that the UPR_{mt} is a potential drug target for depressive disorders.