

Abstract

Mood disorders are serious diseases. Nevertheless, their pathophysiology is not sufficiently clarified. Biological markers that would facilitate the diagnosis or successful prediction of pharmacotherapy are still being sought. The aim of the study was to find out whether mitochondrial functions are affected by antidepressants, mood stabilizers and depression. Our research is based on recent hypotheses of mood disorders, the advanced monoamine hypothesis, the neurotrophic hypothesis, and the mitochondrial dysfunction hypothesis. We assume that impaired function of mitochondria leads to neuronal damage and can be related to the origin of mood disorders. Effects of antidepressants and mood stabilizers on mitochondrial functions can be related to their therapeutic or side effects.

In vitro effects of pharmacologically different antidepressants and mood stabilizers on the activities of mitochondrial enzymes were measured in mitochondria isolated from pig brains (*in vitro* model). Activity of monoamine oxidase (MAO) isoforms was determined radiochemically, activities of other mitochondrial enzymes were measured spectrophotometrically. Overall activity of the system of oxidative phosphorylation was measured electrochemically using high-resolution respirometry. Methods were modified to measure the same parameters in blood platelets of patients with depressive episode and healthy controls.

Though all antidepressants tested inhibited MAO activity, they differed in inhibitory potency, type of inhibition, and specificity for two isoforms. Mood stabilizers did not affect MAO. All drugs tested increased or left citrate synthase (CS) activity unchanged. Activity of electron transport chain (ETC) complexes was decreased. The most affected were complexes I and IV. While respiratory rate of mitochondria was inhibited at higher concentrations of antidepressants, it was not affected by mood stabilizers, olanzapine and ketamine.

Physiological respiration in the blood platelets of depressive patients did not differ from controls; decrease was observed after treatment with antidepressants. Maximal capacity of ETC was decreased both before and after treatment with antidepressants. Ratio of physiological respiration to maximal capacity was significantly increased before the treatment. Effects of antidepressants and mood stabilizers are comprised of marked changes in mitochondrial functions. MAO, CS, complexes I and IV, and respiratory rate of mitochondria were the most affected and are suggested as candidates in searching of new biological markers of mood disorders, targets of new antidepressants or predictors of response to pharmacotherapy.