Activities of respiratory chain complexes and citrate synthase influenced by pharmacologically different antidepressants and mood stabilizers.


Source

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Abstract

OBJECTIVE:

Mitochondrial dysfunctions, impaired bioenergetics and dysfunction of neurotrophins are included in many neurodegenerative and psychiatric diseases. We investigated in vitro effects of pharmacologically different antidepressants and mood stabilizers on mitochondrial enzymes to discover, which mitochondrial functions could be involved in pathophysiology of mood disorders.

METHODS:

In vitro effects of eight pharmacologically different antidepressants (desipramine, amitriptyline, imipramine, citalopram, venlafaxine, mirtazapine, tianeptine, and moclobemide) and three mood stabilizers (lithium, valproate, and olanzapine) on the activities of mitochondrial enzymes (citrate synthase and enzymes in electron transport chain, i.e. complexes I, II, IV) were measured in crude mitochondrial fraction isolated from pig brain.

RESULTS:

Most of the antidepressants and mood stabilizers inhibited the activities of respiratory electron transport chain complexes, complexes I and IV were the most affected. Statistically significant decrease of the complex I activity was caused by desipramine, amitriptyline, imipramine, citalopram, mirtazapine, valproate and olanzapine. Complex II was significantly inhibited only by amitriptyline, imipramine, citalopram and venlafaxine. Complex IV was significantly inhibited by all tested drugs except for
citalopram and moclobemide. Unchanged or slightly increased citrate synthase activity was observed; significant activation of the enzyme was observed after citalopram, tianeptine and olanzapine.

CONCLUSIONS:

Our results indicate that antidepressants may act generally as inhibitors of complex I and complex IV of the electron transport chain. These mitochondrial enzymes are suggested as proper candidates in searching of new biological markers of mood disorders, targets of new antidepressants or predictors of response to pharmacotherapy.

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