

Influence of drug treatment with antidepressants and antipsychotics on plasma urea levels

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Having read with great interest the article by Goto et al¹ and in order to clarify further some of the results presented in this article, especially with regard to the action of atypical antipsychotic drugs on glutamate and the glutamine to creatine ratio, it would seem appropriate to reiterate the comments made by Lozano et al in a presentation at the 55th National Congress of the Spanish Association of Hospital Pharmacists in 2010, where we proposed the likely influence of antipsychotic treatment on nitric oxide, glutamine, and glutamate levels in the brain, as a result of the reaction of nitric oxide with glutamine to yield glutamate and nitrogen gas. A summary of this research is provided as follows.

Nitric oxide is believed to have a role in the pathophysiology of schizophrenia, depression, and anxiety disorders. In this longitudinal cohort study, we measured plasma urea levels to determine the influence of antidepressant and antipsychotic treatment on nitric oxide synthase activity and tissue nitric oxide concentrations in the brain. We recruited two groups, ie, 25 patients treated with the antipsychotic risperidone for at least 6 weeks (AP group) and 25 patients treated with the antidepressant escitalopram for at least 6 weeks (AD group). Student's *t*-test was used for the statistical analysis. The mean plasma urea level in the AD group was 37.7 ± 10.5 mg/dL and in the AP group was 2.6 ± 9.2 mg/dL. The difference between the average value for plasma urea in group AP compared to that obtained for group AD was 11.1 mg/dL ($P < 0.001$).

Preclinical studies have demonstrated that inhibition of nitric oxide synthase produces anxiolytic-like and antidepressant-like behavioral effects, and that nitric oxide may modulate levels of various neurotransmitters in the central nervous system, eg, serotonin, dopamine, gamma aminobutyric acid, and glutamate. Our results suggest that nitric oxide produced by the action of nitric oxide synthase on L-arginine may react with nitrogen in the carbamoyl group on glutamine and, via enzymes with nitric oxide reductase activity, generate nitrogen gas and glutamic acid, thus changing the amount of urea formed by the action of arginase on arginine and, therefore, its concentration in blood. Thus, treatment with antidepressants or antipsychotics could alter the metabolic pathway of arginine to yield urea or nitric oxide/nitrogen gas, increasing (if AP) or decreasing (if AD) urea or nitric oxide/nitrogen gas and, secondarily, excitatory glutamic acid and/or inhibitory gamma aminobutyric acid levels via different pathways in the central nervous system.

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Disclosure

The author reports no conflicts of interest in this work.

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