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Effects of short- and long-term aripiprazole treatment on Group I mGluRs in the nucleus accumbens: comparison with haloperidol

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Abstract

The D2 receptor partial agonist, aripiprazole, has shown increased therapeutic efficacy for schizophrenia, autism and Tourette's syndrome compared to traditional antipsychotics such as the D2 receptor antagonist, haloperidol. Recent evidence suggests this superior profile may be associated with downstream effects on the glutamatergic synapses. Group 1 metabotropic glutamate receptors (mGluRs) and their endogenous modulators, Norbin and Homer1, are regulated by D2 receptor activity, particularly within the nucleus accumbens (NAc), a target region of aripiprazole and haloperidol. This study sought to evaluate the effects of aripiprazole on Group 1 mGluRs, Norbin and Homer1 in the NAc, in comparison to, haloperidol. Sprague-Dawley rats were orally administered daily doses of aripiprazole (2.25 mg/kg), haloperidol (0.3 mg/kg) or vehicle for 1- or 10-weeks. Immunoblot analyses revealed Group 1 mGluR proteins levels were not altered following 1-week and 10-week aripiprazole or haloperidol treatment, compared to vehicle treated rodents. However, 1-week aripiprazole and haloperidol treatment significantly elevated Homer1a and Norbin protein expression, respectively. After 10-weeks of treatment, aripiprazole, but not haloperidol, significantly increased Norbin expression. These findings indicate the antipsychotics, aripiprazole and haloperidol exert differential temporal effects on Norbin and Homer1 expression that may have consequences on synaptic glutamatergic transmission underlying their therapeutic profile.

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