

Abstract

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Effects of myo-inositol versus fluoxetine and imipramine pretreatments on serotonin 5HT2A and muscarinic acetylcholine receptors in human neuroblastoma cells.

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BACKGROUND: myo-Inositol (ml) is a key metabolic precursor to the phosphoinositide (PI) metabolic pathway as a key component of central G-protein coupled receptor signaling systems, including several subtypes of adrenergic, cholinergic, serotonergic and metabotropic glutamatergic receptors. High dose ml has also been shown to be clinically effective in the treatment of obsessive-compulsive disorder, as well as panic and depression, although its mechanism of action remains elusive.

OBJECTIVE: The current study aimed to investigate the possible modulatory role of ml versus fluoxetine or imipramine pretreatments on serotonin-2A receptor (5HT2A-R) and muscarinic acetylcholine receptor (mAChR) function and binding in in vitro systems.

METHODS: After pretreating human neuroblastoma cells with different concentrations of ml, fluoxetine, or imipramine, receptor function was measured by second messenger [3H]-IPx accumulation and [35S]-GTPgammaS binding to G alpha(q) protein. Total [3H]-ml uptake into cells was measured, as well as specific receptor binding to determine receptor binding after the pretreatments.

RESULTS: Results suggest that ml reduces 5HT2A-R function at the receptor-G protein level. While fluoxetine also reduced 5HT2A-R function, but to a lesser degree, imipramine increased 5HT2A-R function, which may explain why ml seems to be effective exclusively in selective serotonin reuptake inhibitor-sensitive disorders. In addition ml, and at high concentrations fluoxetine and imipramine, also reduces mAChR function. Furthermore the results suggest that the attenuating effect of ml on mAChRs is partially dependent on the PI metabolic pathway.

CONCLUSION: The data provide novel information on understanding the mechanism of action of ml in depression and related anxiety disorders and added to the evidence suggesting a role for the cholinergic system in the pathophysiology of depression.

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