

S33-01 - MODULATION OF LIGAND GATED ION CHANNELS BY ANTIDEPRESSANTS

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The classical mechanisms of action of antidepressants suggest that they act through inhibition of monoamine transporters. There is evidence that antidepressants indirectly modulate GABA-A receptors through neurosteroids. We showed that antidepressants may also directly modulate the function of the serotonin type 3 (5-HT₃) receptor in an allosteric fashion. This non-competitive inhibition of receptor function occurred with different classes of antidepressants including tricyclic antidepressants, SSRIs and NARIs. Moreover, these antidepressants were differentially accumulated in lipid rafts. Their concentrations in lipid rafts were related to their ability to allosterically modulate this ligand gated ion channel. However, lipid raft integrity was not a prerequisite for the allosteric modulation of this ion channel by antidepressants. Moreover, differential results were observed with regard to NMDA and GABA-A receptors. Our data show that the allosteric modulation of ligand gated ion channels is an underestimated pharmacological principle which challenges the concept of target specificity of antidepressants for monoamine transporters.