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Atypical antipsychotics: similarities and differences at the synaptic level

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A number of so-called atypical, or new generation, antipsychotic drugs have been introduced into clinical practice in recent years and provide significant advantages in terms of tolerability and, under some circumstances, efficacy. Like classical neuroleptics, all these newer drugs have antagonist actions at dopamine D_2 receptors in the brain. The question has been raised, therefore, of the pharmacological mechanisms which are responsible for the atypical profiles of the new drugs. In a number of cases, antagonism at the 5-HT2A subtype of serotonin receptors may be involved. However, it is clear that this activity is neither sufficient nor necessary to produce an atypical profile. Recent findings with two of the newer drugs, amisulpride and aripiprazole, have swung the spotlight back on to dopamine. Amisulpride has high affinities for dopamine D_2 and D_3 receptors without appreciable affinity for other neurotransmitter receptors. In the clinic it shows efficacy against positive and negative symptoms of schizophrenia without producing Extrapyramidal Side effects. The recently introduced antipsychotic, aripiprazole, also seems to show good clinical efficacy with few adverse effects. This drug also seems to act predominantly at dopamine receptors although a role for serotonin has yet to be completely ruled out. Explanations for the atypical clinical profiles of certain selective dopaminergic antipsychotics include selectivity for dopamine receptors in cortical and limbic brain regions, preferential activity at different dopamine receptors, partial agonist activity, and fast dissociation from dopamine receptors.