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New mechanisms of action for antipsychotic drugs J Csernansky*

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Atypical antipsychotic drugs have now become the leading drug therapy for patients with schizophrenia and other related psychotic disorders. Atypical antipsychotic drugs differ form typical antipsychotic drugs in that they are both more effective, especially for negative symptoms and cognitive deficits, and better tolerated. Perhaps the first atypical antipsychotic drug was clozapine, whose mechanism of action is complex (i.e., antagonist action at various monoamine receptors, especially serotonin receptors), and remains under investigation. For several other atypical drugs, such as risperidone, olanzapine, quetiapine and ziprasidone, their atypical characteristics are attributed to blockade of serotonin (5-HT2A) receptors as well as dopamine (D_2) receptors. Recently, aripiprazole was introduced into clinical use, and appears to have atypical properties as well. However, in the case of this drug, the atypical properties are attributed to its actions as a partial agonist at the dopamine (D₂) receptor. Aripiprazole has several clinical advantages over other antipsychotic drugs including minimal metabolic as well as neurological side-effects. Further, aripiprazole's mechanism of action is unique among both typical and atypical antipsychotic drugs, which suggests that it should is the prototype for a new class of antipsychotic drug.