

04 - Antipsychotic drugs

Antipsychotic drugs

© SPMM Course 3. Modes of therapeutic action for psychotropics

Antipsychotic drugs In general all antipsychotics act via varying degrees of D2 blockade. Atypical drugs show selectivity for D2 receptors and also show high 5HT2: D2 blocking ratio. Specific actions are listed below.

DRUG MECHANISM

Amisulpride Both D2 and D3 antagonism. Similar dose-dependent pre & postsynaptic profile to sulpride. Some degree of limbic selectivity and 5HT7 activity also noted.

Aripiprazole Partial dopamine agonist at D2. Also 5HT2A antagonist. Exhibits a Goldilocks' phenomenon -stabilising action wherein antagonising DA at sites of excessive dopamine such as mesolimbic zones while mimicking DA (agonism) at dopamine deficient zones such as mesocortical areas that are linked negative symptoms. Does not produce much change in tuberoinfundibulum where normal DA levels are expected in schizophrenia. Aripiprazole acts on both postsynaptic D2 receptors and presynaptic autoreceptors.

Asenapine D2 antagonist and serotonin 5HT2A blocker (similar to olanzapine). Has potent alpha-2 blockade effect. Sublingual; allegedly weight and prolactin-neutral. Licensed for use in mania.

Chlorpromazine, promazine The moderate antimuscarinic effect in addition to D2 blockade. Highly sedative phenothiazine drugs.

Clozapine A High ratio of 5HT2 to D2 blockade; also blocks D4 and 5HT6 receptors. Has notable alpha 1 antagonism and anticholinergic and antihistaminic properties. Weak D1 and D2 affinity. Also binds 5HT3. Proposed to have a faster dissociation rate (similar to quetiapine) hence a hit and run profile is noted.

Lurasidone D2 antagonist and serotonin 5HT2A blocker (similar to risperidone). Also has a high affinity for serotonin 5HT7; partial agonist at 5HT1A receptors. Has minimal affinity for alpha-1 (less orthostatic effect) and histamine receptors (thus may be weight neutral)

Olanzapine Atypical antipsychotic. Has high 5HT2 / D2 blockade ratio. Potent D4 blockade and 5HT6 blockade also noted. It has significant anticholinergic and some antihistaminic effects.

Paliperidone A metabolite of risperidone. Similar mechanism of action

Quetiapine Similar to clozapine - hit and run profile on D2. Compared to other atypicals it has somewhat lesser 5HT2A blockade. Significant anticholinergic effects similar to olanzapine.

Risperidone Serotonin-Dopamine Antagonist - Atypical Antipsychotic. Has high 5HT2A antagonistic property. In higher therapeutic doses can bind to D2 in a similar fashion to typicals and can lead to extrapyramidal and prolactin related side effects.

Sulpiride Pure D2 antagonist. At low doses presynaptic receptors blocked (helps negative symptoms?); above 800mg/day doses, affects postsynaptic D2 - reducing positive symptoms.

Thioridazine, pericyazine, D2 antagonists. Marked antimuscarinic effect. Less EPSEs than other typicals.

© SPMM Course pipotiazine Thioxanthenes Exhibit stereoisomerism. D2 antagonists - typical antipsychotics.

Ziprasidone Atypical antipsychotic with 5-HT2A and D2 blockade. Antagonizes 5-HT1D, 5-HT2C, D3, D4 receptors. Poor affinity for muscarinic effects; some antihistaminic property

noted. Agonistic at 5-HT_{1A}; also some serotonin and norepinephrine reuptake inhibition noted. Zolpidem Atypical antipsychotic with 5HT_{2A}, 5HT_{2C}, D₁, D₂, D₃, D₄ antagonism. Potent noradrenaline reuptake inhibitor. Potent antihistaminic activity and some NMDA antagonism.

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