Antipsychotics: Mechanisms underlying clinical response and side-effects and novel treatment approaches based on pathophysiology

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This shows elevated striatal dopamine synthesis and release capacity in dorsal regions of the striatum underlies the positive symptoms of psychosis and suggests reduced [dopamine release](https://www.sciencedirect.com/topics/neuroscience/dopamine-release" \o "Learn more about dopamine release from ScienceDirect's AI-generated Topic Pages) in cortical regions contributes to cognitive and negative symptom

Current drugs act downstream of the major dopamine abnormalities and may worsen cortical dopamine function. GABAergic and glutamatergic regulation of dopamine neurons

New approaches include targeting dopamine synthesis and capacity, autoreceptors, trace-amine receptors and other mechanisms.

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Non-dopmaminergic approaches such as those addressing inflammation may prove to be disease modifying.

Dopamine synthesis in the striatum = postive symptoms,

Reduced dopamine release in cortical regions contributes to cognitive and negative symptoms.

[Schizophrenia](https://www.sciencedirect.com/topics/neuroscience/dementia-praecox) is a common [mental disorder](https://www.sciencedirect.com/topics/neuroscience/psychopathology" \o "Learn more about mental disorder from ScienceDirect's AI-generated Topic Pages) characterised by positive symptoms, such as delusions and hallucinations, negative symptoms such as avolition and social withdrawal, and [cognitive impairments](https://www.sciencedirect.com/topics/neuroscience/cognitive-disorders" \o "Learn more about cognitive impairments from ScienceDirect's AI-generated Topic Pages) ([Revier et al., 2015](https://www.sciencedirect.com/science/article/pii/S002839081930262X?via%3Dihub" \l "bib287)). It typically presents in late adolescence to early adulthood, starting with a prodromal phase of subtle changes in thinking and behaviour ([Howes and Murray, 2014](https://www.sciencedirect.com/science/article/pii/S002839081930262X?via%3Dihub" \l "bib125)).

Treatment resistance (Howes et al, 2017)

[Antipsychotic](https://www.sciencedirect.com/topics/neuroscience/antipsychotic) drugs are effective in treating the acute manifestations of the illness and in reducing the risk of relapse ([Leucht et al., 2017](https://www.sciencedirect.com/science/article/pii/S002839081930262X?via%3Dihub" \l "bib192)),

1. Common effects: monoaminergic dysfunction in scz – core to understanding the mechanism of action of AP
2. Receptor binding profiles of commonly used AP

But – imaging studies show an increase in striatal D2/3 receptors in some patients, but no signif. Increase in AP naïve patients (in mea-analyses., and no clear change in cortical dopamine D2/3.