

12 - 12. Some clinical implications

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β ADRENOCEPTOR Chronic antidepressant treatment induces a reduction in β adrenoreceptor density around 2 weeks after starting antidepressants; this correlates with therapeutic effects.

Unmedicated suicide victims show higher density of β adrenoreceptors. β blockade can reduce peripheral features of anxiety driven by sympathetic overdrive. **5HT & DEPRESSION** An increased density of 5HT₂ binding sites has been shown in post mortem studies of depressed / suicidal patients. The increase in 5HT_{2A} receptors is most prominent in dorsolateral prefrontal cortex and in platelets of medication naïve patients. A reduction in 5HT_{1A} receptors has also been noted in cortex

Long-term antidepressant treatment has been shown to reduce 5HT₂ receptors and increase 5HT_{1A} function. But these changes may not be causative of antidepressant action as they predate any clinical response to antidepressant therapy

Most directly acting 5HT_{1A} agonists have poor antidepressant activity.

Ach & LEWY BODY DEMENTIA Brain acetylcholine levels are reduced in DLB similar to Alzheimer's. Cortical choline acetyl transferase (ChAT) is reduced to a greater extent (85%) in patients with hallucinations in Lewy body dementia than in those without hallucinations (50%). This may partially explain the altered sleep-wake patterns seen in DLB and also the response of hallucinations to acetylcholinesterase inhibitors **ABERRANT SALIENCE** Kapur proposed that in the normal individual, the role of mesolimbic dopamine is to attach significance or 'salience' to an external stimulus, or an internal thought. This converts a neutral piece of information into an attention grabbing one (Kapur, 2003).

In acute psychosis where hyperdopaminergic state is noted in mesolimbic system, insignificant events and perceptions receive inappropriate salience leading to delusional elaborations.

Antipsychotics are claimed to "dampen the salience" of these abnormal experiences - do not erase the symptoms - but provide the platform for a process of psychological resolution.

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□ <http://omim.org/entry/107930> □ Kapur, S. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am J Psychiatry* 2003; 160 □ Angelucci et al. BDNF in schizophrenia, depression and corresponding animal models. *Molecular Psychiatry* (2005) 10, 345-352 □ Artigas F. Serotonin receptors involved in antidepressant effects. *Pharmacology & Therapeutics*, 2013; 119-31

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Revision #1

Created 2026-01-04 20:03:06 UTC by Omar Ayman

Updated 2026-01-04 20:03:06 UTC by Omar Ayman