09 - Anti dementia drugs

Anti dementia drugs

© SPMM Course Anti dementia drugs DRUG MECHANISM Donepezil, Galantamine, Rivastigmine Cholinesterase Inhibitors. The act by inhibiting acetyl cholinesterase enzyme that breaks down acetylcholine centrally. Rivastigmine inhibits both the acetyl and butylcholinesterase while donepezil and galantamine are acetyl specific. Galantamine also has nicotine agonistic properties. Memantine Blockade of N-methyl-d-aspartate (NMDA) glutamate receptors. Unlike ketamine, which is a high-affinity noncompetitive blocker, memantine is a non-competitive blocker with low affinity and binds only to actively open NMDA channels. Its receptor dissociation rate is relatively fast, and so it does not accumulate and interfere with normal NMDA activity. Acetylcholine is inactivated by both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Cholinesterase inhibitors increase the amount of ACh available through inhibition of these enzymes. An acetylcholinesterase inhibitor can work at either of two sites on AChE, an ionic subsite or a catalytic esteratic subsite; Tacrine and donepezil act at the ionic while physostigmine and rivastigmine act at the catalytic esteratic subsite. Tacrine, and to some extent rivastigmine are non-selective inhibitors of both AChE and BChE. CNS specific inhibition of AChE can occur with donepezil. Binding to the AChE sites may be either reversible or irreversible, and may be competitive or noncompetitive with acetylcholine. Galantamine is a competitive drug while tacrine is a non-competitive inhibitor. AChE tetramer, G4, is located on the presynaptic membranes while a monomer, G1, is found on postsynaptic membranes. Although G4 is decreased along with the neuronal loss in AD, postsynaptic cholinergic receptor neurons and G1 ACh are not decreased significantly with AD or aging. Rivastigmine and to some extent galantamine are highly selective for the postsynaptic G1 monomer while donepezil is not selective.

RILUZOLE

It is approved for use in Motor Neuron Disorder. It is unclear whether this would help features of fronto-temporal dementia associated with MND. It prolongs survival by nearly 10% for more than a year of treatment. Riluzole’s mechanism of action is via 1. Sodium channel blockade 2. High-voltage calcium channel blockade 3. NMDA-glutamate receptor antagonism. It preferentially blocks the sodium channels in damaged neurons, reducing calcium flow and indirectly preventing excitotoxic damage.

Revision #1
Created 2026-01-04 20:04:26 UTC by Omar Ayman
Updated 2026-01-04 20:04:27 UTC by Omar Ayman