Binding profiles of antipsychotics to mouse cerebral cortical muscarinic receptors using [*N*-methyl-^{3}H]scopolamine ([^{3}H]NMS)

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Antipsychotics are often used as the first-line treatment for behavioral and psychological symptoms of dementia (BPSD). However, the potential anticholinergic effects of antipsychotics could counteract therapeutic effects of cholinesterase (ChE) inhibitors for Alzheimer's disease (AD), which increases in brain acetylcholine levels. This study was carried out to investigate the inhibitory effects of 26 clinically available antipsychotics on [^{3}H]NMS specific binding in mouse cerebral cortex in order to predict which of these drugs may possess anticholinergic properties that could attenuate the therapeutic effects of ChE inhibitors within clinically relevant dosages. Of the tested 26 drugs (10^{-5} M), the following 10 antipsychotics inhibited specific binding of 0.5 nM [^{3}H]NMS by >45%: chlorpromazine, levomepromazine, prochlorperazine, timiperone, zotepine, pimozide, blonanserin, olanzapine, quetiapine, and clozapine. Furthermore, the pK_i values of chlorpromazine (6.40 ± 0.08), levomepromazine (6.22 ± 0.07), zotepine (6.21 ± 0.03), olanzapine (6.85 ± 0.07), and clozapine (6.83 ± 0.05) overlapped with their clinically achievable blood concentrations. Therefore, these antipsychotics could attenuate the effects of ChE inhibitors, and thus, should not be recommended for the treatment of BPSD in AD patients.