Determination of the pharmacological properties and binding mechanisms of amphetamine-type stimulants on nicotinic receptors

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Amphetamine-type stimulants (ATS) are currently the second most prevalent drug of abuse among adolescents. However, with no fully effective long-term treatments, more knowledge about potential therapies is required. Interestingly, ATS addiction has an associated increase in activity of striatal cholinergic interneurons. Moreover, drugs targeting the nicotinic acetylcholine receptors have been proposed as potential therapeutic targets. Indeed, the cholinergic interneurons of the striatum are widely recognized as the major regulator of striatal dopamine release. Still, before effective nicotinic-based treatments are identified, more knowledge about the design of nicotinic drugs is required. Because of this, we plan on identifying the structural elements in ATSs that impart drug potency, efficacy, and pharmacological response (agonism vs. antagonism) on nicotinic receptors; as well as their binding mechanisms. In order to evaluate the binding mechanisms of ATSs and nicotinic receptors, *in silico* docking analyses will be performed with PiAMPH, DiMETH and METH. These same drugs will then be employed in Two Electrode Voltage Clamping (TEVC) procedures on oocytes to determine drug expression, response dichotomy and response magnitude on nicotinic receptors.