**A novel translational assay of response inhibition and impulsivity; effects of prefrontal cortex lesions, drugs used in ADHD, and serotonin 2C receptor antagonism.**

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Neuropsychopharmacology. 2013 May 9. doi: 10.1038/npp.2013.112. [Epub ahead of print]

Animal models are making an increasing contribution to our understanding of the psychology and brain mechanisms underlying behavioral inhibition and impulsivity. The aim here was to develop, for the first time, a mouse analogue of the stop-signal reaction time task with high translational validity in order to be able to exploit this species in genetic and molecular investigations of impulsive behaviours. Cohorts of mice were trained to nose-poke to presentations of visual stimuli. Control of responding was manipulated by altering the onset of an auditory 'stop-signal' during the go response. The anticipated systematic changes in action cancellation were observed as stopping was made more difficult by placing the stop-signal closer to the execution of the action. Excitotoxic lesions of medial prefrontal cortex resulted in impaired stopping, whilst the clinically effective drugs methylphenidate and atomoxetine enhanced stopping abilities. The specific 5-HT2C receptor antagonist SB242084 also led to enhanced response control in this task. We conclude that stop-signal reaction time task performance can be successfully modelled in mice and is sensitive to prefrontal cortex dysfunction and drug treatments in a qualitatively similar manner to humans and previous rat models. Additionally, using the model we show novel and highly discrete effects of 5-HT2C receptor antagonism that suggest manipulation of 5-HT2C receptor function may be of use in correcting maladaptive impulsive behaviors and provide further evidence for dissociable contributions of serotonergic transmission to response control.Neuropsychopharmacology accepted article preview online, 9 May 2013; doi:10.1038/npp.2013.112.