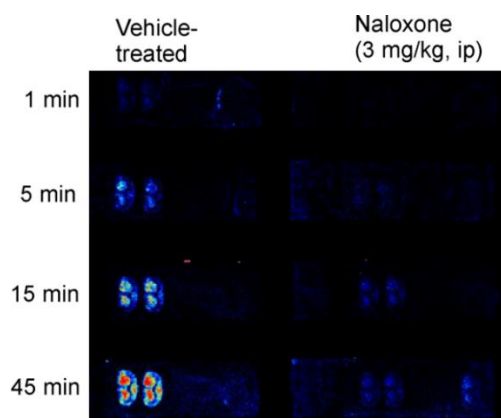


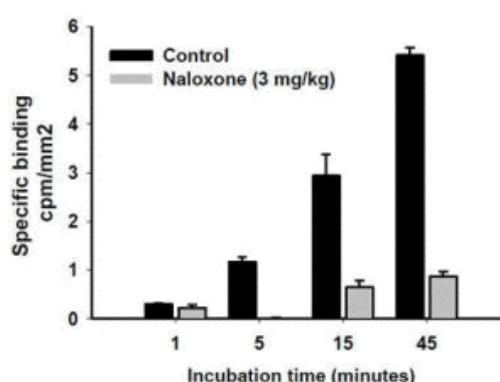
### EX VIVO RECEPTOR OCCUPANCY

Fig. 1. Autoradiographic binding of [ $^3$ H]DAMGO to striatal sections from rats given naloxone (3 mg/kg, i.p.) or vehicle, 20 minutes prior to sacrifice. After being cut, sections were incubated *in vitro* in [ $^3$ H]DAMGO for between 1 to 45 minutes. Binding of [ $^3$ H]DAMGO to opiate receptors in the sections from the drug-treated animal is reduced at all incubation time points due to occupancy of opiate receptors in the tissue by the drug.

(a) Autoradiographic image



(b) ROI quantification of radiotracer binding



### IN VIVO RECEPTOR OCCUPANCY

Fig. 1. *In vivo* CB1 receptor occupancy of a test drug determined by inhibition of [ $^3$ H]SR141716A binding in the rat brain. The test drug was given by oral gavage 1 hour prior to sacrifice and [ $^3$ H]SR141716A via a tail vein 30 minutes prior to sacrifice. Plotted values are ratios of radioactivity in a receptor-rich region (cerebellum or hippocampus) relative to that in a receptor-poor reference region (brain stem) and are the means of 5 - 6 animals per dose. At the highest dose, test drug reduced both hippocampal:brain stem and cerebellum:brain stem ratios to close to one, indicating complete occupancy of brain CB1 receptors.

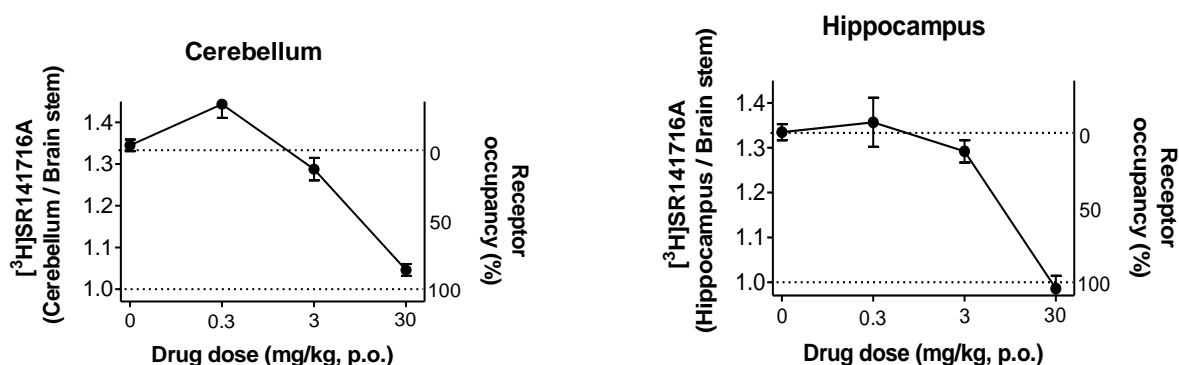
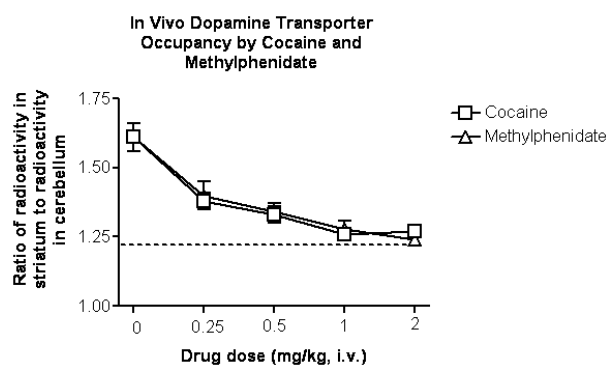


Fig. 2.



*In vivo* dopamine transporter occupancy of cocaine and methylphenidate as determined by inhibition of [<sup>3</sup>H]cocaine binding in the striatum in mice. Values are ratios of radioactivity in striatum (receptor-rich region) to cerebellum (reference region) and are the means of 5 - 6 animals per dose. Both cocaine and methylphenidate reduced specific [<sup>3</sup>H]cocaine binding with 50%

inhibition at about 0.25 mg/kg for both drugs. Dotted line indicates the level of non-specific binding, as determined by administration of a blocking dose of a high-affinity cocaine analogue.