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**Title:** The role of the dopamine D<sub>4</sub> receptor (D4R) in cocaine self-administration  
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The D4R has received considerable attention due to its relationship in certain personality traits and psychological disorders, such as gambling (Perez de Castro I et al., 1997), substance abuse (Lusher et al., 2001), Attention Deficit Hyperactivity Disorder (ADHD) (Burgos-Arcos, et al., 2004), schizophrenia (Seeman et al, 1993) and bipolar disorder (Muglia et al., 2002). Previous studies have supported the idea that reinforcing effects of cocaine are likely exerted in the mesolimbic regions in mammals, particularly in the hippocampus, caudate putamen and nucleus accumbens (Kuhar et al 1991). These same regions have a high concentration of D4R. Mutant mice lacking the D4R have been shown to be supersensitive to the psychomotor stimulant effects of ethanol, methamphetamine, and cocaine as compared to the wild type (Rubinstein et al., 1997). Another study determined that the D4R plays a role in vulnerability to stimulant abuse (Katz et al., 2003). In the present study we examined the cocaine self-administration behavior of knock-out (D4R<sup>-/-</sup>), heterozygous (D4R<sup>+/-</sup>) and wild-type (D4R<sup>+/+</sup>) mice. Following 18 days of daily (60 minute) cocaine (1 mg/kg/infusion) self-administration sessions, mice were randomly selected to follow an extinction or abstinence regiment. Extinction trials consisted of substituting saline for self-administration and continued until the animal reached a criteria of 3 consecutive days of 10% from baseline response. Abstinence (2 weeks) trials consisted of mice kept in their home cages without any type of exposure to cocaine-associated stimuli. Reinstatement of cocaine self-administration was tested in both extinction and abstinence mice either once they met criteria for extinction or two weeks after abstinence. During reinstatement, all mice were pretreated with a 1 ml intraperitoneal (i.p) injection of cocaine (1mg/kg). In this study we expect to examine the role of the D4R in cocaine self-administration maintenance, extinction, abstinence and reinstatement.

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