

Medial prefrontal cortex, but not nucleus accumbens dopamine nerve terminals become hypersensitive following cocaine self-administration

*De Vries TJ, Vanderschuren LJMJ\*, Schoffeleers ANM*

Research Institute Neurosciences Vrije Universiteit, Drug Abuse Program, Dept of Medical Pharmacology, VU Medical Center, Amsterdam, \*Rudolf Magnus Institute of Neuroscience, Dept of Pharmacology and Anatomy, University Medical Center Utrecht, Utrecht

The sensitizing properties of drugs of abuse are believed to play an important role in the development and persistence of drug-seeking behaviour (Robinson and Berridge, 1993). Our studies have supported this view, by showing that the ability of a particular drug to elicit a sensitized locomotor response in opiate and psychostimulant treated rats was strongly associated with the ability of that same drug to provoke a drug seeking response in rats after long-term extinction of self-administration behaviour. With regard to the underlying neuronal mechanisms of drug sensitization, many studies have pointed to a role of the nucleus accumbens dopamine system. Indeed, we and others have shown that the repeated administration of morphine, amphetamine, cocaine, nicotine or alcohol, results in a long-lasting enhancement of dopamine release in this area. In agreement with these findings, we recently observed that direct infusion of the dopamine releasing agent amphetamine in the nucleus accumbens elicits a sensitized locomotor response in amphetamine pre-treated rats, with a particular involvement of the shell region. In contrast, infusion of amphetamine in either shell or core only marginally induced drug seeking in cocaine trained rats. This suggests that the substrates mediating drug sensitization and drug seeking may differ. On the other hand, recent neurochemical experiments reveal that, in contrast to repeated forced injections of drugs of abuse, self-administration of cocaine did not result in hypersensitivity of nucleus accumbens dopaminergic nerve terminals, but caused a robust sensitization of medial prefrontal cortex dopamine neurons. Taken together, our data indicate and support previous findings that (1) the neuroadaptations produced by addictive drugs depend heavily on the paradigm used and (2) the medial prefrontal cortex dopamine system may play a crucial role in relapse to drug seeking.

T.J. De Vries, Department of Medical Pharmacology, VU Medical Center, Van der Boerhorststraat 7, 1081 BT Amsterdam, The Netherlands. t 020 4448101, e-mail [tj.devries@vumc.nl](mailto:tj.devries@vumc.nl)

posters Neuroscience 2