Differences in cellular mechanisms underlying the differential response to amphetamine in apomorhine-susceptible and apomorphine-unsusceptible rats

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Individual differences in responses to addictive drugs such as amphetamine and cocaine is a well known phenomenon. Additionally, it is known that (among others) the dopaminergic system in mesolimbic brain areas such as the nucleus accumbens plays an important role in determining these individual differences.
In the dopaminergic nerve terminal two different dopamine pools are present: the reserpine (RES)-sensitive dopamine pool and the alpha-methyl-para-tyrosine (aMpT)-sensitive dopamine pool. These pools can be depleted by reserpine and aMpT, respectively. Amphetamine is known to act primarily on the latter pool, by releasing dopamine from this pool through the dopamine transporter.
Two types of rats that differ in their dopaminergic system were used in this study. The apomorphine-susceptible (APO-SUS) rats have a more extensive and more reactive dopaminergic system than the apomorphine-unsusceptible (APO-UNSUS) rats. These rats were tested in the prepulse inhibition (PPI) paradigm to evaluate whether there was a differential response to amphetamine and whether this response could be blocked by aMpT. We found that amphetamine produces a dose-dependent decrease in PPI in both APO-SUS and APO-UNSUS rats and that the effect is stronger in APO-SUS rats; namely APO-SUS rats respond to all doses tested, whereas the APO-UNSUS rats showed only a decrease in PPI at the two highest doses. Furthermore we found that the effect of amphetamine can be blocked by aMpT and, moreover, that this effect could only be blocked in the APO-UNSUS rats, but not in the APO-SUS rats. These data suggest that (a) APO-SUS rats are more sensitive to amphetamine than APO-UNSUS rats and (b) the aMpT sensitive pool in APO-UNSUS rats is smaller than in APO-SUS rats, which might explain the lower sensitivity of APO-UNSUS rats to amphetamine.

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