Prefrontal DA release and cognitive flexibility

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We are interested in the neurobiological basis of cognitive flexibility, the ability to adjust goal-directed behaviour in response to changes in environmental demands. This capacity is severely disturbed in schizophrenia and in patients with lesions of the prefrontal cortex (PFC).
We showed that reversal learning in rats depends on the integrity of the medial PFC (de Bruin et al, 2000). The task we used is a two-lever discrimination task, in which the relation between response and reward is reversed and/or extinguished. PFC function has been claimed to depend on the activity of dopamine (DA) and, indeed, we also observed impaired reversal learning after local blockade of DA D1-receptors in the medial PFC. In both cases, impairment was restricted to the first reversals, indicating PFC involvement in initial adaptation of behavior.
To further study the relationship between prefrontal DA and cognitive flexibility we used an adapted version of the serial reversal task and measured DA and noradrenaline (NA) during performance of either a first or a third reversal, or extinction.
The results show that DA efflux is increased (50%) during performance of the control task. Rats performing the first reversal showed a higher (75%) and more extended increase of DA, while rats performing the third reversal showed no difference compared to their controls. Although NA was increased during task performance as well, no extra increase during the first reversal was observed. Neither DA nor NA efflux showed any activation during the extinction.
Conclusion: These results corroborate our previous findings after local application of dopamine receptor antagonists and indicate a selective involvement of prefrontal DA in initial reversal learning.
To further study the role of DA we developed a model in which cognitive flexibility is disturbed. Currently we are testing the effects of neuroleptics on this model and on DA release.

J.P.C. de Bruin et al. (2000) Progr. Brain Res.126: 103-113

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session 32