Cognitive flexibility, serotonin and the prefrontal cortex of the rat

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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 ability requires a conversion of different functions, like response-selection and inhibition, which has been shown to require an intact prefrontal cortex (PFC). Animal research has shown a functional specialisation of the PFC in which medial PFC is involved in cognitive flexibility in spatial learning tasks whereas the orbital PFC is involved in the 'updating' of existing stimulus – reward associations and the utilization of these associations to guide behaviour.
Neurochemically, serotonin (5-HT) has been suggested to be of importance for cognitive flexibility when affect guides decision-making. In a series of tryptophan depletion studies others have reported that healthy volunteers were found to show impaired reversal-learning and reduced ability to discriminate between the magnitudes of rewards in a gambling task, indicating that 5-HT is involved when affective cues are used to guide behaviour. Based on these findings, we hypothesised that 5-HT in the PFC is of particular importance for behavioural adaptations when stimulus – reward associations change and affect guides decision-making. In a series of experiments, we aim to clarify this involvement by manipulating and measuring the release of 5-HT during behavioural tasks.
Preliminary results with acute tryptophan depletion in rats show decreased availability of plasma tryptophan but no change in 5-HT efflux in the medial PFC. This suggests that effects previously found with tryptophan depletion might not always be attributable to changes in 5-HT function. Future experiments, including microdialysis and lesion studies, will follow to further clarify the relationship between 5-HT and cognitive flexibility.

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