METAPLASTIC TREATMENTS WITH KETAMINE AND MK-801 AFFECT INSTRUMENTAL APPETITIVE MEMORY RECONSOLIDATION IN RATS

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Reconsolidation is the mechanism that restores previously consolidated memory traces after their reactivation. Memory reactivation induces destabilization, a labile phase during which synapses can be enhanced or weakened, resulting in memory restabilization or disruption. NMDA receptors, and more precisely GluN2B and GluN2A, were shown to modulate respectively the destabilization and restabilization of previously consolidated memories. These receptors are also involved in metaplasticity.

Aims: to investigate the effect of NMDA channel blockers on destabilization and reconsolidation of food instrumental memories when given under a 'metaplasticity' protocol. Therefore, we tested whether MK-801 or ketamine given one day prior to food instrumental memory retrieval may reduce reinstatement of food-seeking behaviour in rats previously trained to food self-administration.

Methods: after forced abstinence, intraperitoneal 4 mg/kg MK-801 or intravenous 10 mg/kg ketamine were given to rats 24 hours before re-exposure to training context and lever responding, up to 20 lever pressing without contingency.

Results: MK-801, but not ketamine, inhibited reinstatement compared to vehicle and control groups treated with MK-801 or ketamine but without retrieval. To investigate the molecular changes induced by MK-801 or ketamine, we also analysed the expression pattern of different glutamatergic receptors in specific rat brain areas involved in memory processes. Interestingly, preliminary data showed that the level of GluN2B in amygdala was significantly decreased 24 hours after the treatment with MK-801 but not ketamine.

Conclusion: we suggest that previous day treatment with MK-801, but not ketamine, reduces the reinstatement of food-seeking behaviour through a GluN2B-NMDA-dependent inhibition of instrumental memory reconsolidation.