The effect of the antipsychotic drug remoxipride on memory; a preclinical study utilizing the novel object recognition task

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Conclusions

Our results show that remoxipride demonstrated an enhanced effect on recognition memory in a dose dependent manner. Remoxiprides mechanism of action may hereby be a valuable tool in the development of novel drugs with improved effect on cognitive function.

Introduction

There is a great need of new, pro-cognitive drugs in the treatment of schizophrenia as the related cognitive impairments remains the most challenging cluster of symptoms to ameliorate with current antipsychotic drugs. Clinical and preclinical studies suggest that the pathophysiology of the cognitive dysfunctions in schizophrenia involves dysregulation in cortical glutamate trasmission[1,2,3]. Interestingly, previous preclinical studies suggest that the antipsychotic drug remoxipride might have glutamate modulating ability, as it has been suggested to act as a mGlur 2/3 agonist in addition to its dopamine D2 antagonistic effect. Furthermore, remoxipride has also been shown to prevent cortical glutamate release produced by NMDA-R antagonists (e.g. ketamine and phencyclidine)[4]. With this background, the aim of this study was to investigate the effect of remoxipride on recognition memory by using the novel object recognition task in rats.

References

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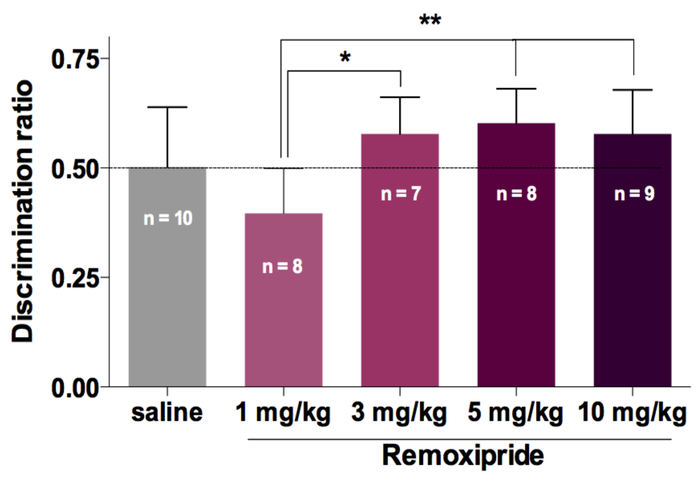
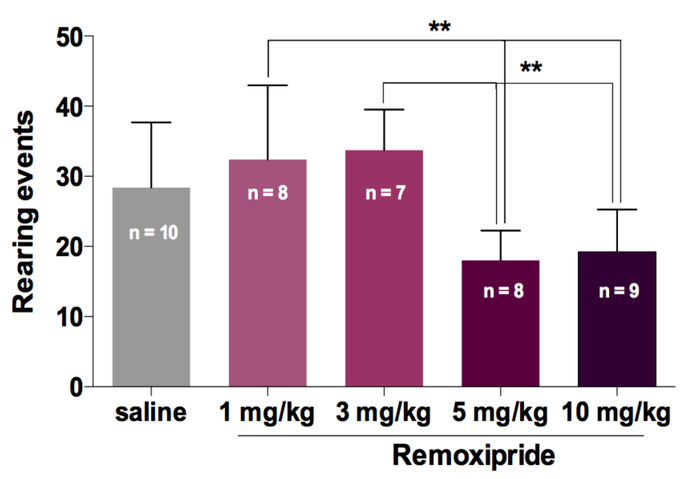
Results

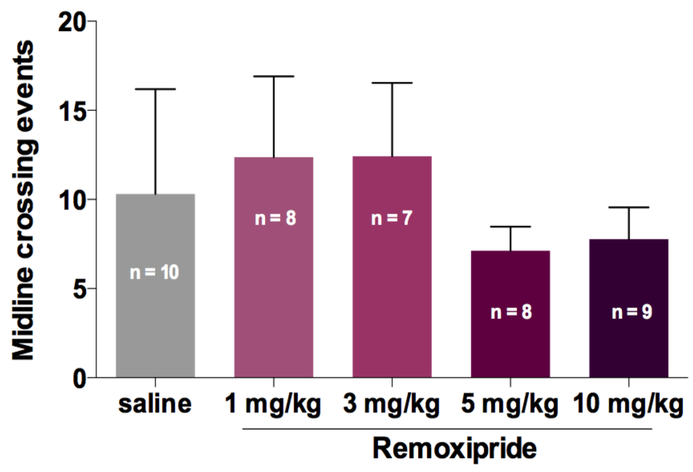
1. The antipsychotic drug remoxipride show an enhancing effect on recognition memory in a dose dependent manner



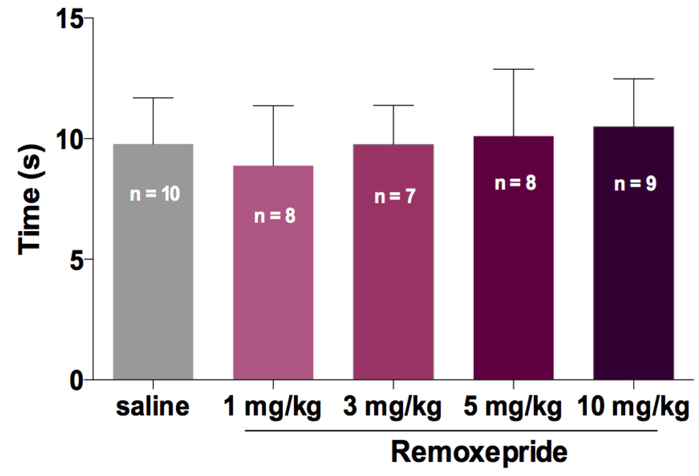
2. Higher doses of remoxipride decrease rearing frequency

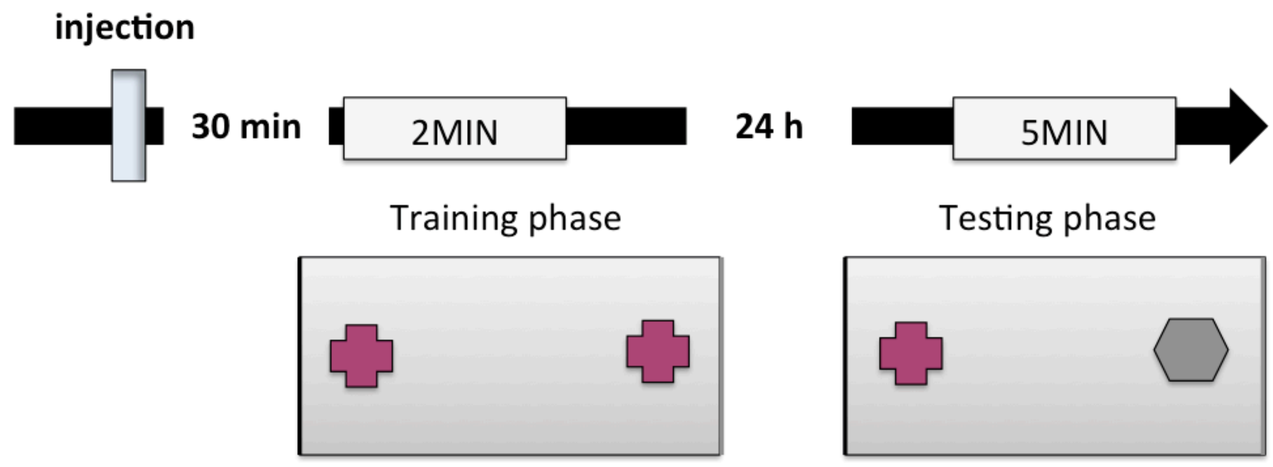


3. Higher doses of remoxipride, result in lower locomotor activity



4. The total amount of exploration was not affected by remoxipride

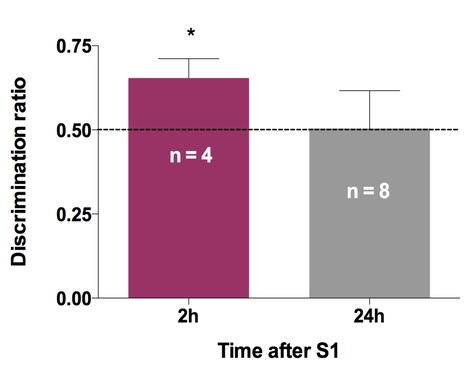




Methods

Novel Object Recognition Task

NOR is based on rats natural curiosity and the premise that rats prefer to explore novel objects over familiar ones[5]. The task consists of 2 phases, a training phase (S1) and a test phase (S2). 30 minutes prior to the S1 phase, remoxipride in multiple doses (1mg/kg, 3mg/kg, 5mg/kg and 10mg/kg) or saline (0.9% NaCl) were systemically administered. During the S1 phase, rats were presented to two identical objects. After a retention time of 24 hours, animals were introduced to a familiar and a novel object (S2 phase). A discrimination ratio was calculated based on the time that the animal spent interacting with each object during the test phase. A discrimination ratio higher than 0.5, indicates that the rat spent more time interacting with the novel object. As validation allowed exclusion of both object (p=0.0756) and side preference (p=0,7962), it could be concluded that the animal recognizes the familiar object.



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No conflict of interest to disclose

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