Evaluation Of Sub-Chronic Ketamine Treatment In A Rodent Model Of The Iowa Gambling Task

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Introduction

• The Iowa Gambling Task (IGT) is a choice-based task which assesses impulsivity, where patients must choose one of four options in order to optimise monetary gains.
• Choices that give large rewards are linked with large punishers or monetary losses and vice versa. Optimum gains are made by choosing small reward options the most and high-risk choices are associated with high levels of impulsivity and has been shown to be higher in schizophrenics.
• This has been adapted to rodents with the rIGT by Zeeb et al (2009) where rodents must choose between four illuminated holes in order to gain maximum food pellets within a 30 minute period. The punishment is represented as a time-out period which has the indirect effect of reducing the number of pellets that can be gained (1) (see figure 1).
• Schizophrenia is associated with a wide-range of symptoms including cognitive deficits (2).
• Aberrant glutamatergic transmission is thought responsible for these deficits, therefore ketamine (weak NMDA-receptor antagonists) can be used to model schizophrenia in rodents (3).
• Nicotine has been shown to improve attentional performance in patients with schizophrenia (4).

Aims and Hypotheses

• To assess the impact of sub-chronic ketamine exposure on ability of rats to make choices within the rIGT and therefore assess impulse behaviour.
• To determine whether nicotine can restore any alterations in choice produced by the sub-chronic ketamine exposure since it has been shown to improve cognition in other tasks (5).

References


Experimental Design

- Rats were trained to nose-poke into a hopper and then follow it up by nose-poking into an illuminated light which was then associated with a reward. Training was judged as being completed when the rats were repeatedly being successful in achieving 30 correct responses within a 10 second stimulus.
- The rats underwent injections daily for 5 days.
- The rats were randomly separated into two groups (n=12) with one group being treated with saline injections and the other group being treated with ketamine (10mg/kg IP). The rats underwent injections daily for 5 days.
- Both groups of rats were each tested with a randomised sequence of nicotine doses (0, 0.05, 0.1, 0.2, 0.4) administered 10 min prior to rIGT sessions.
- Rats then carried out the rIGT task once again and choice selection was assessed to determine the impact of nicotine on impulsivity.

Details of the rGT

| Figure 1. This diagram depicts the relative risk/reward of each choice associated with the illuminated holes in the rIGT. P2 is the optimal choice selection with P5 being the least optimal. |

Results

Figure 3. Sub-chronic ketamine treatment produced no significant differences between choice selection in the P1 and P4 selections. There was a significant increase (p<0.001) in the optimal selection (P2) with the ketamine treated rats compared to the vehicle group.

Figure 4. (a) Nicotine pre-treatment had no significant effect on choice selection in the rats in the vehicle group. (b) Nicotine pre-treatment also had no effect on choice selection in the ketamine treated group.

Conclusions

- Sub-chronic ketamine exposure increased optimal choice selection and decreased sub-optimal choice which is contradictory to published literature on impulsivity in patients with schizophrenia.
- The overall finding from this study suggests that the sub-chronic ketamine exposure decreases impulse behaviour in rats.
- Nicotine treatment had no effect on choice selection in control subjects and had no effect in restoring the altered baseline performance in the rIGT.