CDPPB A NEW HOPES FOR SCHIZOPHRENIA?

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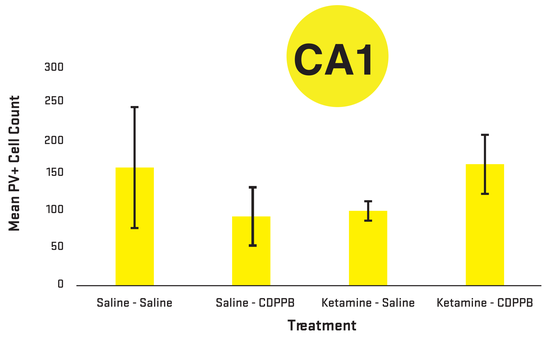
INTRODUCTION

The present study will use immunohistochemical techniques to compare PV+ cell counts in the CA1 region of the HPC and prelimbic (PL) of the PFC of rats administered a rescue dose of CDPPB, after a repeated dosing regimen of Ketamine.

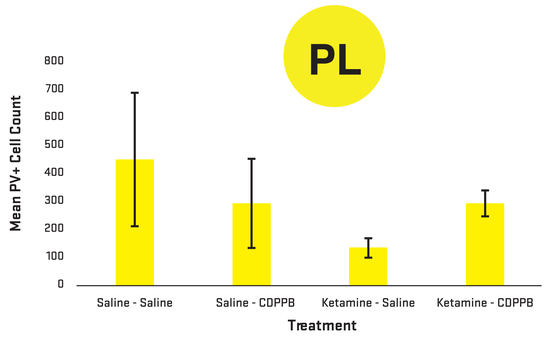
- Schizophrenia is characterized by positive, negative and cognitive symptoms[1]
- Current medications insufficiently address the negative and cognitive symptoms[2]
- Ketamine and other NMDAR antagonists induce schizophrenia-like effects in rodents, impairing the functioning of the medial pre-frontal cortex (PFC) and the hippocampus (HPC)[3]
- NMDAR antagonists lead to a decreased inhibitory effect on glutamatergic interneurons resulting in excitotoxicity and cell death[4]
- Specifically parvalbumin (PV) positive interneuron counts have been shown to be decreased in schizophrenic brains[5]
- 3-cyano-N-(1,3-diphenyl-1H-pyrazol-5-yl)benzamide (CDPPB) has been shown to rescue working memory and other cognitive deficits induced by NMDAR antagonists[6,7]

RESULTS



Comparison of the number of parvalbumin cells within CA1 region. For each treatment saline-saline (n=3), Ketamine-saline (n=4), saline-CDPPB (n=3) and Ketamine-CDPPB (n=4) within CA1 region the average automated cell counts were compared.

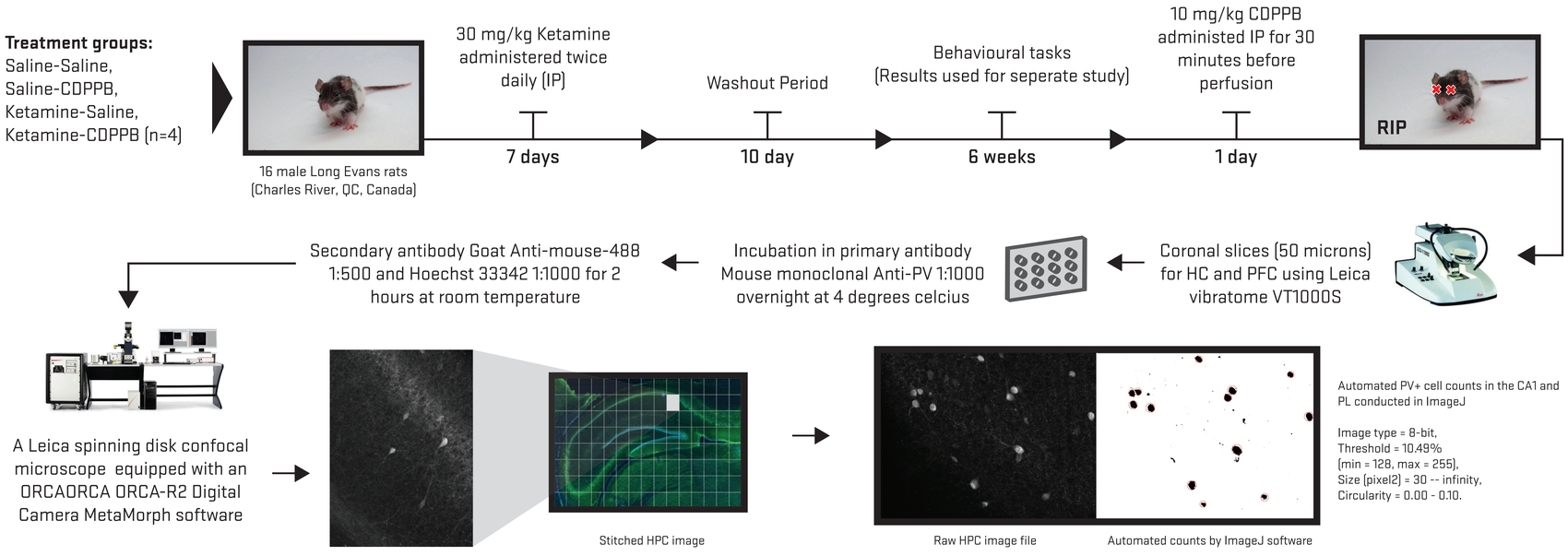
No significant differences were found



Comparison of the number of parvalbumin cells within PL region. For each treatment saline-saline (n= 4), Ketamine-saline (n=4), saline-CDPPB (n=3) and Ketamine-CDPPB (n=3) the average automated cell counts were compared.

No significant differences were found

MATERIALS AND METHODS



DISCUSSION

- CDPPB did not significantly reverse the decrease in PV+ cell counts in CA1 or PL induced by Ketamine
- However, the trend (qualitative analysis) shows that PV+ interneurons from the Ketamine-CDPPB group in both HPC and PFC are greater than the Ketamine-Saline group
- Limitations: small sample size (n=4) which would decrease the statistical power of the experiment, inconsistencies in automated counting methodology (inter-rater reliability), rats were sacrificed after 30 minutes of CDPPB injection, and therefore behavioural testing was not done after CDPPB administration
- Alternatively, Ketamine and CDPPB may exert their effects via changing the density of NMDA receptors on parvalbumin cells. A study on wildtype rats showed that repeated administration of Ketamine increased the density of NMDA receptors but not AMPA receptor in HPC[8]
- Another study has shown that activation of NMDAR receptors with mGluR5 positive modulators decreased gamma oscillations[9]
- Future studies should be conducted to examine the effect of CDPPB on the oscillation of the PV+ cells and the direct effect of these oscillations in improvement of cognitive symptoms

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