Sub-chronic PCP treated rats demonstrate pessimism in a task of optimistic cognitive bias: A novel approach for investigating the disruption of anticipatory motivation in schizophrenia

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Introduction & Methods

- The deficit in anticipatory motivation for pleasurable activities is considered to be one of the main negative symptoms of schizophrenia.
- Sub-chronic treatment with phencyclidine (PCP), a non-competitive NMDA receptor antagonist, has been widely used by us and other researchers for modelling cognitive deficits in the disease (1). However, to date there is no validated method for investigating anticipatory motivation experienced in the disease in an animal model. Our aim is to address this issue by exploring the cognitive bias of PCP treated rats using a novel task for optimistic cognitive bias (2).

- Adult female hooded-Lister rats (160-200 g) were divided into vehicle and PCP groups (n=10, each). The protocol was adapted from that described by Brydges et. al (2). In this task, rats were introduced to white chocolate drops as high value (HV) rewards and 1/2 honey nut cheerios as low value (LV) rewards and trained to associate each reward with a particular grade of sandpaper (fine or coarse) lined on the tunnel of the apparatus. After training, rats were subjected to a pre-treatment test for determination of their natural optimistic bias which was defined when an animal made a choice for the HV reward, chocolate, when introduced to an ambiguous stimulus (medium grade of sandpaper). PCP (2 mg/kg; i.p.) or saline (0.1 ml/100g; i.p.) was administered twice a day for 7 days followed by wash-out (7 days). Then both groups were finally subjected to post-treatment testing. Data were analysed by Student’s t-test and one-way ANOVA.

The Task of Optimistic Cognitive Bias

35 days period

Results

- Phase A (Habituation 1): Groop familiarization to the maze & rewards (10 min/day) Duration: 2 days

- Phase B (Habituation 2): reward-bowl odor pairings 2 sessions/5/day Duration: 3 days

- Phase C (Training 1): learning reward-sandpaper pairings 4 trials/day (5 trials: 2 chocolate trials, 2 cheersio trials) Duration: 3 days

- Phase D (Training 2): same as Phase C except that the rewards are treated progressively Duration: 4 days

- Phase E (Testing 1): Discrimination testing Reward-bowl odor pairings 4 trials/day (5 trials: 2 chocolate trials, 2 cheersio trials) Duration: 3 days

- Phase F (Treatment & Imaging): Sub-chronic PCP vehicle administration followed by a wash out period Duration: 14 days

- Phase D2 (Post-treatment testing) same as Phase F Duration: 3 days

- Data analysis

Conclusions

- These preliminary data suggest for the first time that optimistic bias, as evaluated in a modified version of the sandpaper task was negatively affected by sub-chronic PCP administration. Therefore it may be used as a novel test for investigating the efficacy of novel compounds to reduce blunted affect, a core negative symptom of schizophrenia.