Differential effects of PCP in an effort based reward task and a sucrose preference task

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Introduction

•Schizophrenia consists of positive and negative symptoms together with cognitive deficits. Current antipsychotic drugs treat the positive symptoms but have limited efficacy against cognitive deficits and negative symptoms. The negative symptoms include avolition (related to motivation) and anhedonia (inability to experience pleasure)

•NMDA receptor antagonists such as phencyclidine and ketamine induce behaviours in humans that resemble the various symptom domains of schizophrenia, including negative symptoms (Javitt and Zukin 1991) However, there is limited information on whether PCP-can produce negative symptom-like behaviours in rodents

•Previous studies have suggested that the consumatory elements of reward processing (liking) can be distinguished from the motivational aspects (wanting) (Berridge and Robinson 2003)

•AIM, To determine whether PCP can produce negative like symptom in the rodent using two tasks designed to tap into different aspects of reward function. Firstly by measuring motivation for a reward with an effort based task and secondly, consumption rates in a non effortful sucrose consumption task

Methods

Subjects
Male hooded Lister rats (Harlan UK) weighing ~250g at the beginning of the study. They were single housed under a 12 hour light dark cycle, lights on at 8:00am. Temperature and humidity were maintained at 20-22ºC and 55% respectively. All animals were maintained at 85% of their free feeding weight for the duration of testing.

Materials
Effort based reward
The animals were tested in an elevated, high sided, uniform grey, polyvinyl chloride (PVC) T-maze after the design of (Walton et al 2002). The start arm was connected to two goal arms all 60cm in length, 10cm wide with 30cm high walls, with a brass food well 2cm in diameter placed at the far end of each goal arm 3cm from the far wall. Climbing barriers were constructed from wire mesh in the shape of a right angled triangle. To obtain the high reward the animals had to scale the vertical wall of the climbing barriers but were able to descend to the reward area down a varying degree of slope depending on the barrier height. 3 barriers heights were used: 15cm, 20cm and 25cm.

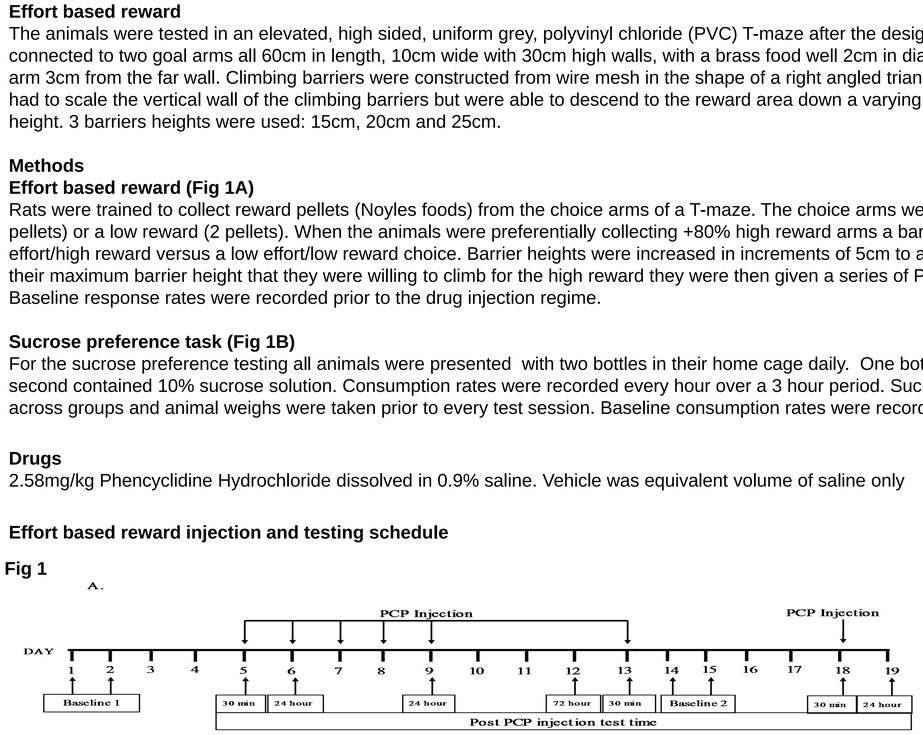
Methods
Effort based reward (Fig 1A)
Rats were trained to collect reward pellets (Noyles foods) from the choice arms of a T-maze. The choice arms were baited with either a high reward (4 pellets) or a low reward (2 pellets). When the animals were preferentially collecting +80% high reward arms a barrier was introduced to create an high effort/high reward versus a low effort/low reward choice. Barrier heights were increased in increments of 5cm to a max of 25cm. When animals had reached their maximum barrier height that they were willing to climb for the high reward they were then given a series of PCP injections and tested for arm choice. Baseline response rates were recorded prior to the drug injection regime.

Sucrose preference task (Fig 1B)
For the sucrose preference testing all animals were presented with two bottles in their home cage daily. One bottle contained normal tap water and the second contained 10% sucrose solution. Consumption rates were recorded every hour over a 3 hour period. Sucrose bottle location was counterbalanced across groups and animal weighs were taken prior to every test session. Baseline consumption rates were recorded prior to the drug injection regime.

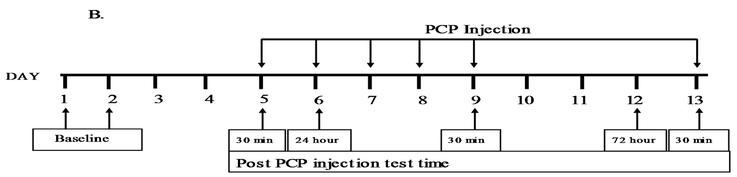
Drugs
2.58mg/kg Phencyclidine Hydrochloride dissolved in 0.9% saline. Vehicle was equivalent volume of saline only

Effort based reward injection and testing schedule

Fig 1

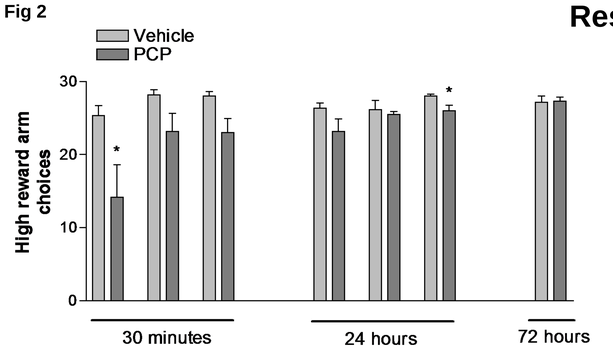


Sucrose preference task injection and testing schedule



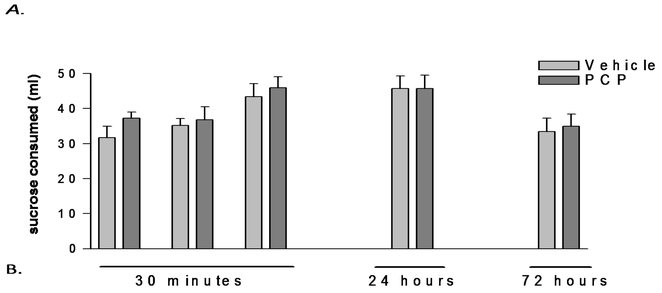
Results

Fig 2



Effort based reward
A significant reduction in high effort/high reward arm choices 30 minutes post PCP injection was seen ($F_{(1,11)} = 5.0.13$ $P < 0.05$) and also 24 hours post PCP ($F_{(1, 11)} = 7.53$ $P < 0.05$). At 72 hours post injection no effects of drug were noted.

Fig 3



Sucrose preference
There were no changes in sucrose consumption following PCP treatment. This was the case for 30 minute, 24 hour and 72 hour post injection time points

Water consumption rates
PCP did not alter water consumption rates, which were relatively low, with all animals showing a clear preference for the sucrose solution throughout the testing period (Fig 3A).

Summary and Conclusion

•The results demonstrate that PCP reduces the amount of effort that a rat is willing to expend in order obtain a reward in a T-maze effort-based reward task.
• In contrast, PCP treatment had no effect in the sucrose preference test in which minimal effort is required to obtain a reward.
•The differential effects of PCP on performance in these tasks, suggests that PCP impairs motivational aspects of reward seeking without affecting the consummatory aspects of reward.
• Overall these data suggest that PCP may mirror the amotivational elements of the negative symptoms of schizophrenia. Drugs that reverse PCP-induced deficits in effort-based reward behaviours and in the neural systems which are involved in informing decision making about a given reward are likely to be predictive for treating the negative symptoms of schizophrenia.

REFERENCES
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