EFFECT OF PHENCYCLIDINE ON HIPPOCAMPAL SENSORY GATING UNDER ISOFLURANE ANAESTHESIA IN THE RAT

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Sensory gating can be assessed using an auditory conditioning-test paradigm which measures the reduction in the auditory evoked response produced by a test stimulus following an initial conditioning stimulus (Bickford et al., 1990). Schizophrenic patients demonstrate lack of attenuation of the test response (Cadenhead et al., 2000) while a similar deficit in the N40-wave evoked potential is observed in a rodent model of schizophrenia (Bickford et al., 1990). This study examined auditory gating in the rat hippocampus following single dose administration of phencyclidine (PCP).

Extracellular single-unit and local field potential (LFP) activity was recorded simultaneously using a 16-channel multi-electrode arrays (Teflon-coated stainless steel, 50µm diameter microwires, NB Labs, Texas USA) in the dentate gyrus, CA1 and CA3 regions of the hippocampus in isoflurane-N_2O:O_2 anaesthetised adult male Lister-hooded rats (250g-450g). Paired auditory stimuli consisting of 3 kHz tones of 10ms duration, intensity 90dB, with a 0.5s inter-stimuli interval and 10s inter-trial intervals over 128 trials were presented binaurally. The effect of PCP (1mg/kg, i.p., n=11 rats) on gating of the N40 LFP wave was assessed as the Test:Condition response amplitude ratio (T/C %); a value of <50% was indicative of gating. Auditory stimuli were presented 15min and 45min after drug administration to assess time course effects on gating and data were analysed using Neuroexplorer (NEX, USA) and Prism (GraphPad, USA).

The CA3 and dentate gyrus (n=8 rats) showed auditory evoked LFP responses, whereas the CA1 (n=3 rats) did not. However, auditory gating was only observed in 5/8 rats, with the dentate gyrus indicating better gating (T/C = 17±3%; mean±s.e.m.n=5) than in CA3 (T/C = 27±3%). PCP disrupted gating in CA3 (T/C = 79±4%; $p<0.0001$) but not in the dentate gyrus (T/C = 15± 2) 45min after i.p. administration. Single-unit activity in the dentate gyrus and CA3 demonstrated inhibitory (40/87 units), excitatory (17/87) or no (30/87) responses to the auditory conditioning stimulus. Clozapine (5mg/kg i.p., n=3 rats) alone was without effect yet prevented deficit in sensory gating induced by PCP (T/C = 28±2%).

This study shows that a single administration of PCP selectively disrupts sensory gating in the CA3 region of the hippocampus in the isoflurane anaesthetised rat. Similar deficits are observed in schizophrenic patients and this method may provide an animal model with good predictive validity, a view substantiated by the fact that clozapine corrects the sensory gating deficits induced by PCP.

Bickford *et al.,* (1990) *Biological Psychiatry* **27**:183-192
Cadenhead *et al.,* (2000) *American Journal of Psychiatry* **157**: 55-59.