

Electrophysiological properties of the hippocampus-medial prefrontal cortex pathway in the sub-chronic phencyclidine model for schizophrenia

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Introduction

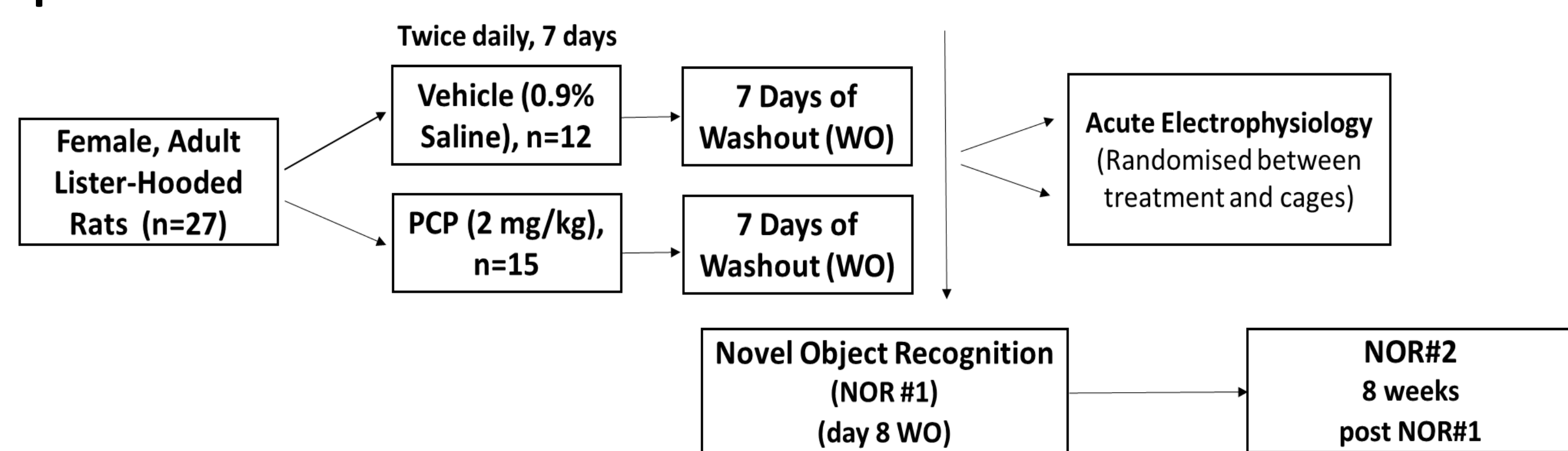
- The functional coupling between the ventral hippocampus (VH) and medial prefrontal cortex (mPFC) is integral to **context dependent memory retrieval, working memory and goal directed behaviour**.
- Synchronised activity between hippocampal formation and PFC during memory relevant tasks has been reported in humans (Anderson et al., 2010, *Cerebral Cortex* 20 (7), 1604-1612).
- Disruption to VH-mPFC in schizophrenia (SZ) is thought to be responsible for deficits in these cognitive processes (Godsil et al., 2013, *Eur Neuropsychopharm* 23, 1165-1181).
- The disrupted functional connectivity has also been shown in the sub-chronic Phencyclidine (PCP) model for schizophrenia (Young et al., 2015, *Neuroscience* 278, 157-163).
- the underlying mechanisms for this remain relatively unexplored.

Aims

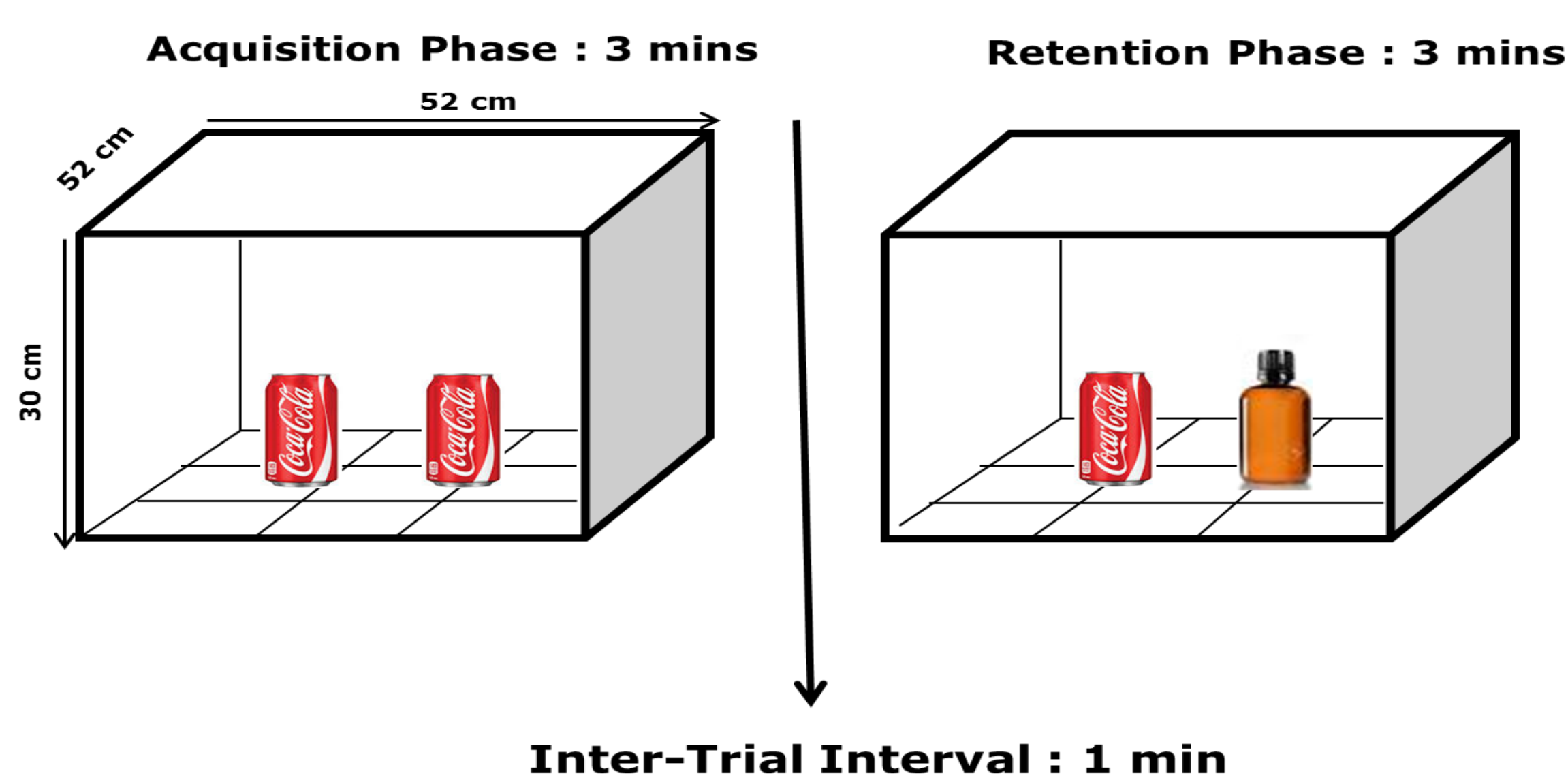
- To replicate the object recognition memory (NOR) cognitive deficit in the scPCP model.
- To test whether this NOR deficit correlates with short- and /or long-term plasticity changes in the pathway between ventral hippocampus and rat medial prefrontal cortex.

Methods

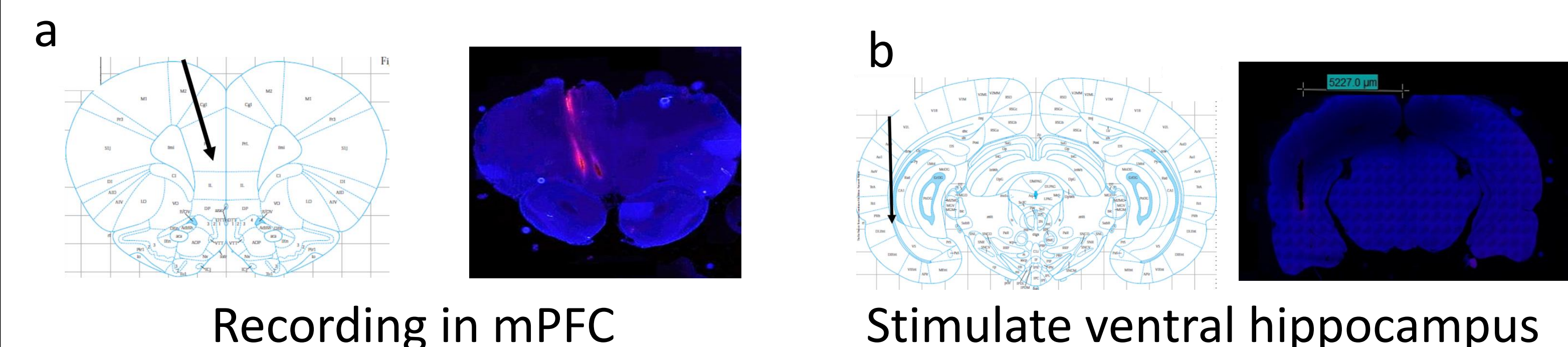
Experimental Outline



Novel Object Recognition (NOR)



Acute Electrophysiological Recordings



Recording Protocol Evoked Recording

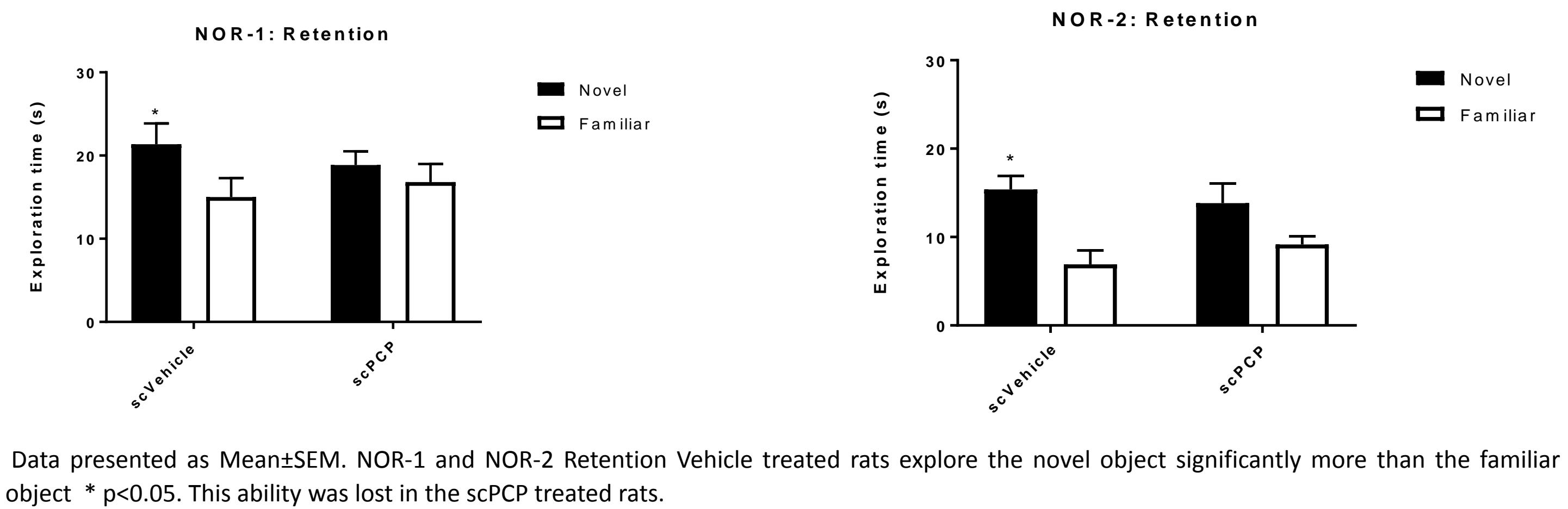
- Input/Output Curve** 20 Pairs, 100-800uA. *The following all set to 50% intensity from the I/O curve*
- Paired-Pulses** 20 pairs, 25-1000ms IPI
- High frequency stimulation (HFS): 20 pulses** at 200Hz, 5 repeats, separated by 2s.
- Low frequency stimulation (LFS): 900 pairs** with 50ms inter-pulse interval at 1Hz
- Baseline recording** Pre-Post HFs and Post-LFs: 30, 60, 30min; Pairs, 50ms IPI every 30s

Electrode Placements

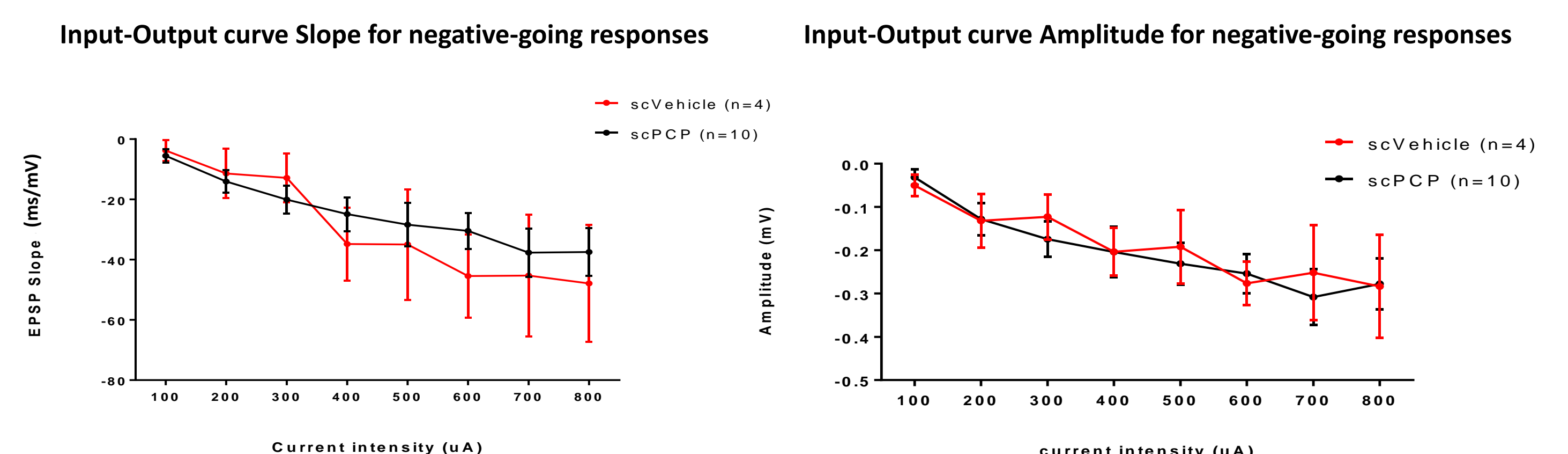
- a) Recording:** B+3.2 mm, Lat 1.5 mm, Depth 4 mm, 10°. 2x16 or 4x8 (Buzsaki) electrode configuration (NeuroNexus Tech., USA);
- b) Stimulating:** B-6.5 mm, Lat 5.5 mm, Depth 4.4-5.4 mm. Twisted pair of Teflon-insulated stainless steel wires, 125um (AdventRM, UK)

Results

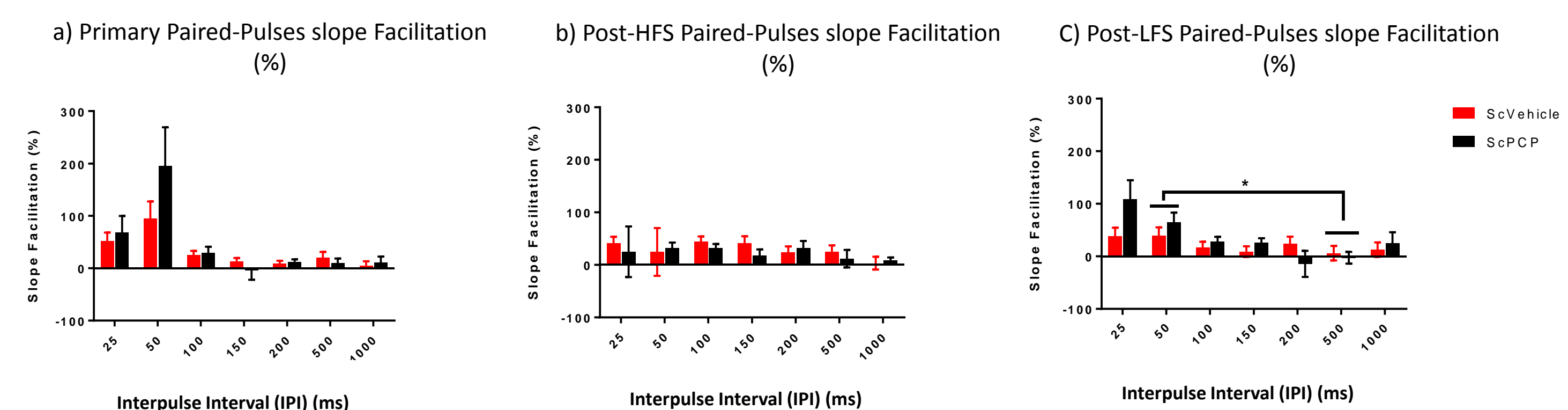
scPCP Rats Show Persistent NOR Deficit



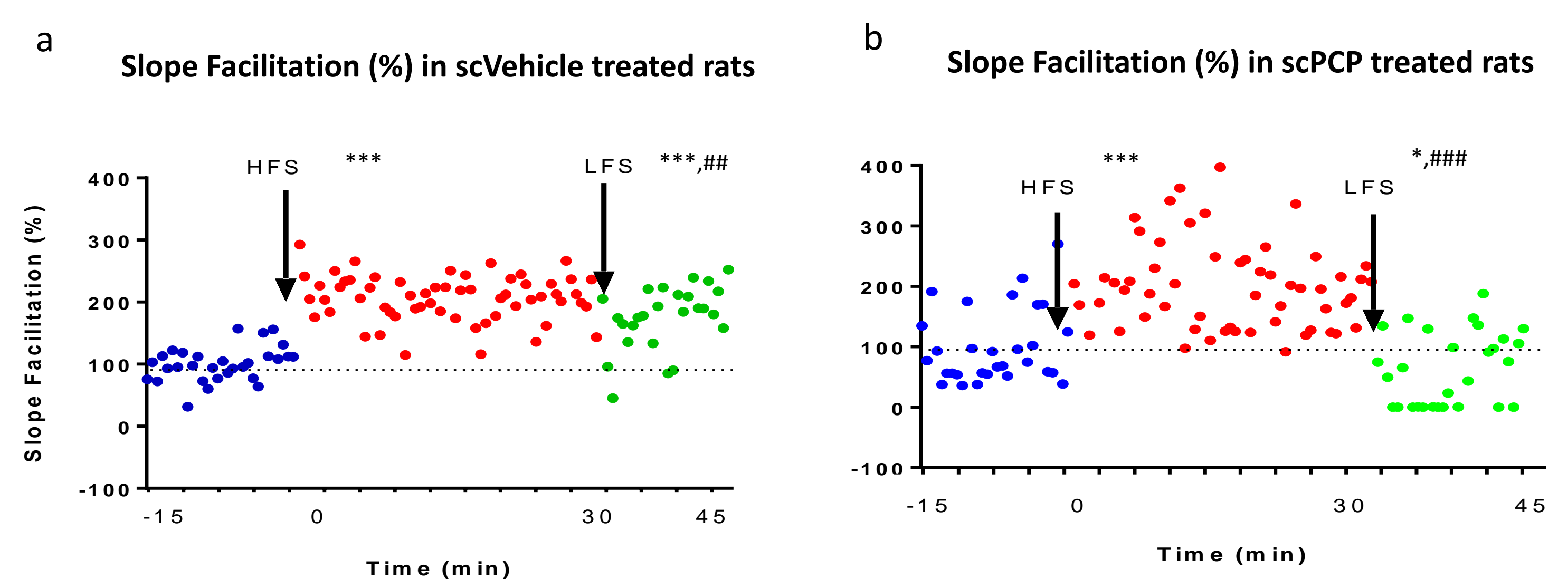
Connectivity Between vHipp and mPFC is Similar for scPCP and Controls



Short-term Synaptic Plasticity is Similar Between scPCP and Controls



Depotentiation of LTP is Much Stronger in scPCP Rats



Conclusions

- Synaptic connectivity between ventral hippocampus (vHipp) and mPFC is unaffected in scPCP rats
- Short-term synaptic potentiation in the vHipp→mPFC pathway is unaffected in scPCP rats.
- Long-term potentiation induction in the the vHipp→mPFC pathway is normal in scPCP rats.
- Changes in short-term potentiation after LTP suggest a pre-synaptic locus in both vehicle and scPCP rats.
- LTP stability in scPCP rats is much more sensitive to LFS patterns.** LFS reverses LTP completely to values below baseline, suggesting an LTD-like effect. This LTP instability may explain some of the cognitive deficits associated with schizophrenia.