

Further characterisation of the rat model of Tourette-related striatal disinhibition: in vivo electrophysiological and behavioural studies

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Background:

Tourette's syndrome, characterised by tics, has been linked to reduced GABAergic inhibition, so-called neural disinhibition, in the striatum (Jackson et al., 2015, *Trends CognSci*). Dorsal striatal microinfusion of GABA-A antagonists like picrotoxin produces tic-like movements in rodents and primates (Bronfeld et al., 2013, *FrontSystNeurosci*; Klaus&Plenz, 2016, *PLoS Biol.*)

Methods:

Here, we infused young adult male Lister hooded rats unilaterally with picrotoxin (300ng/0.5ul) or saline (0.5ul) into the anterior dorsal striatum and recorded electrophysiological and behavioural measurements to characterise further the neuro-behavioural impact of striatal disinhibition.

Results:

Electrophysiological recordings under isoflurane in the striatum showed that picrotoxin disinhibition, apart from evoking large LFP spike-wave discharges, with sharp multi-unit bursts during the negative spike, markedly enhanced burst firing, similar to findings in prefrontal cortex and hippocampus (Bast et al., 2017, *BrJPharmacol*). In freely moving rats, striatal picrotoxin reliably induced tic-like contralateral forelimb movements. Automated photobeam measurements revealed that striatal disinhibition increased locomotor activity and fine motor counts. Fine motor counts showed a similar time course to tic-like movements, suggesting an automated method to quantify these movements. Prepulse inhibition (PPI) of acoustic startle depends on the striatum and is disrupted in Tourette's (Swerdlow, 2013, *NeurosciBiobehavRev*). Striatal disinhibition in rats did not affect PPI, but tended to reduce startle during the first test block, before habituation led to similarly low startle responses in both infusion conditions (infusion-X-block: $F(2,26)=3.2$, $p=0.058$).

Conclusions:

Our findings confirm that striatal disinhibition causes marked spike-wave discharges in striatum and tic-like movements. In addition, such disinhibition markedly enhances striatal burst firing and increases locomotor activity, but does not reproduce PPI deficits seen in Tourette's.