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Prolonged striatal disinhibition as a chronic animal model of tic disorders

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Highlights

- The chronic model is an adaptation of the acute striatal disinhibition model.
- Mini osmotic pumps were used for prolonged bicuculline infusion to the striatum.
- Motor tics were expressed throughout the infusion period (multiple days).
- Tics were accompanied by stereotypical LFP spikes throughout the period.
- Neuronal activity around the tic time was stereotypic and stable across days.

Abstract

Background

Experimental findings and theoretical models have associated Tourette syndrome with abnormal striatal inhibition. The expression of tics, the hallmark symptom of this disorder, has been transiently induced in non-human primates and rodents by the injection of $GABA_A$ antagonists into the striatum, leading to temporary disinhibition.

New method

The novel chronic model of tic expression utilizes mini-osmotic pumps implanted subcutaneously in the rat back for prolonged infusion of bicuculline into the dorsolateral striatum.

Results

Tics were expressed on the contralateral side to the infusion over a period of multiple days. Tic expression was stable, and maintained similar properties throughout the infusion period. Electrophysiological recordings revealed the existence of tic-related local field potential spikes and individual neuron activity changes that remained stable throughout the infusion period.

Comparison with existing methods

The striatal disinhibition model provides a unique combination of face validity (tic expression) and construct validity (abnormal striatal inhibition) but is limited to sub-hour periods. The new chronic model extends the period of tic expression to multiple days and thus enables the study of tic dynamics and the effects of behavior and pharmacological agents on tic expression.

Conclusions