Effects of anti-seizure compounds in a *DishBrain* system containing hyperactive glutamatergic neurons

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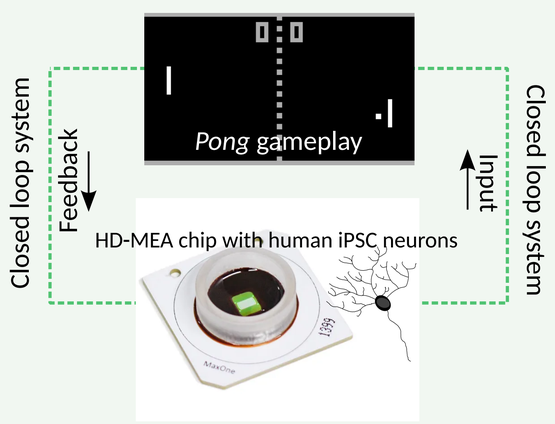
DishBrain[1] is a novel *in vitro* model of neural information processing. Human neurons are presented structured information representing the game *Pong* and are able to interact with it through their activity.

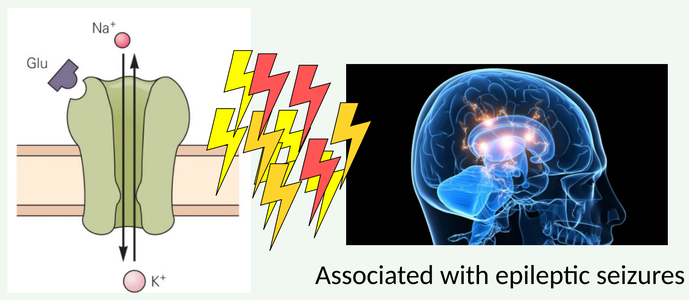
Glutamatergic neuron hyperactivity is seen in pure glutamatergic cultures, and as a clinical feature is associated with a number of psychiatric and neurological conditions[2].

We used *DishBrain* to determine whether modulation of gameplay performance via common anti-seizure drugs in a highly enriched glutamatergic culture is possible.

DishBrain platform



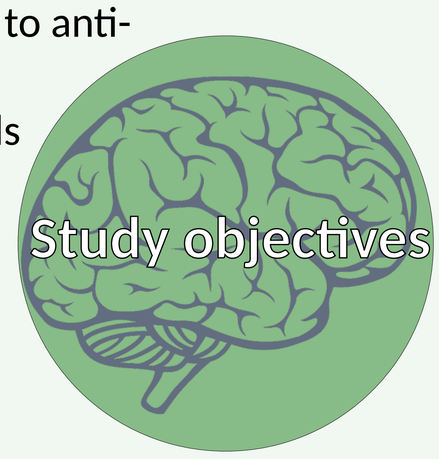
Glutamatergic hyperactivity



Associated with epileptic seizures

Excess glutamatergic neurotransmission

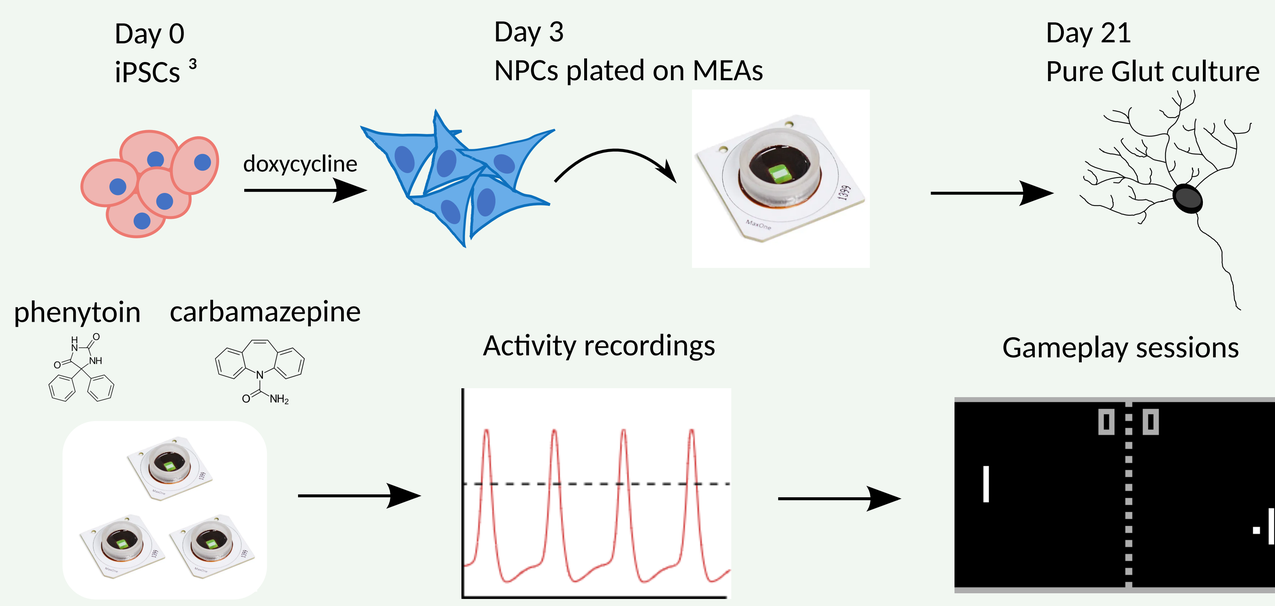
Measure neuronal **responses** to anti-seizure compounds



Generate **dose-response** relationships for anti-seizure compounds

Investigate effects of common anti-seizure medications on gameplay performance in the *DishBrain* platform

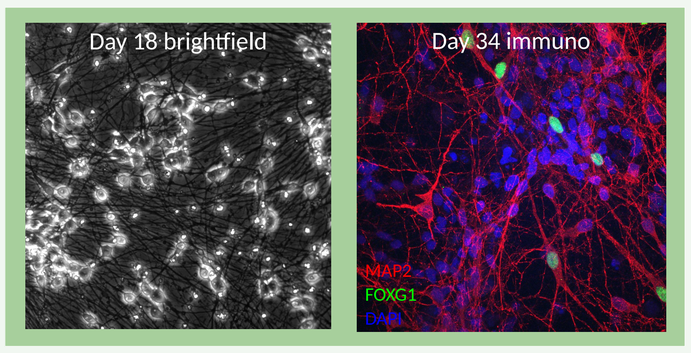
Study design



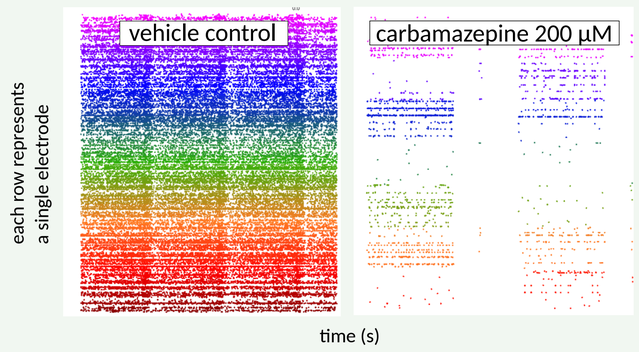
Anti-seizure compound effects on glutamatergic hyperactivity

Cultures set up in parallel to MEA chips were immunoreactive for neuronal and glutamatergic markers. MEA recordings revealed spikes corresponding with action potentials.
Carbamazepine (200 µM) reduced mean and maximum firing rate significantly compared to time-matched vehicle control ($p < 0.05$).

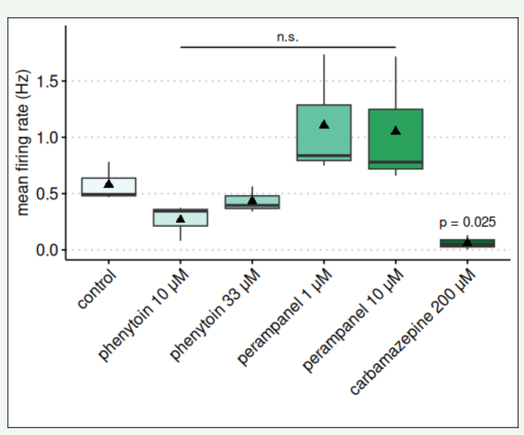
Induced NGN2 glutamatergic neurons



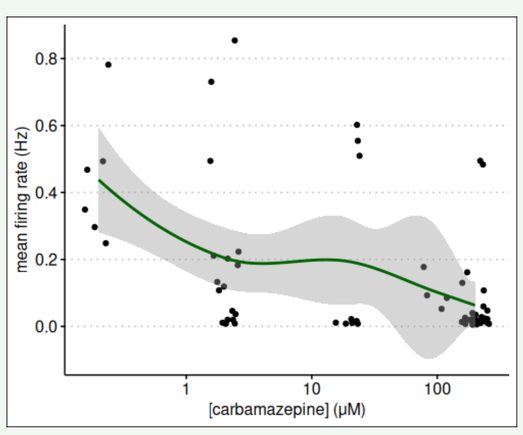
Neuronal firing (each dot = one action potential)



Anti-seizure compound effects on activity



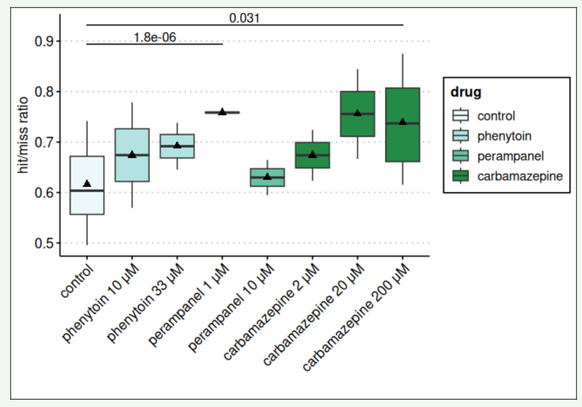
Carbamazepine-activity dose-response curve



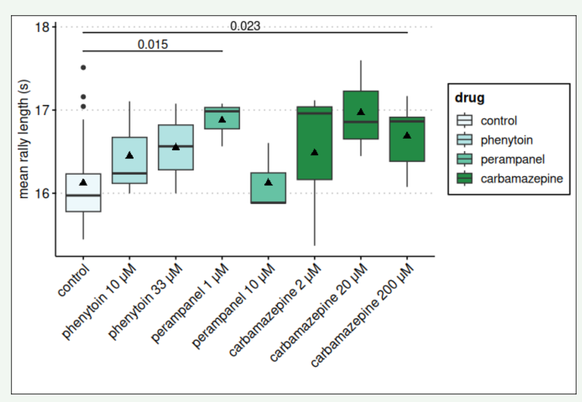
DishBrain gameplay

Perampanel 1 µM and carbamazepine 200 µM improved hit/miss ratio and mean rally length in active gameplay sessions ($p < 0.05$).

Anti-seizure compound effects on *Pong* hits



Anti-seizure compound effects on *Pong* rallies



Key findings

Carbamazepine reduced the firing rate of highly enriched glutamatergic cultures.
Dose-response relationships were generated with anti-seizure compounds in this assay.
Perampanel and carbamazepine improved gameplay performance in the *DishBrain* system.

Significance

We show varying performance in an *in vitro* neural processing model of glutamatergic hyperactivity using therapeutic interventions.

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References

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