SYNAPCELL

THE AMYGDALA -KINDLING RAT MODEL

Accelerating the Identification of Novel Antiseizure Medications

Breaking the Drug-Resistance Barrier in Epilepsy: The Role of Smarter Animal Models

Epilepsy is a chronic neurological disorder marked by recurrent spontaneous seizures due to pathological hyperexcitability and abnormal neuronal discharges. The most common epileptic syndrome in adults is temporal lobe epilepsy. Despite the introduction of over 20 new drugs in 30 years, 30% of patients remain drug-resistant.

The search for more effective and tolerable treatments continues, requiring optimization of animal models for drug discovery. Animal models must be **easy to perform**, **cost-efficient**, and **predictive** of clinical activity.

Different types of seizures on one model

The amygdala-kindling rat model offers the possibility to test a compound on two different types of seizures.

Highly predictive

Predictive for detecting clinically effective drugs of focal onset and secondarily generalized seizures.

A standard procedure

A protocol developped by SynapCell that is robust, reproducible and provides coherent data over different cohorts.

The Amygdala-Kindling Rat Model

- Ideal to assess pharmacodynamics of anti-seizure medications.
- Behavioral and cortical activity readouts are associated through EEG and video recordings
- Combined with a cross-over design, provides a decision-enabling platform to identify novel compounds for the prevention, treatment, and modification of Epilepsy.

Case Study: Amygdala Kindling Protocol

Step 1

Electrode **implantation**
Animal selection (EEG)

Step 2

Afterdischarge threshold is determined.
Daily stimulations at 60Hz until 3 consecutives stage 5 are observed.

Step 3

Stimulation at threshold intensity associated with video and EEG recording.

Step 4

Signal analysis Afterdischarge Duration (focal seizures) & Racine scale (convulsive seizures)

Method and results

Kindling Process

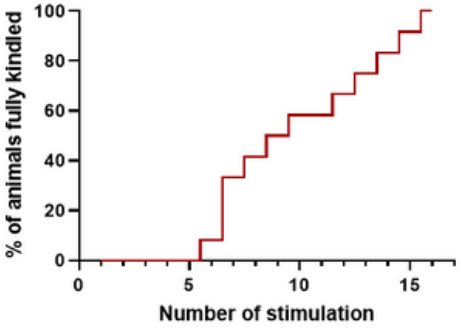

Fig. 1 *- Plot representing the % of animals validated during the kindling acquisition process.*

Pharmacology Process

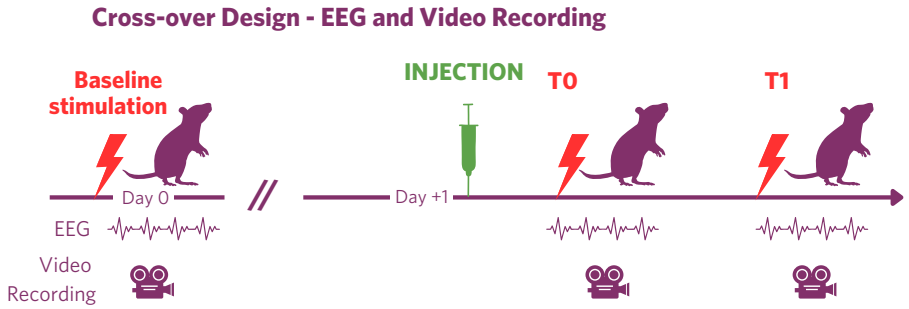

Fig. 2 *- Stimulation at threshold intensity associated with video and EEG recording.* All EEG recordings and behavioral manifestation monitoring are done in freely moving rats following a cross-over design.

Afterdischarge Duration

Valproate – Multiple Mechanisms of Actions

Vehicule i.p
Valproate 200 mg/kg i.p

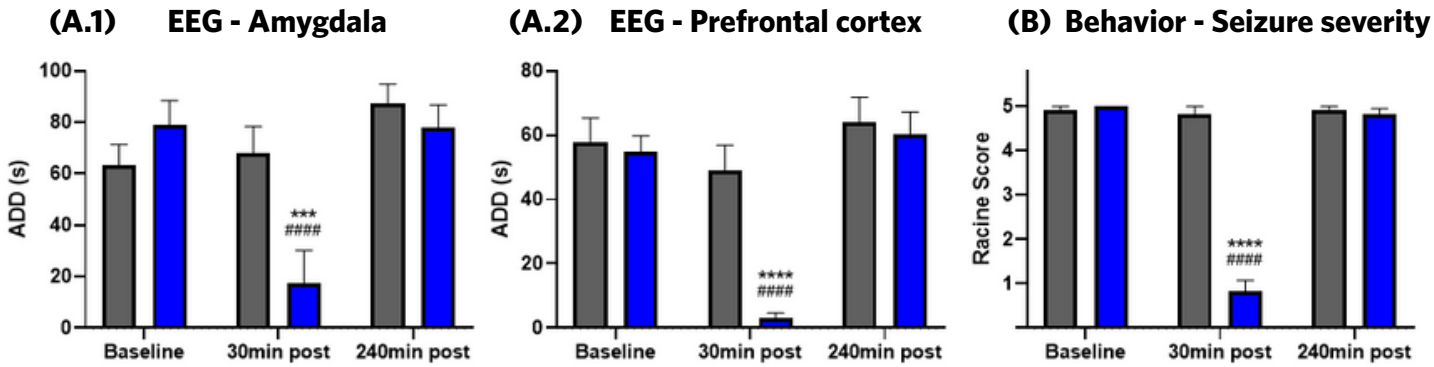

Fig. 3 *- (A) Mean afterdischarge duration (ADD) values ± S.E.M in the left amygdala complex (A.1) and prefrontal cortex (A.2) at different time points.*
(B) Mean behavioral seizure stage values ± S.E.M at different time points.

Valproate at 200 mg/kg produced seizure control as measured by a reduction in motor components of the seizure and a reduction in ADD at the first time point.