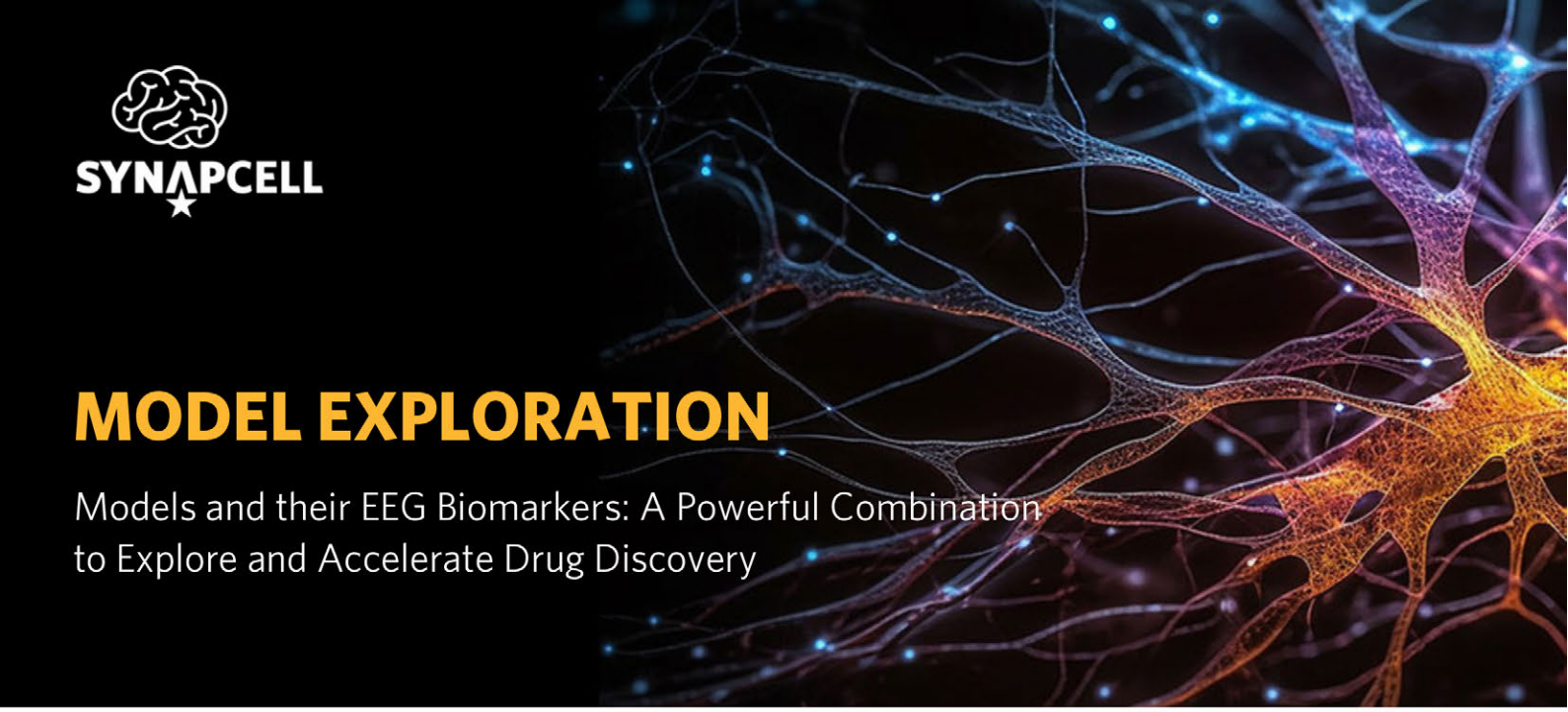


MODEL EXPLORATION

Models and their EEG Biomarkers: A Powerful Combination to Explore and Accelerate Drug Discovery

The Challenges of CNS Models

A large hurdle in drug development is that, although many therapeutics show promising results in rodent models, the therapeutic value does not always translate to human patients in clinical trials. **There is a need to look for a biomarker that is translational, objective and quantitative, in order to maximize chances of success.**

Why EEG Phenotyping ?

EEG Phenotyping consists in identifying, in an animal model, an abnormal brain-wave pattern relevant to the disorder of interest, whether it be common brain disorders or orphan diseases.

Objective & Reliable

SynapCell's EEG technology is stable in time, can be recorded in rodents and humans alike. The technology is even sensitive enough to distinguish brain activity between genders.

Improve Model Predictability

SynapCell's powerful model exploration solution allows you to carry out reverse translational studies by replicating in rodents what can be seen in humans.

A True Drug Discovery Tool

A translational model & biomarker can be used to better understand mechanisms leading to CNS diseases, validate drug targets, and provide the necessary confidence that a therapy will ultimately benefit patients.

How Do We Phenotype a Model?

Biomarker Identification

- Identify or confirm a disease phenotype
- Can be based on litterature or investigated in an unexplored model

Biomarker Validation

- Reverse with reference compounds, to investigate the pharmaco-sensitivity of the pattern
- Convert aberrant EEG oscillations into a relevant biomarker

Compound Testing

- Discriminate the level of efficacy of different compounds

Case Study: Characterizing a Genetic Model

Step 1

Electrode **implantation**
Model selection (EEG)

Step 2

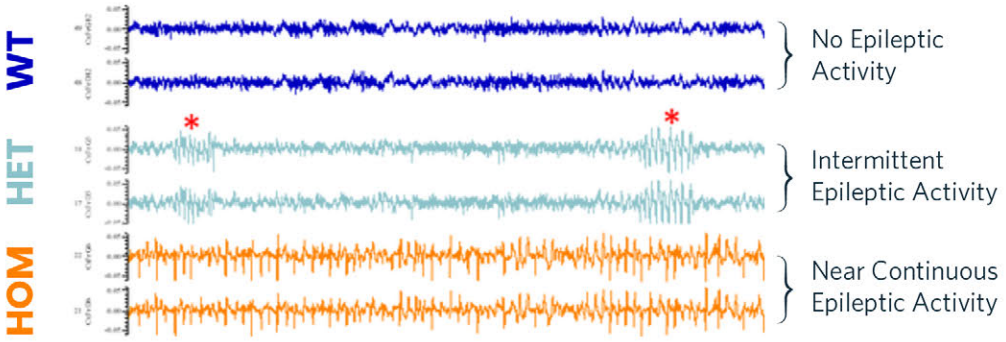
EEG recording

Step 3

Epileptic activity : **Qualitative** evaluation **Quantitative EEG** of entire signal

Qualitative & Quantitative Results

Qualitative Evaluation



The epileptic activity of this model is intermittent in the case of Het mice and near continuous in the case of Hom. mice. It seems that the number of copies of the mutation is proportional to the epileptic activity.

***Fig 1**. Pattern categories vs phenotypes of Heterozygote and Homozygote mice. Red stars : cluster of epileptic discharges.*

Quantitative EEG of Entire Signal

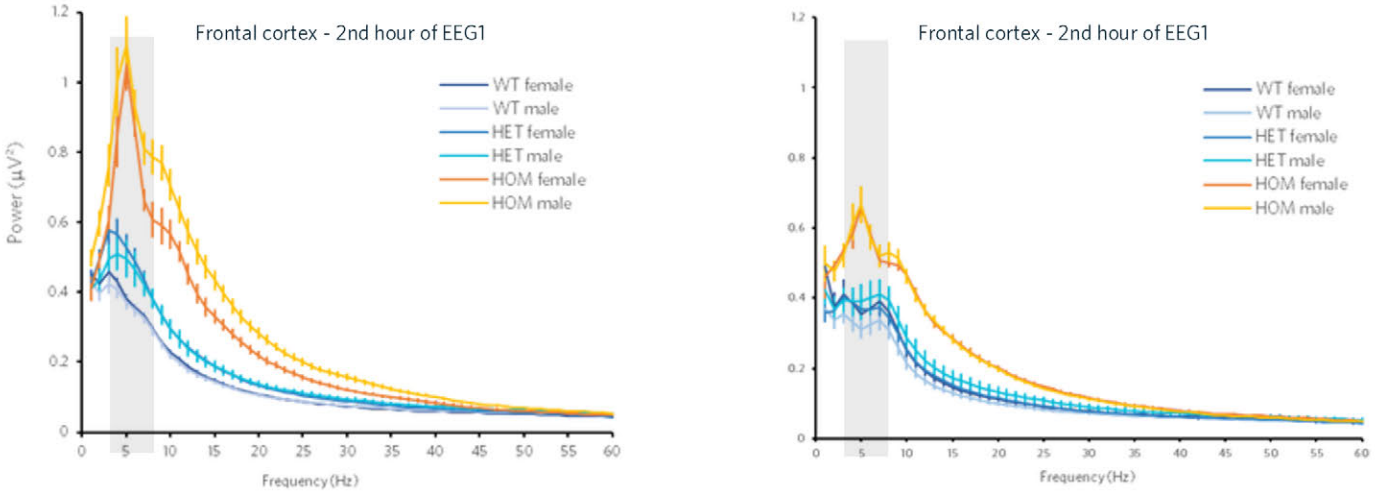


***Fig 2.** EEG Power spectra of Frontal cortex (left) and Parietal cortex (right) in Het male and female mice and Hom male and female mice.*

A clear gradation in power can be observed in the frontal cortex between 4 and 30 Hz, from the WT spectrum at the lowest power to the Homozygote spectrum at the highest. This power increase is found in the parietal cortex but to a lower extent.