

Differential effect of neuropeptides on excitatory synaptic transmission in human epileptic hippocampus

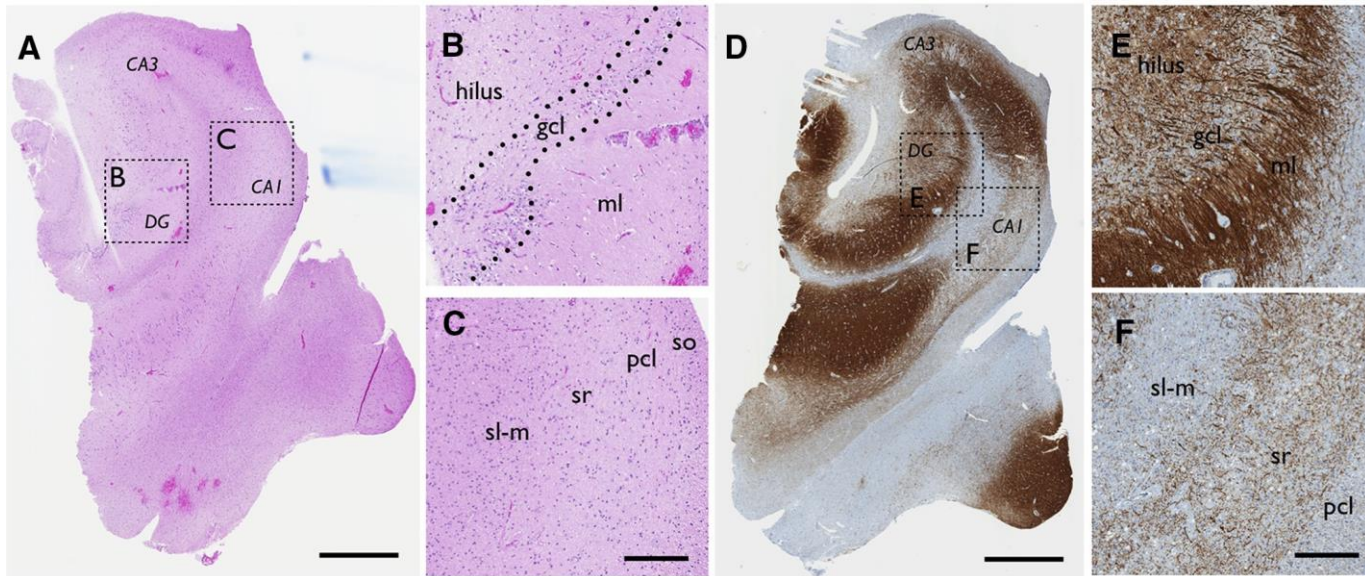
Marco Ledri, PhD

Lund University - Epixchange

Neuropeptides

- Neuropeptide Y (**NPY**) and **galanin** are small endogenous peptides with seizure-suppressant properties
- They **reduce** pre-synaptic **glutamate** release
- Tested both *in vitro* and *in vivo*, in several **animal models**
- Delivered via **AAV** and expressed in epileptic focus
- Proposed as candidates for clinical trials in humans
- What are their effects on **human pharmaco-resistant** epileptic tissue?

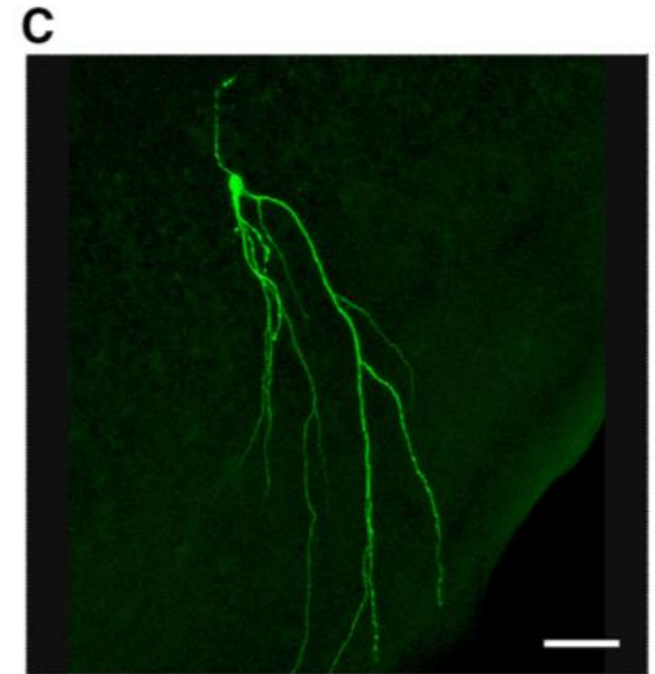
Human hippocampus



- 13 patients
- diagnosed with **pharmacoresistant** temporal lobe epilepsy
- **Hippocampal focus**
- **Sclerotic hippocampus**

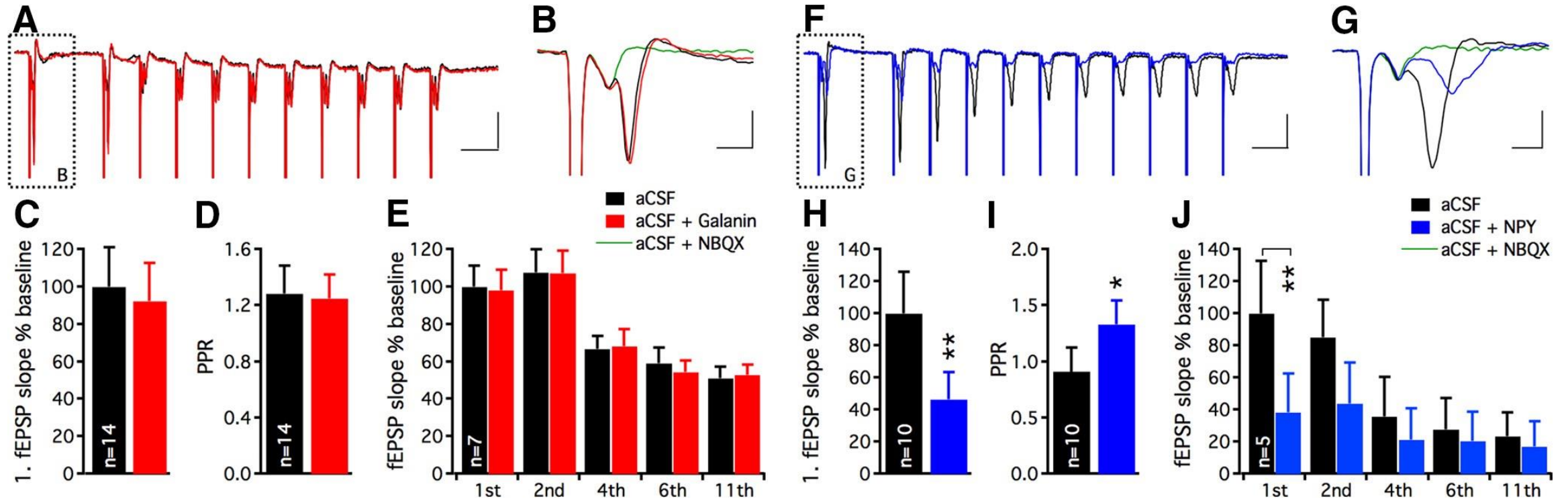
Human hippocampus

- Hippocampal tissue was sliced with a vibratome
- Transferred to electrophysiology setup
- **Single-cell** and **field** recordings
- **NPY** and **galanin** were applied in the bath



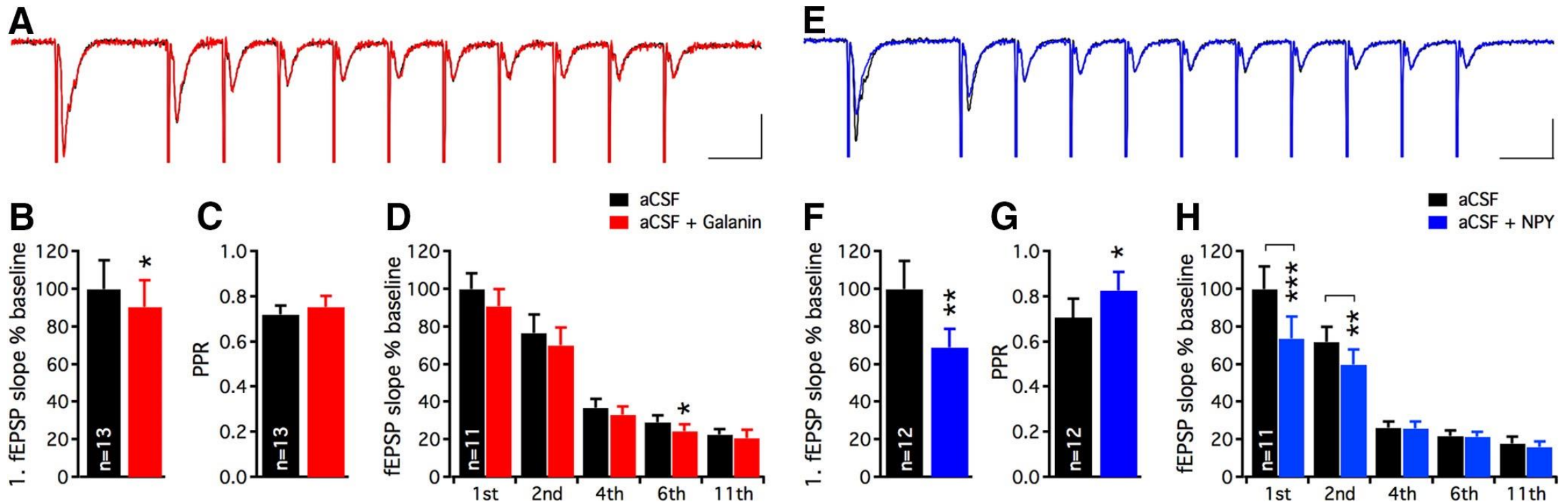
NPY but not galanin decreases glutamatergic synaptic transmission

CA1



NPY but not galanin decreases glutamatergic synaptic transmission

Dentate gyrus

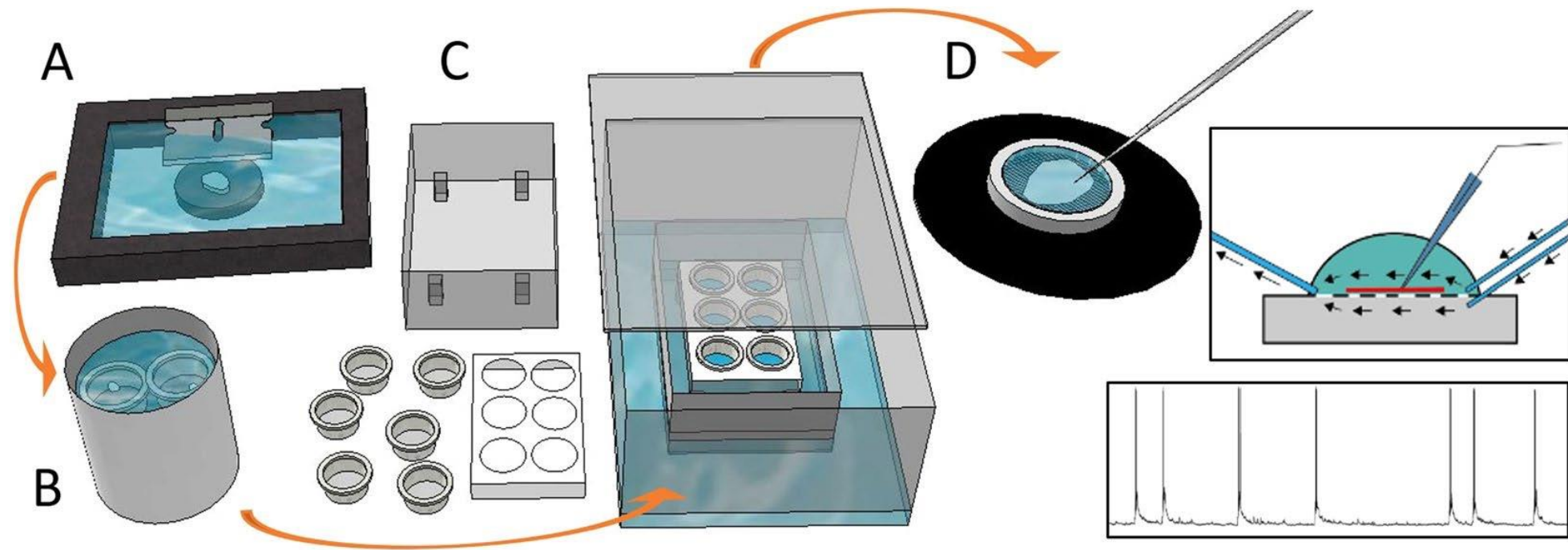


Challenges

- Availability of human resected hippocampal tissue is limited
- Can we extend the viability for increased experimental output?
- Can we induce epileptiform activity?
- Can we test viral vector approaches in human tissue?

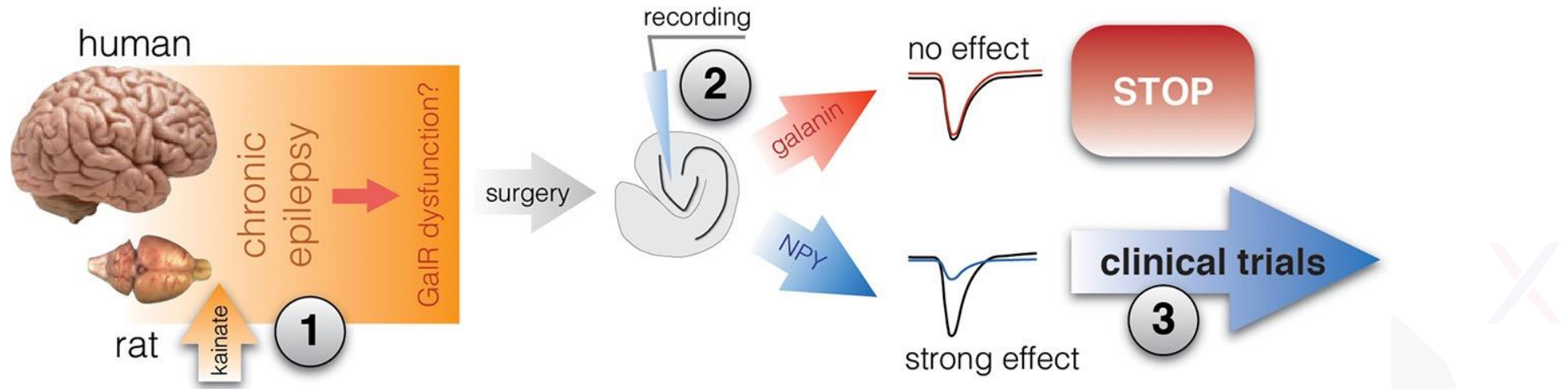


The way forward



Prolonged life of human acute hippocampal slices from temporal lobe epilepsy surgery (Wickham J et al., Sci. Rep. 2018)

The way forward



Translational road-map for clinical trials with gene therapy in epilepsy

Thank you !

Marco Ledri

Marco.Ledri@med.lu.se

