Stiftung zur Förderung der Erforschung von Ersatz- und Ergänzungsmethoden zur Einschränkung von Tierversuchen

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# Project

## Screening and evaluation of antiepileptic compounds in vitro: organotypic cultures of hippocampus as a model of ictaform activity and epileptogenesis

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## *Screening and evaluation of antiepileptic compounds in vitro: organotypic cultures of hippocampus as a model of ictaform activity and epileptogenesis*

In vitro models of pharmacosensitive ictaform activity, pharmacoresistant ictaform activity and epileptogenesis are being developed on the basis of organotypic slice cultures of hippocampal formation with or without entorhinal cortex (Fig. 1). Slice cultures (on average 25/animal) are prepared from 6 to 10-day old rats and cultured under 5%CO2 for up to 3 months. Ictaform activity is induced either by tetanic stimulation of Schaffer collaterals in CA1 (Fig. 2) or by omitting Mg2+ from the medium or adding a K+-channel blocker (Fig. 3). Single neuron and neuron population activities as well as extracellular K+ concentrations are recorded with microelectrodes and ion sensitive electrodes, resp. Effects of drugs are quantified on the basis of certain parameters of ictaform activity (among others: duration and frequency of tonic/clonic ictaform activity, associated changes of extracellular K+ concentrations).
So far we have have worked out a model of pharmacosensitive ictaform activity (tetanic stimulation of the hilus of DG or Schaffer collaterals in CA1; see Fig. 2) and a model of pharmacoresistant ictaform activity (low magnesium or blockade of K+-channels; see Fig. 3).

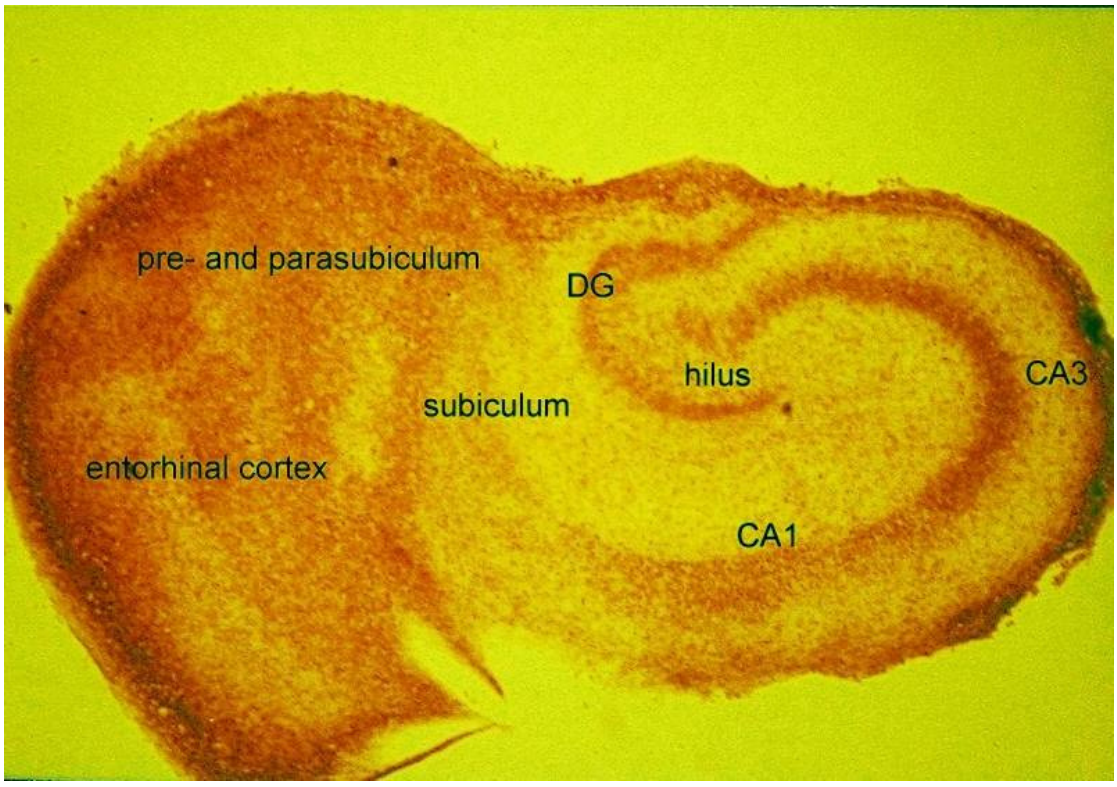


Fig. 1
Organotypic culture of rat hippocampal formation and entorhinal cortex. 10 days in vitro; Nissl stain. DG: gyrus dentatus.

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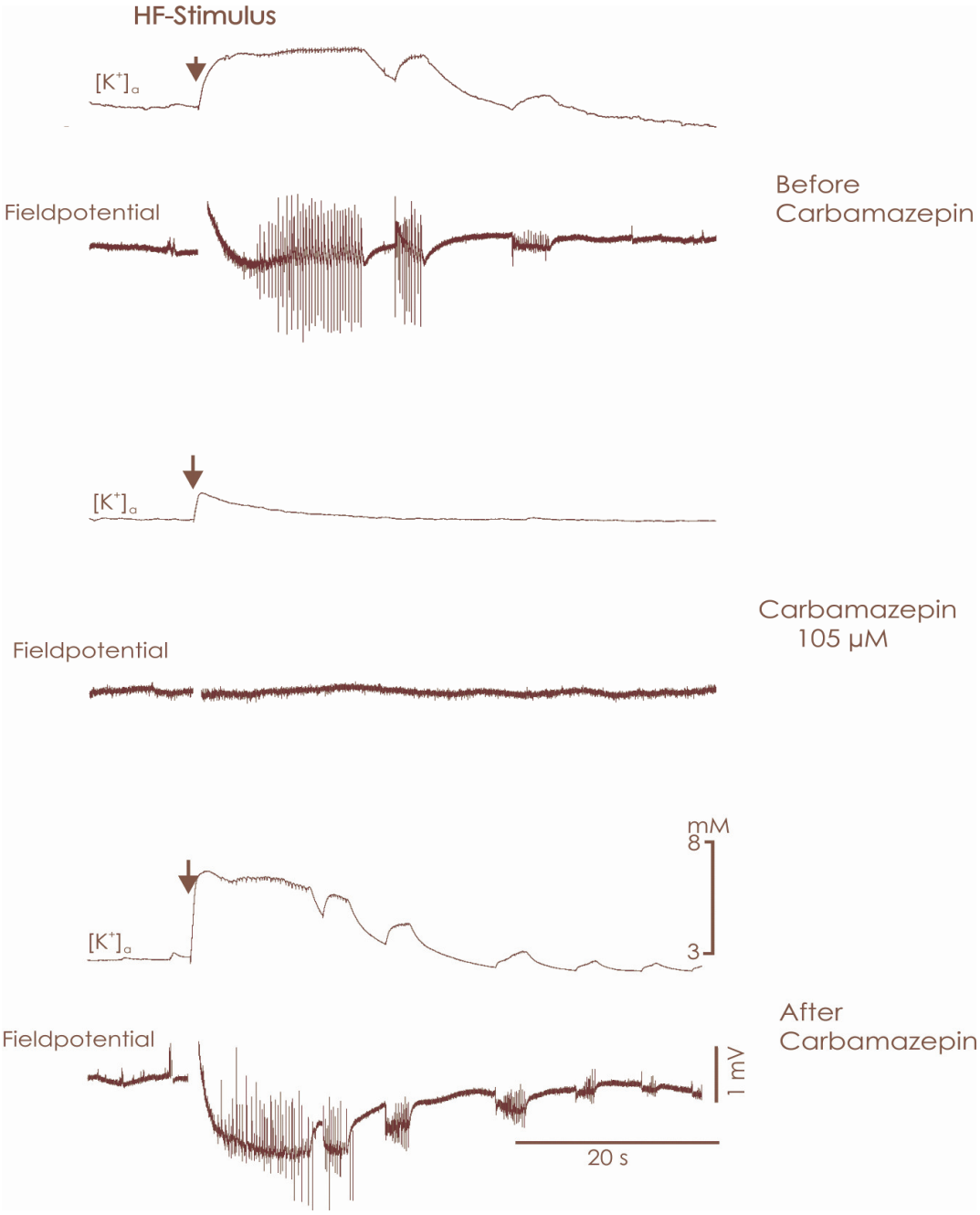


Fig 2.
Carbamazepine (105 µM) suppresses ictaform activity induced by high frequency stimulation (HF-Stimulus) of Schaffer collaterals in CA1 of hippocampus. $[K^+]_o$ : extracellular potassium concentration.

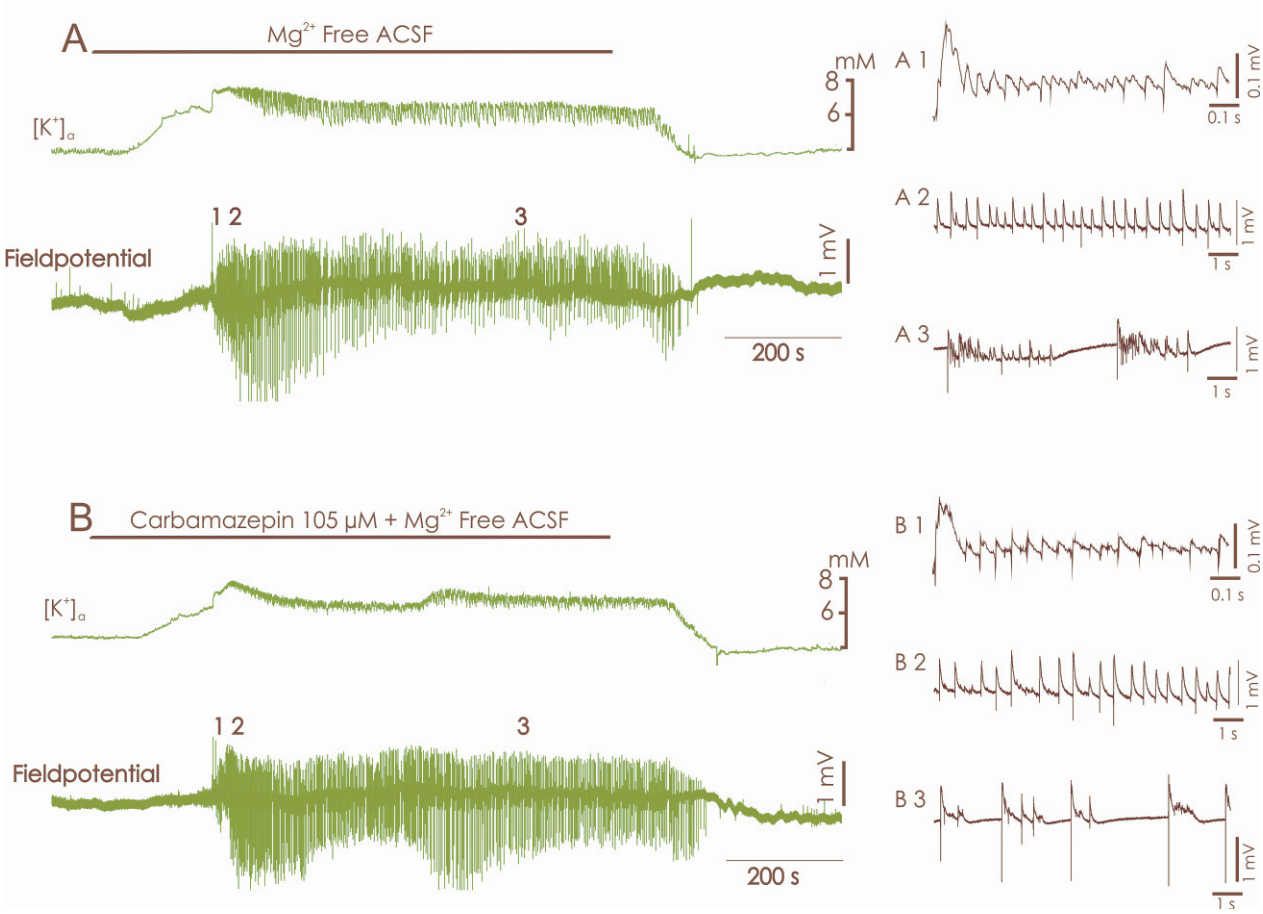


Fig.3
Carbamazepine (105 µM) does not block induction of ictaform activity induced by low magnesium. Clear drug effects are nevertheless present: The frequencies of field potential oscillations during the tonic phase decrease (compare A1 and A2 with B1 and B2, resp.; clonic events increase in frequency and decrease in duration (compare A3 with B3). Same experiment as in Fig. 2. $[K^+]_o$ : extracellular potassium concentration.

***Literature:***

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