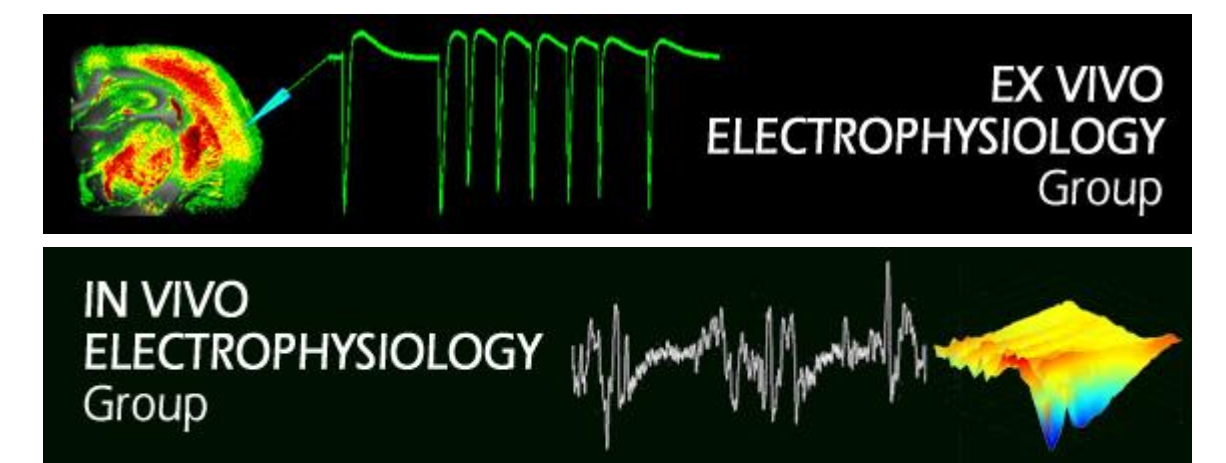


Fumonisin B1 alters the sensitivity of neuronal networks after acute treatment



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Introduction

Fumonisin B1 (FB1) is a mycotoxin produced by microscopic moulds (mostly *Fusarium* species) which **may** infect our major crops. The toxin **can** inhibit the development of these plants but **may have** also harmful effects on the animals or humans consuming the infected crops.

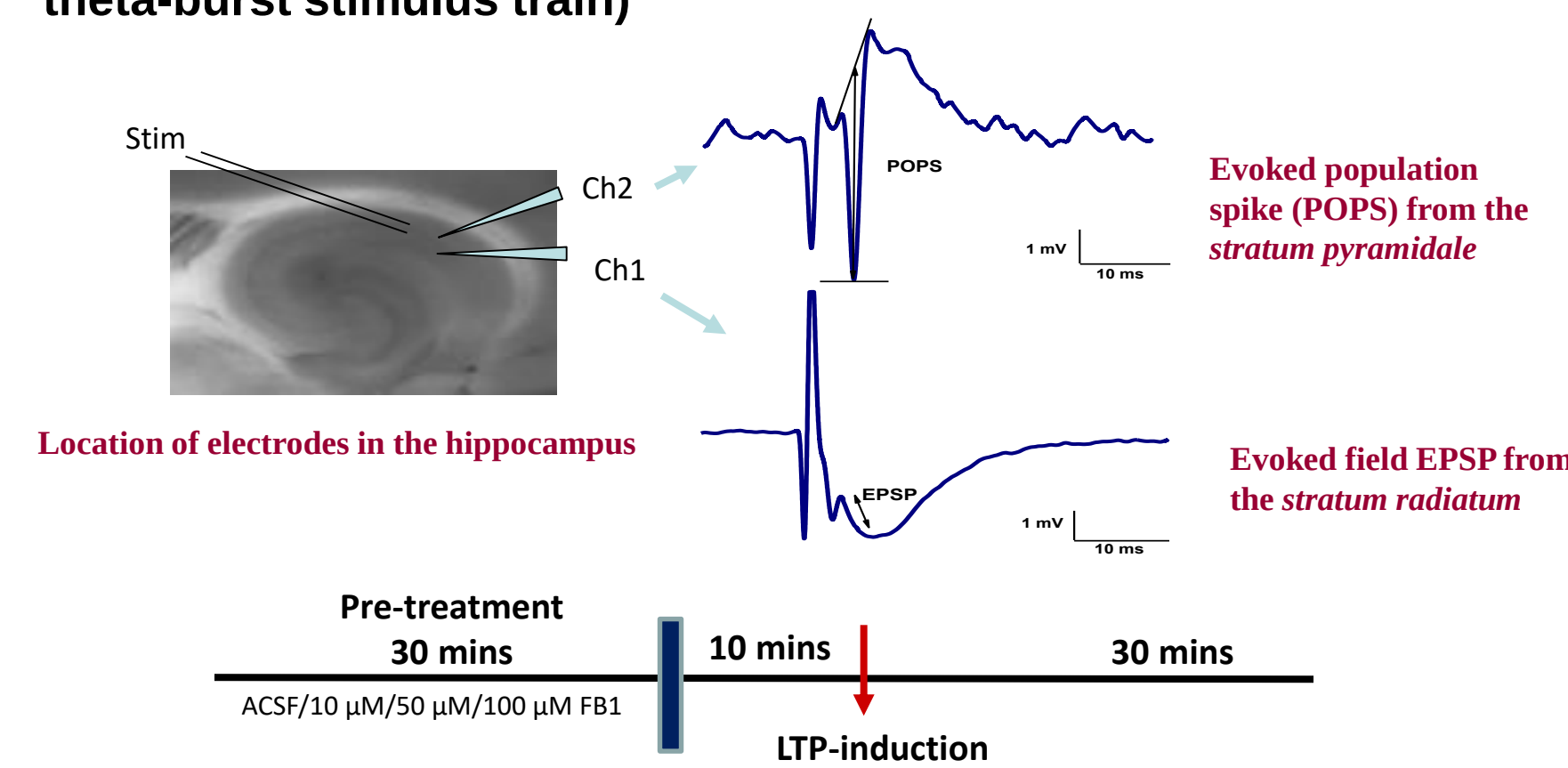
The main mechanism of action of FB1 is the alteration of sphingolipid biosynthesis which leads to impaired membrane characteristics and thus altered neuronal functions. It has been known that the toxin has inhibitory effects on neuronal network activities in case of chronic consumption, but according to new calcium imaging data, it has also acute excitatory effects on neural cell cultures. After these studies, we decided to examine with electrophysiological methods whether FB1 alters neuronal network activities *ex vivo* or *in vivo* after acute treatment.

Materials & methods

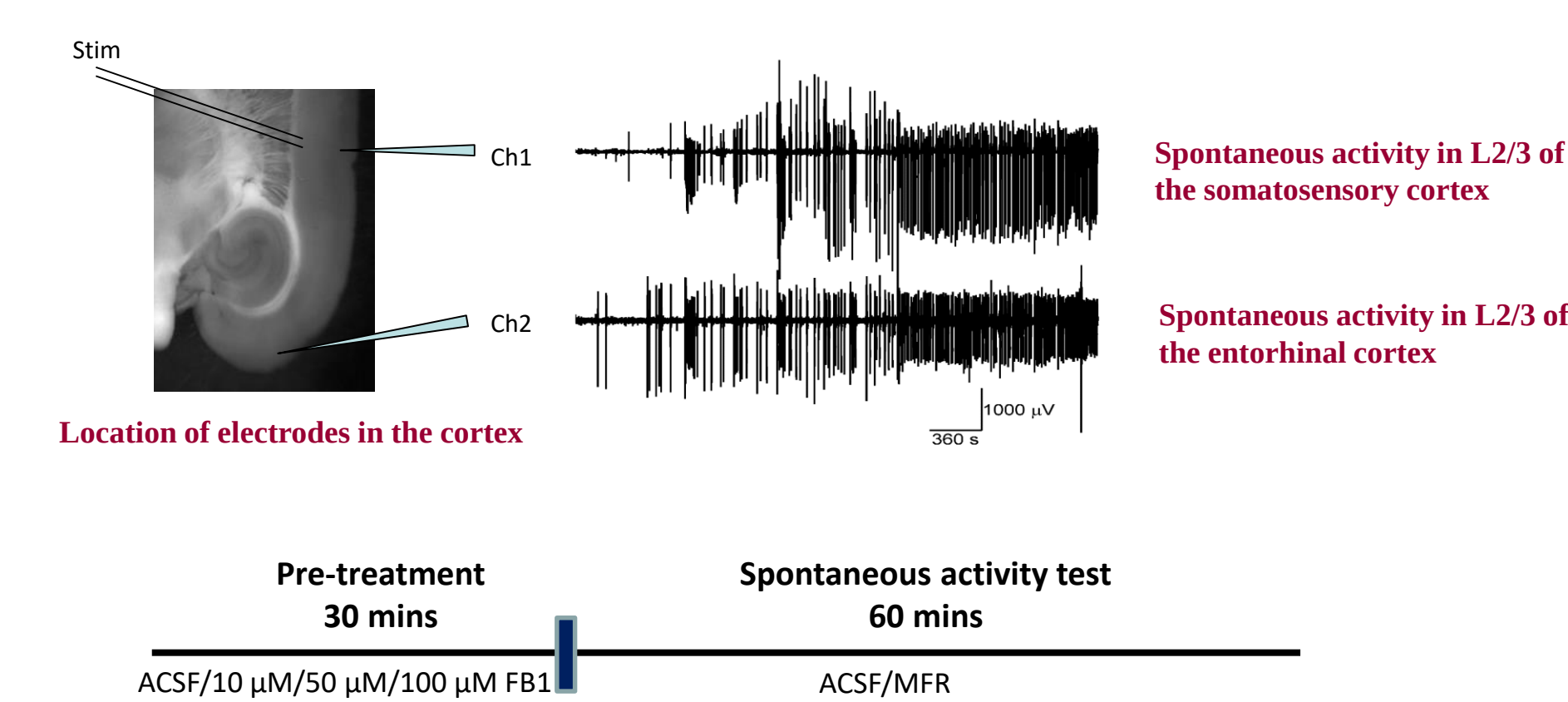
Ex vivo electrophysiology

- Male Wistar rats (age of 1.5 – 3 month)
- 400 μm thick surviving brain slices
- Pre-treatment for 30 mins with 10, 50 or 100 μM FB1-containing ACSF (artificial cerebro-spinal fluid)
- Recording of electrically evoked and spontaneous field potentials

- Coronal sections for hippocampal recording
- Registration of FB1-effects on long-term potentiation (LTP, induced with a special theta-burst stimulus train)



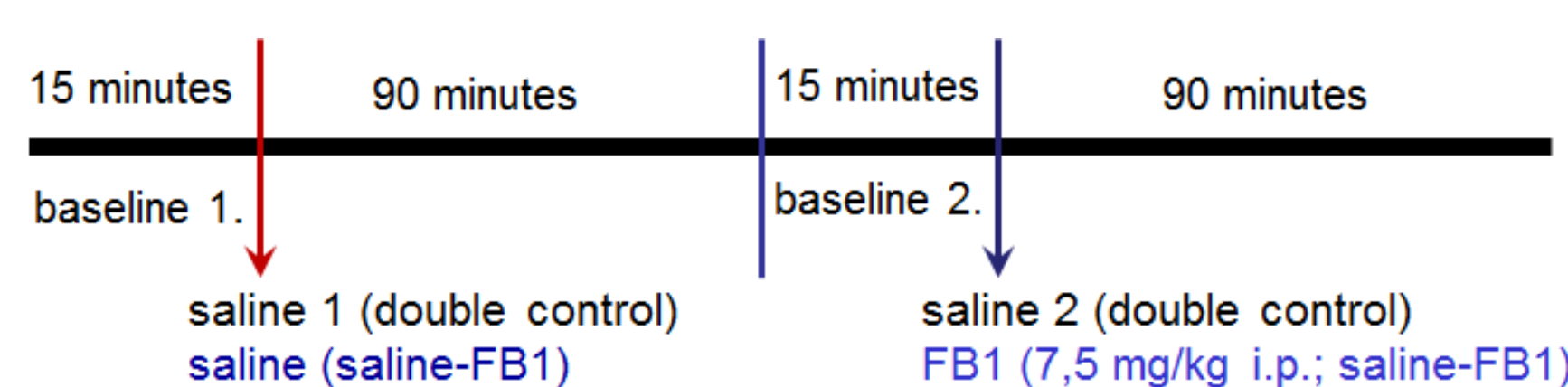
- Horizontal sections for recording from the secondary somatosensory and lateral entorhinal cortices
- Registration of FB1-effects on epileptiform activity (induced with magnesium-free ACSF – MFR)



- Statistical analysis: one-way ANOVA with Student-Newman-Keuls post hoc test
- $p < 0.05$ *
- $p < 0.01$ **
- $p < 0.001$ ***

In vivo electrophysiology

- male Wistar rats (300-465 g; $n=12$)
- urethane anesthesia (1.2 g/kg i.p.)
- i.p. injection with saline or 7.5 mg/kg FB1
- two rat groups: saline-saline (double control; $n=6$) and saline-FB1 ($n=6$)
- evoked field potential (EFP) registration in the hindlimb area of the S1 after stimulation of the tibial nerve (frequency: 0.1 Hz)
- 210 minutes-long recordings

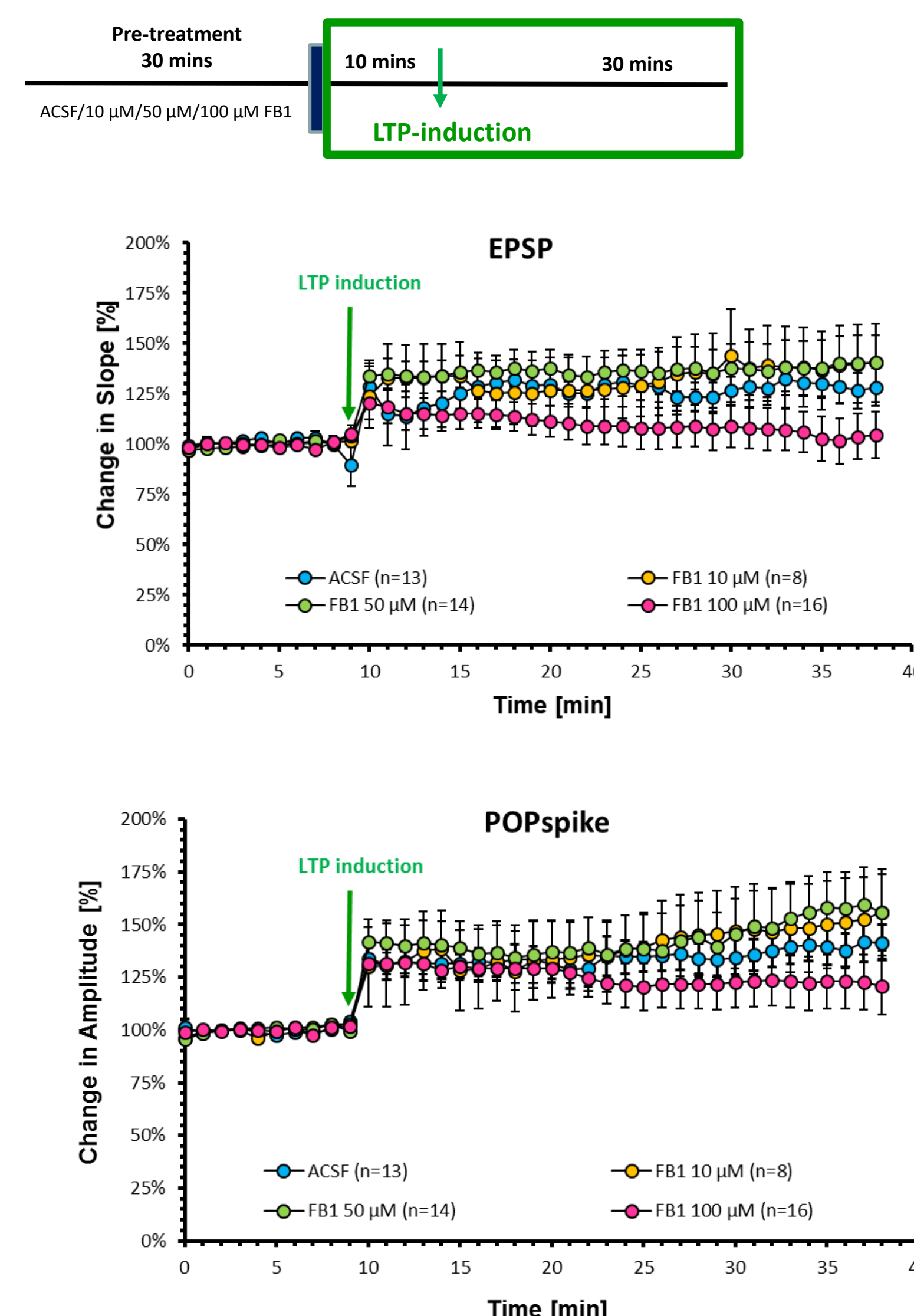


- EFP analysis: amplitude, latency, slope (first 3.5 ms of the responses), AUC (area under the curve; integral; first 21 ms-long epoch of the EFPs) calculation
- statistical analysis: one-way ANOVA with Student-Newman-Keuls *post hoc* test

Results

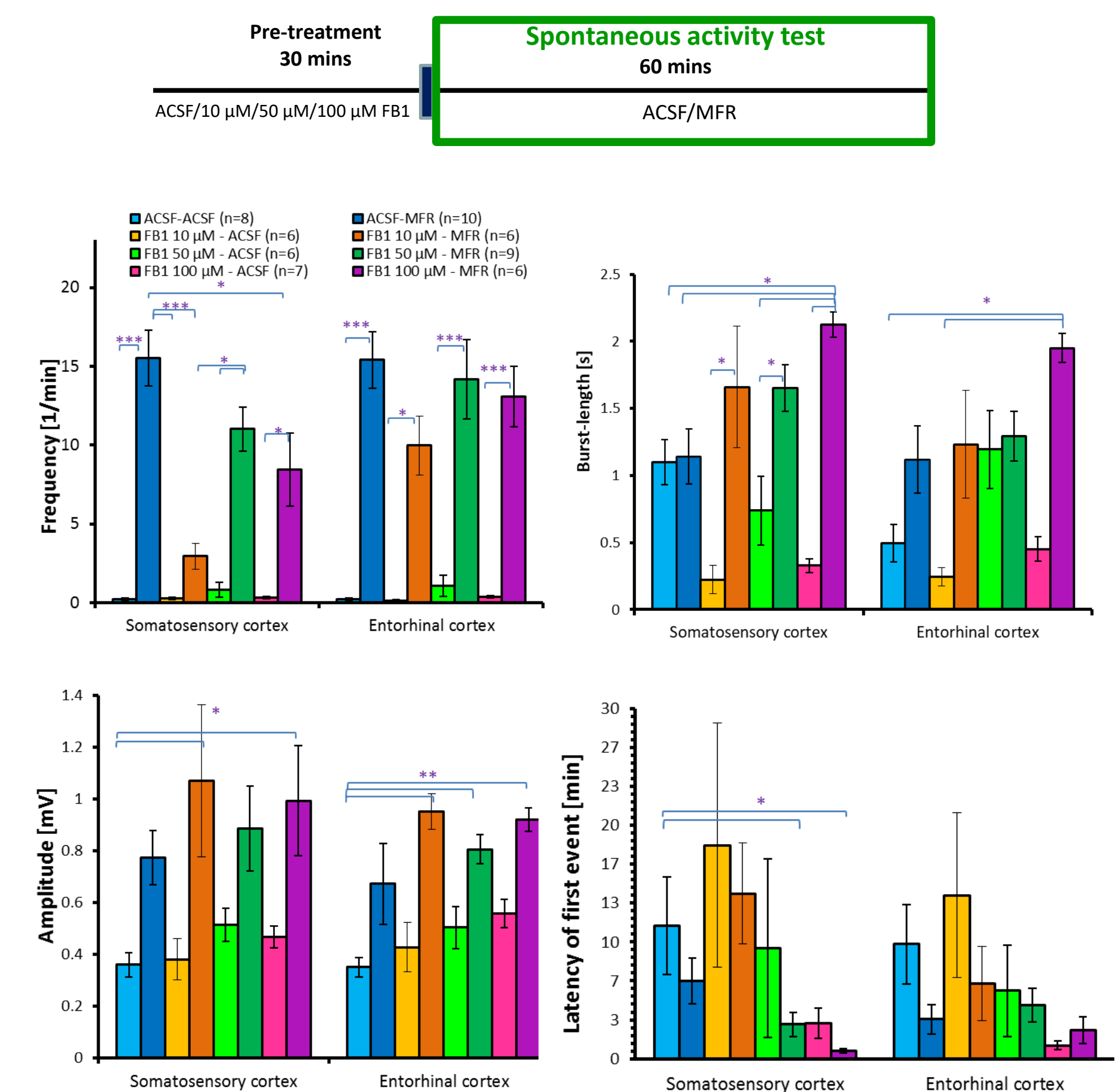
Ex vivo electrophysiology

LTP in hippocampus



Hippocampus: treatment with the lower concentrations of FB1 tended to increase the effect of the potentiation. In contrary, treatment with the higher FB1 dose tended to inhibit the maintenance of LTP.

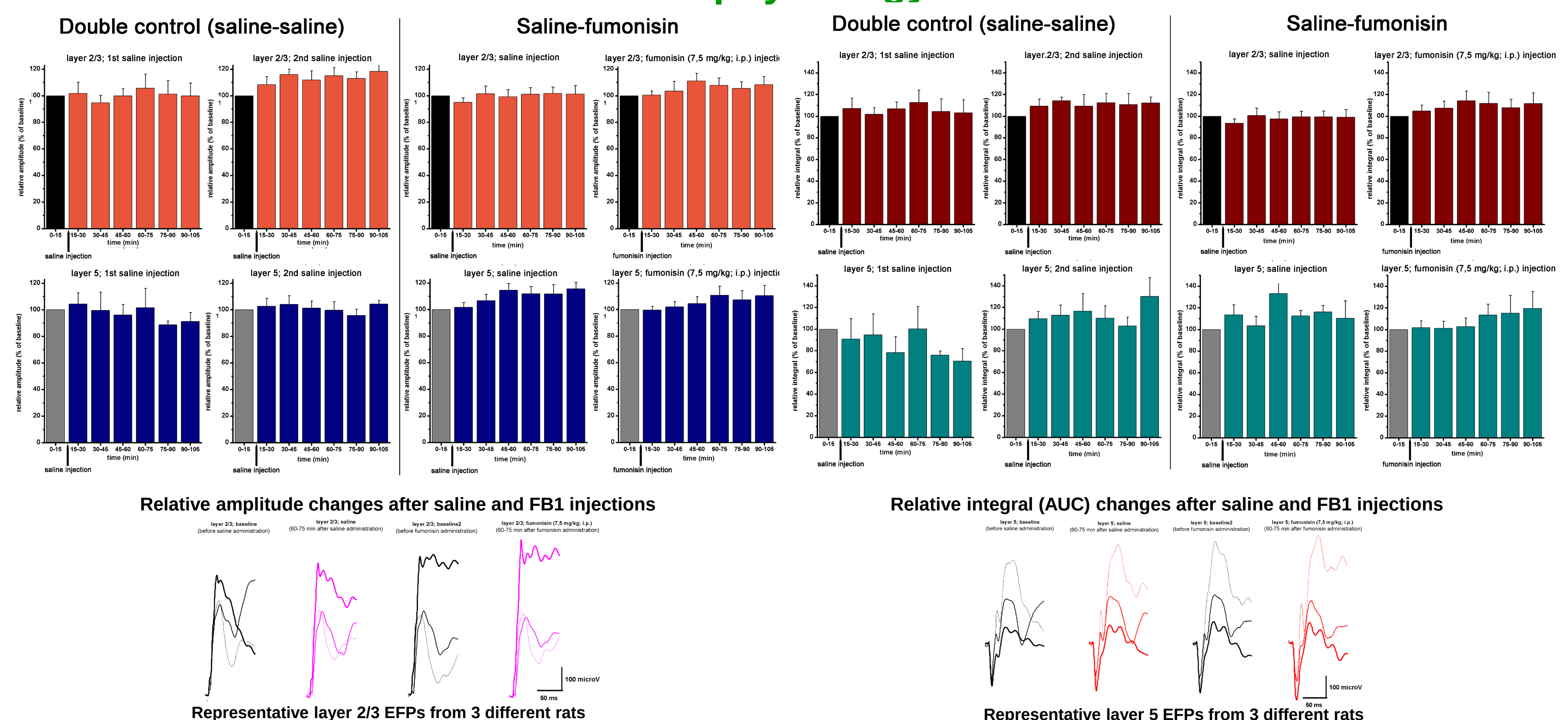
Epileptiform activity in the cortex



Cortex: MFR, as expected, increased the frequency of events and amplitude of bursts which appear earlier compared to those recorded in ACSF.

FB1 treatment clearly altered the effects of MFR. Frequency of events became lower because of the increasing length of bursts. Furthermore, the amplitude grew and latency times became shorter.

In vivo electrophysiology



No significant changes were found in any of the somatosensory EFP parameters analyzed (amplitude, latency, slope, AUC) after saline as well as FB1 injections (7.5 mg/kg i.p.) compared to corresponding baseline (pre-injection) values. Small, non-significant deviations of the analyzed EFPs parameters can be attributed to the fluctuations of anesthetic depth over time.

Discussion

We confirmed that FB1 has acute excitatory effects on neuronal networks after direct *ex vivo* exposure of rat brain slices to toxin-containing ACSF. Efficacy of LTP-induction was altered in a concentration-dependent fashion and epileptiform activity evoked with MFR was enhanced. Although the current experiments do not provide information concerning the exact molecular mechanism of action, our results may be explained by the previously described phenomenon that FB1 exerts an excitatory effect on neurons by elevating intracellular Ca^{2+} concentration. In future we plan to examine this effect on the single cell level with patch clamp recordings.

Acute FB1 treatments in urethane-anesthetized rats *in vivo* did not affect the parameters of somatosensory EFPs. Lack of effect can be explained by different causes. First, FB1 may be ineffective to alter neuronal functions along the involved somatosensory pathway. However, a more likely explanation can be that FB1 could not penetrate across the blood-brain barrier (BBB) to yield effective concentration in the central nervous system at healthy conditions *in vivo*. Thus, FB1-evoked changes seen during *ex vivo* experiments may be prominent when BBB functions are corrupted due to different pathological conditions.

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