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The Acute Effects of Fumonisin B1 on Brain Slice Preparations

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MOMENTUM OF INNOVATION

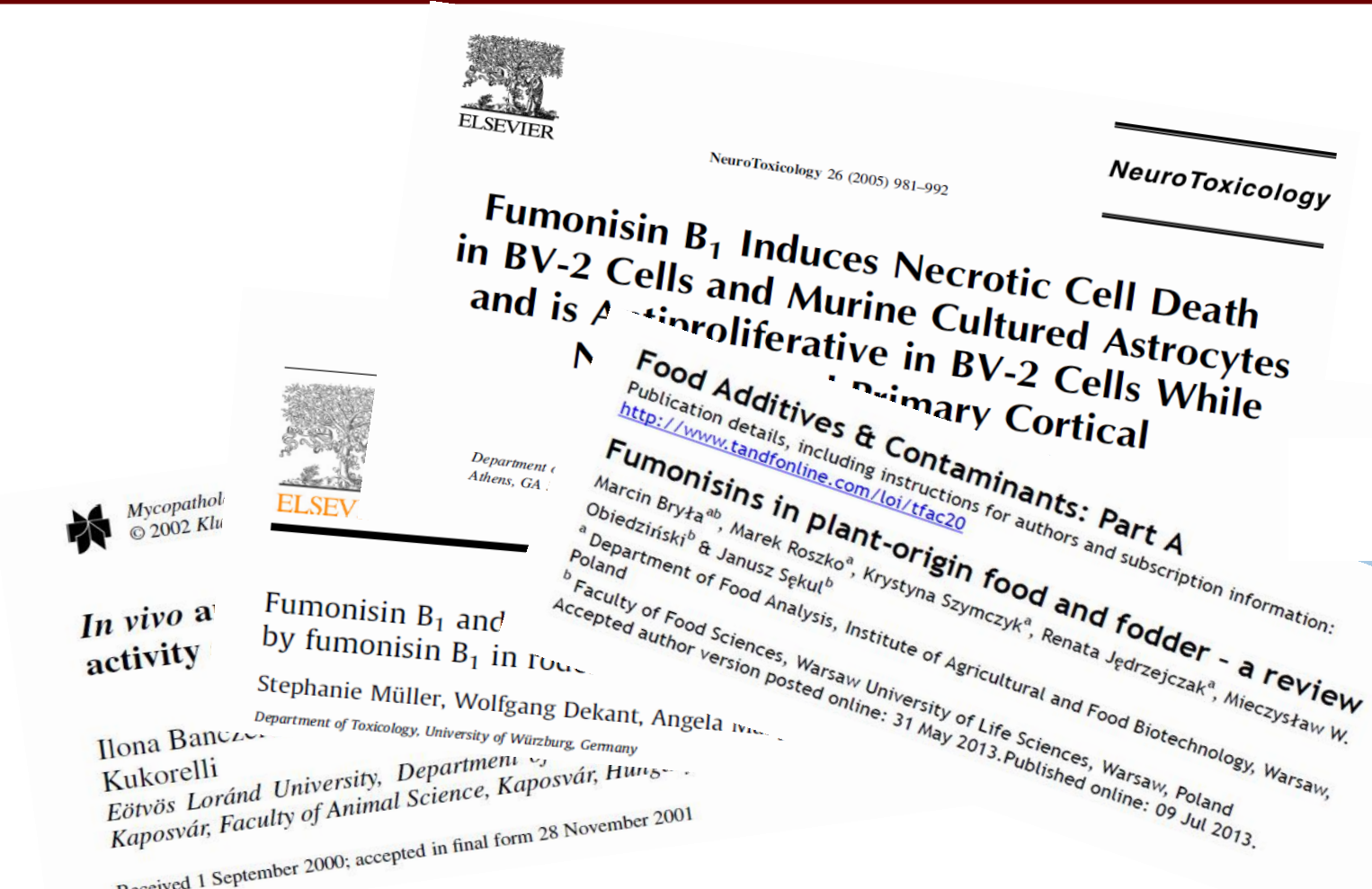
Introduction

Fumonisin B1 (FB1) is a mycotoxin produced by *Fusarium* species. These moulds are spread worldwide and infect our most important crops; toxins may be present even in processed food. Mycotoxins have harmful effects on the health of humans and animals, thus they constitute a serious public health and economical issue.

It is well-known that FB1 disturbs sphingolipid biosynthesis, thus impairs the structure of cell membranes and alters myelinisation¹; this explains its effects on nervous system. With chronic intake FB1 can influence the processing of sensory information, spinal reflexes and learning processes^{2,3}. Recent research revealed that the toxin has also direct acute excitatory effects on neuronal cultures; it increases intracellular calcium concentration⁴.

In this study we intended to examine if the toxin also had similar effects on brain slice electrophysiology.

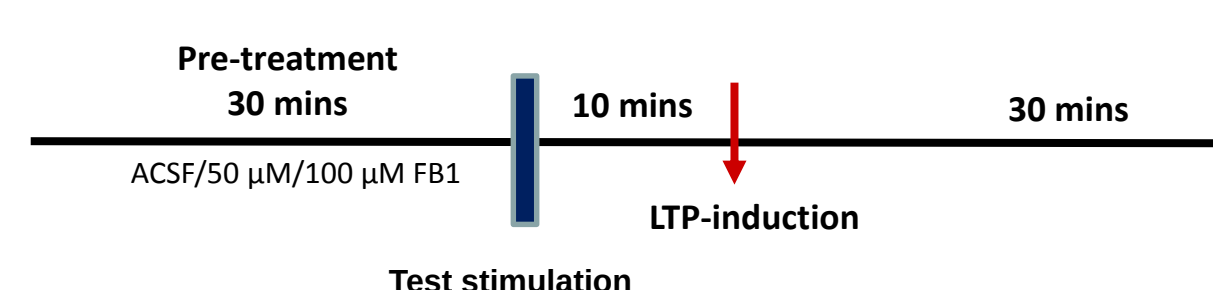
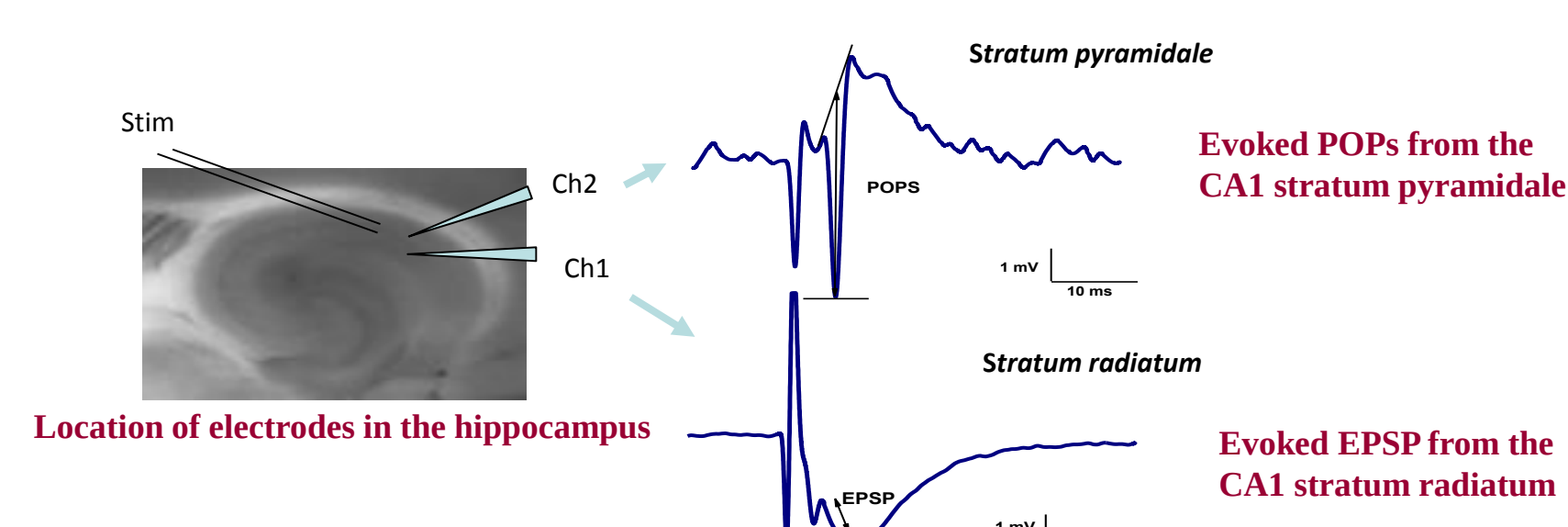
Citations: ¹Stockmann-Juvala H., Savolainen K. (2008), *Human & experimental toxicology*, 27, 11: 799–809.
²Banczerowski-Pelyhe et al. (2002), *Mycopathologia*, 153, 3: 149–56.
³Banczerowski-Pelyhe et al. (2008), *Cerebral Research Communications*, 1947–1950.
⁴Domijan et al. (2012), *Neuroscience*, 202, 10–6.



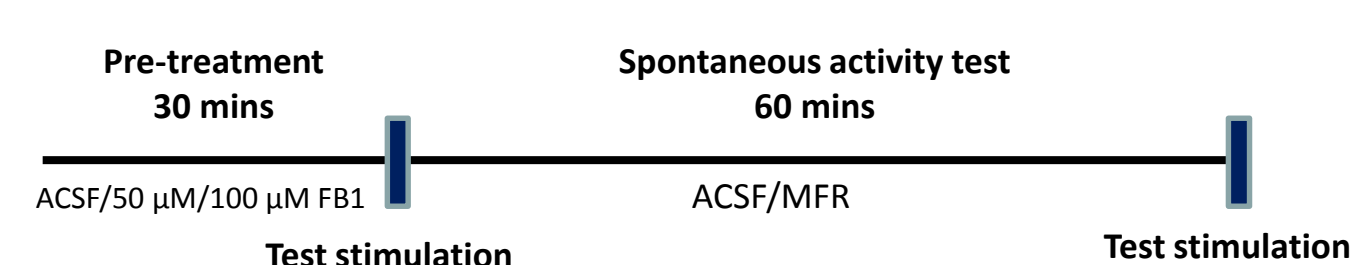
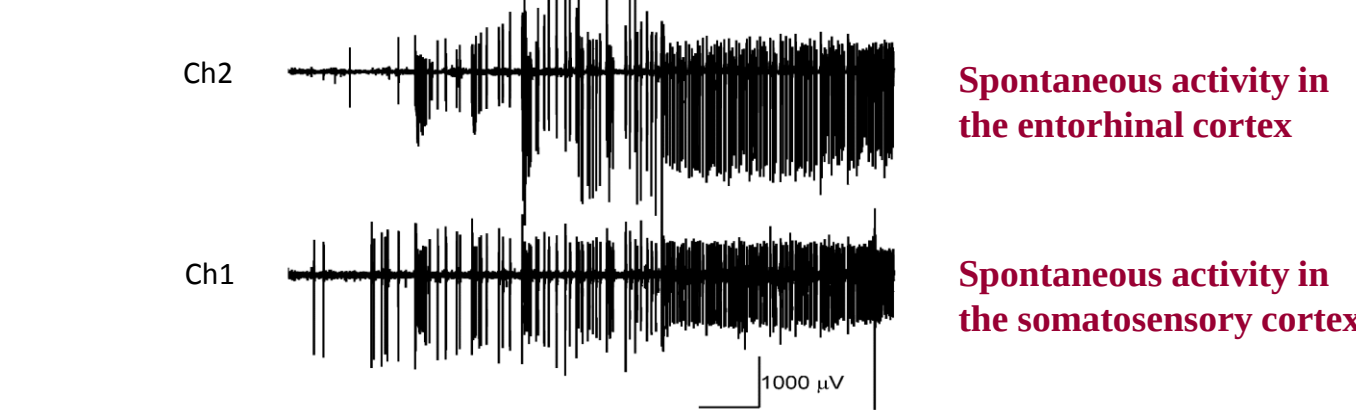
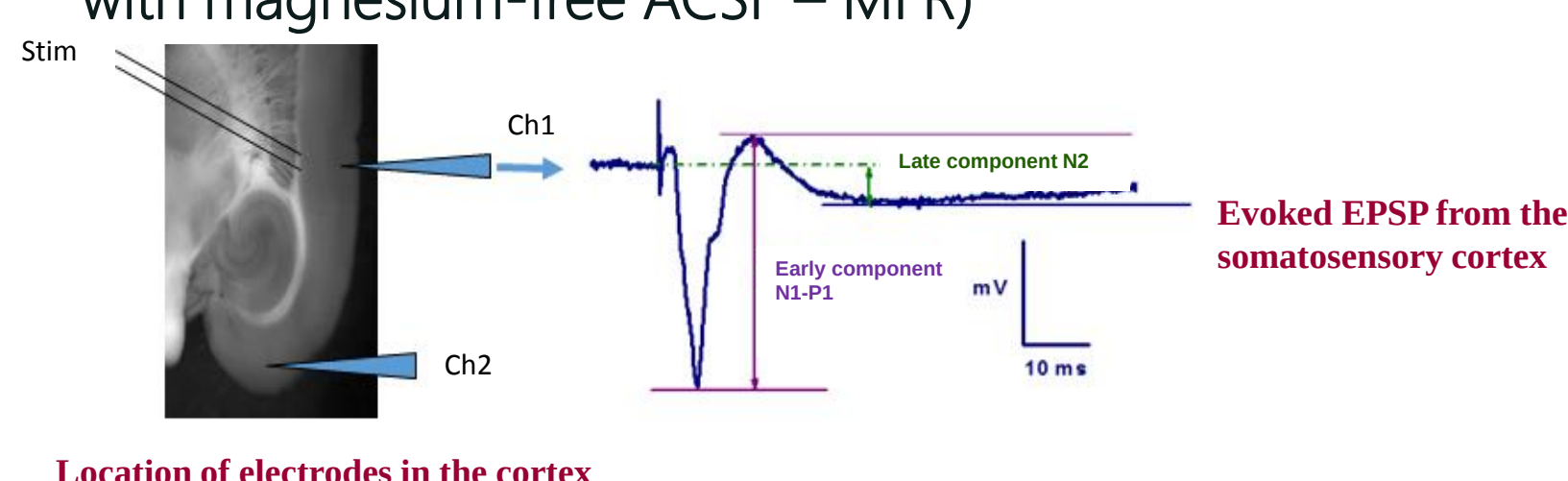
Materials & methods

- Male Wistar rats (age of 1.5 – 3 month)
- 400 μm thick surviving brain slices
- Pre-treatment for 30 mins with 50 μM 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)



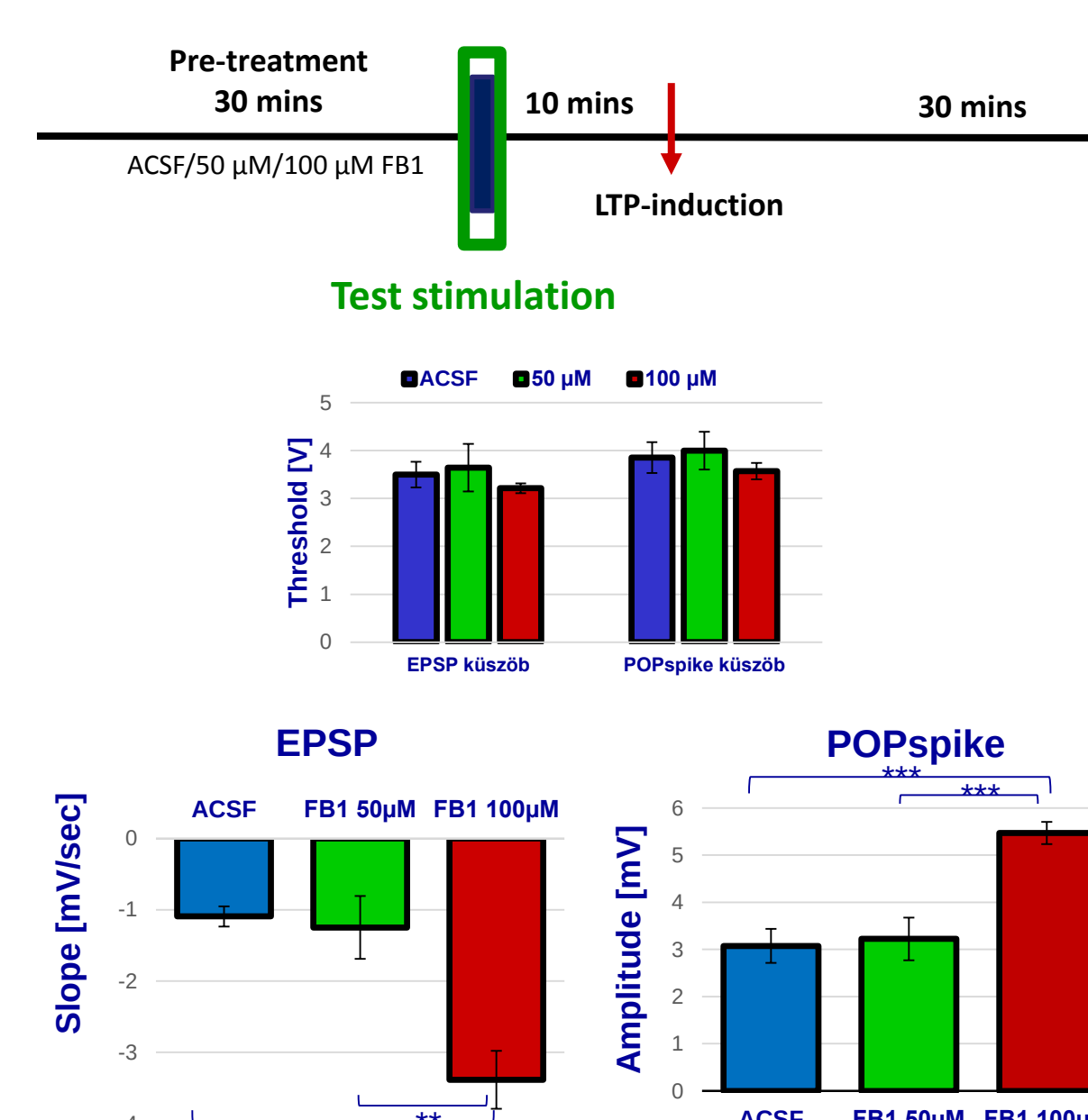
- Horizontal sections for recording from the secondary somatosensory and lateral entorhinal cortices
- Registration of FB1-effects on epileptiform activity (induced with magnesium-free ACSF – MFR)



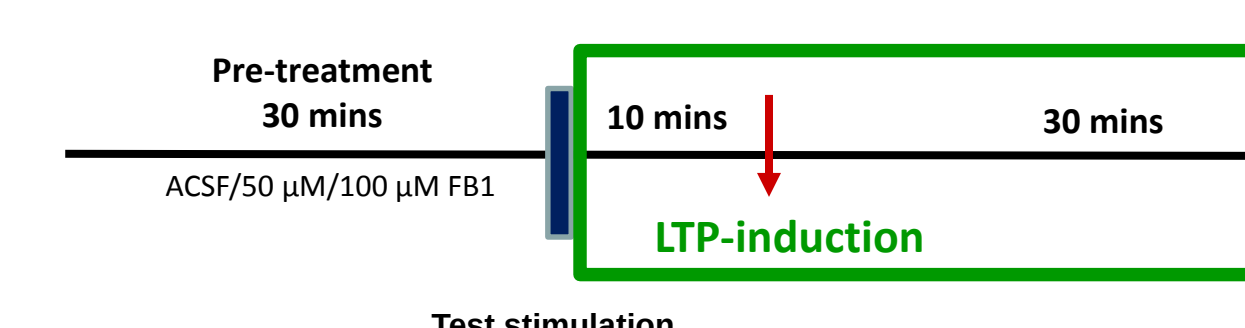
- Statistical analysis: two-sample t-test:
 - $p < 0,05$ *
 - $p < 0,01$ **
 - $p < 0,001$ ***

Results

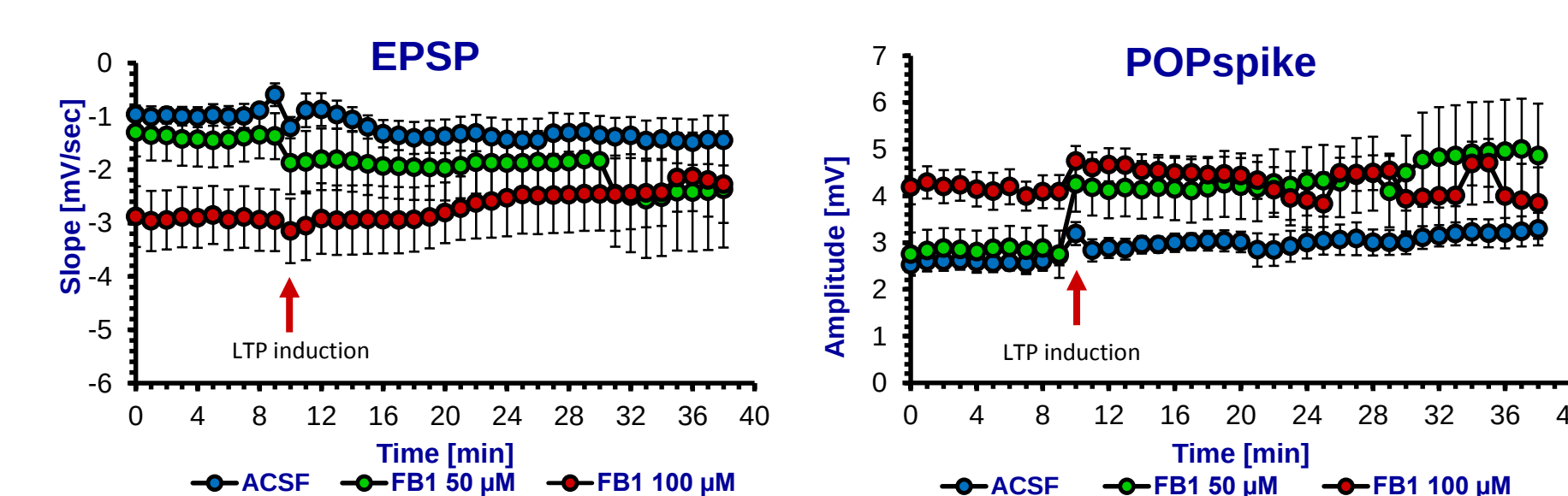
Hippocampus



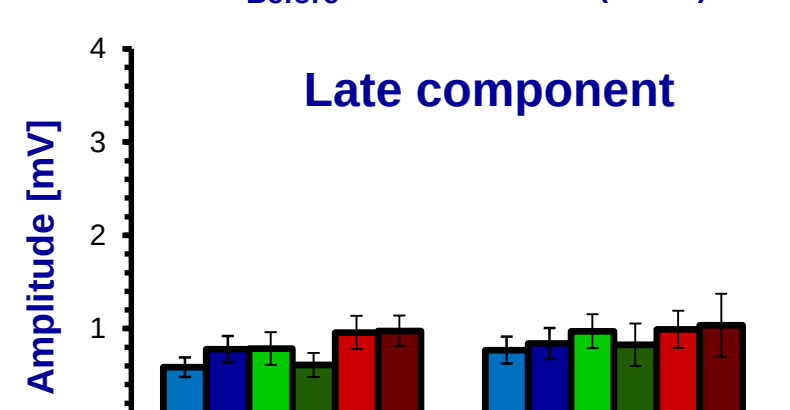
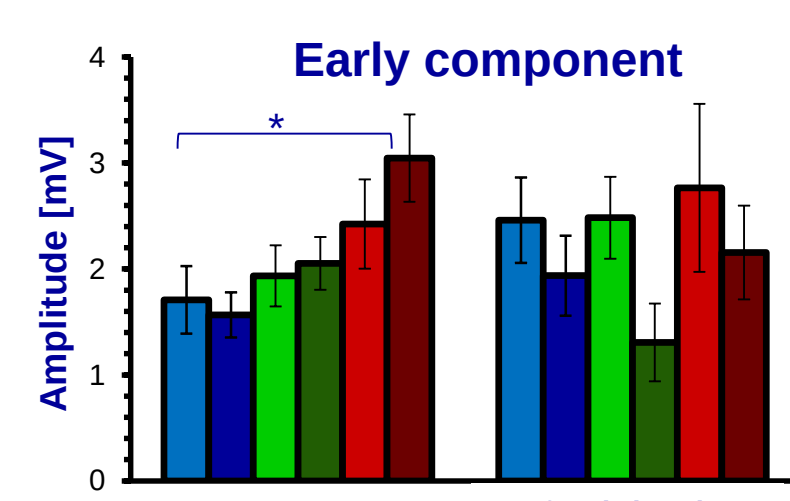
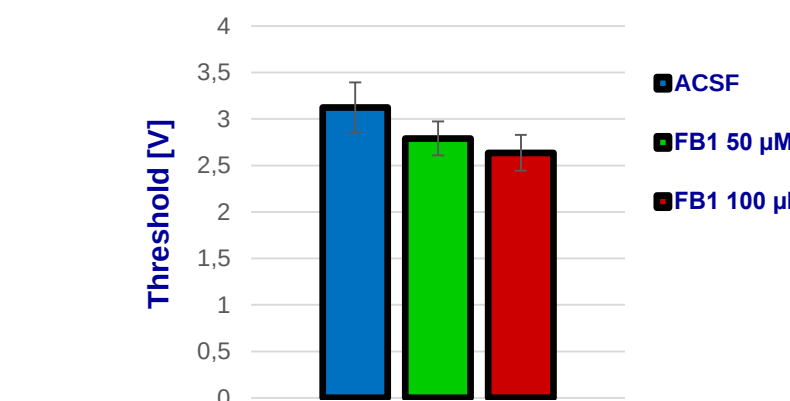
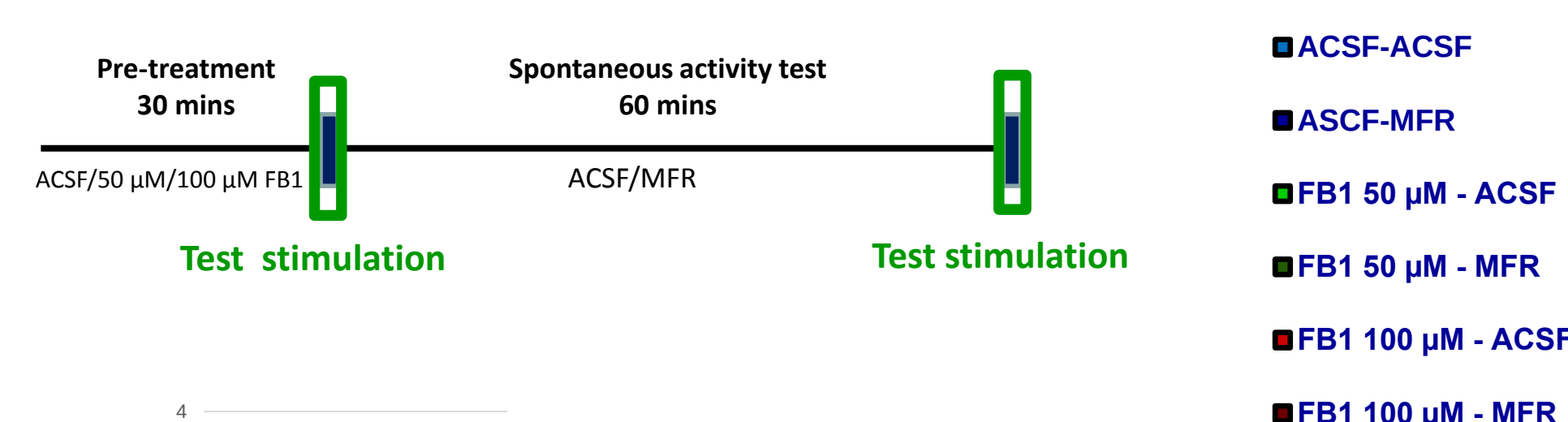
Although stimulation thresholds were similar in each treatment group, we can see significant differences in the amplitudes of evoked potentials according to the toxin concentrations, right after the pre-treatment.



Treatment with the lower concentration of FB1 doesn't change the basic activity but increases the effect of the potentiation. In contrary, treatment with the higher FB1 concentration increases only the basic activity of neurons but inhibits the potentiation.



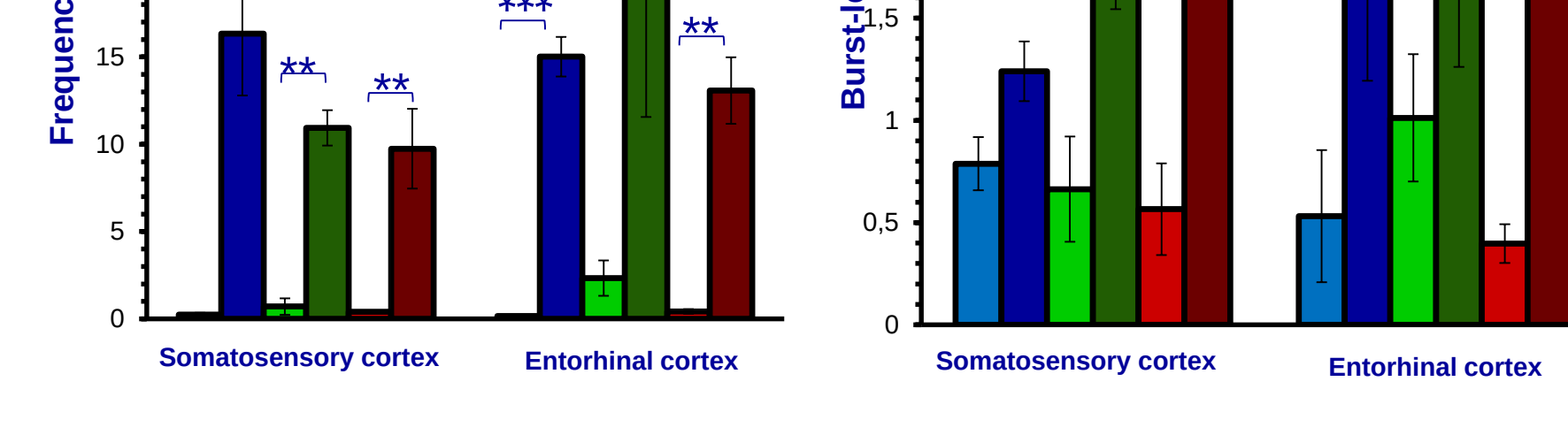
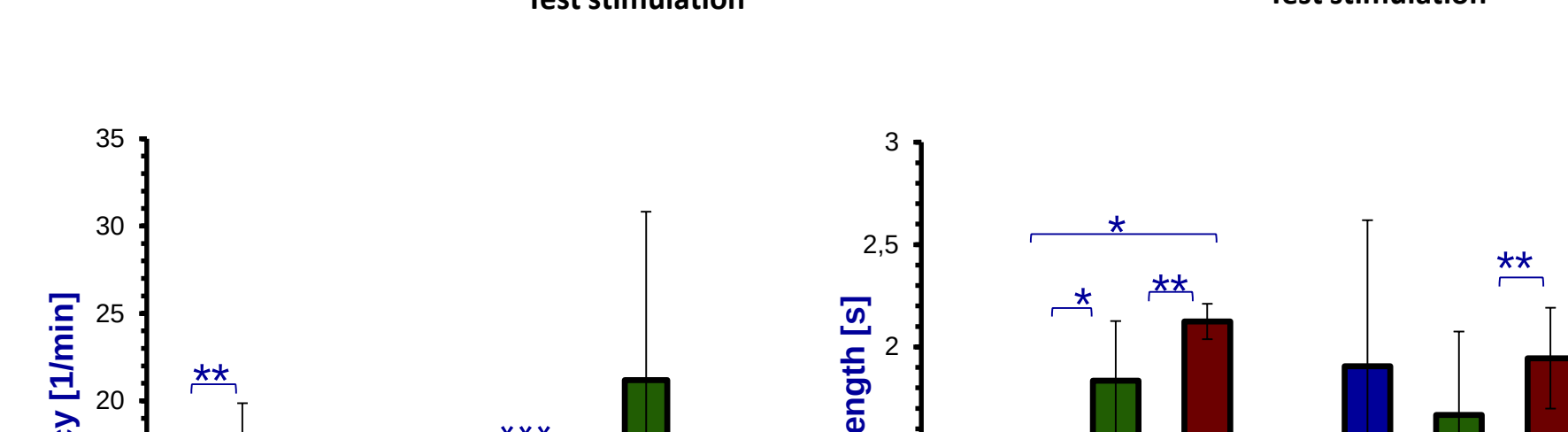
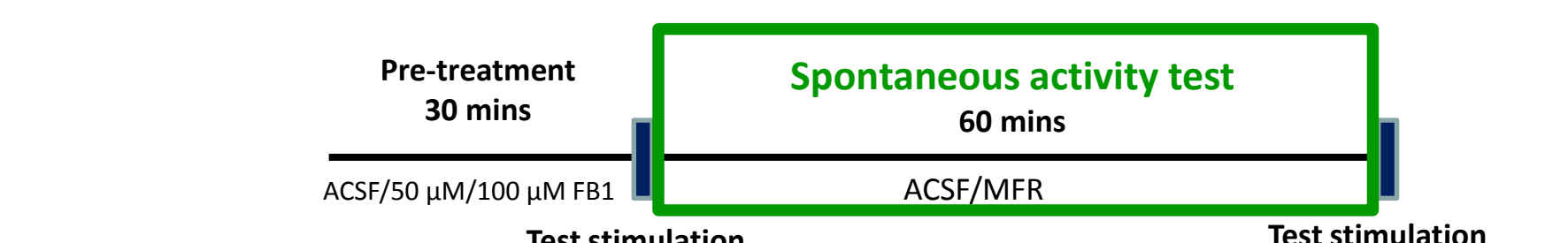
Sensory and entorhinal cortices



In the cortex, higher concentration of the toxin increased evoked potentials, mostly the early component.

MFR, as expected, increased the frequency of events and amplitudes of bursts which appear earlier compared to those recordable in ACSF.

Nevertheless treatment with FB1 alters the effects of MFR. Frequency becomes lower because of the increasing length of bursts. Furthermore amplitudes grow and latency times become shorter.



Discussion

In the hippocampus, during the stimulation tests right after the treatment, the toxin in the lower concentration didn't have significant effects on the neurons, while in case of the higher concentration, we observed an increase in amplitude of evoked potentials. After the induction of LTP (long-term potentiation), we could see that treating with the higher concentration made the initial excitatory effect result in the depletion of neuronal networks, and the setback of the effect of the potentiation.

In the cortex during stimulation tests we've experienced similar results as in the hippocampus since the lower concentration had lesser effect on the neurons, while the higher concentration increased the evoked potentials significantly. In case of spontaneous activity recorded in the convulsant (MFR), the impact of the elevation of toxin concentration was clearly excitatory. FB1 treatment causes longer lasting bursts which occur earlier with higher amplitudes.

Altogether we can say that the toxin influences the basic excitability of neuronal networks in brain slices and also elementary processes of learning (LTP). Pathological, epileptic events were also altered, parallel with the increasing sensitivity of neurons. 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.

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