



Effect of *Fusarium* mycotoxins on behavior and neuronal network activity after subchronic exposure in rat



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Background

Mycotoxins are toxic secondary metabolites produced by microscopic fungi; the most common *Fusarium* toxins – fumonisin B1 (FB1), deoxynivalenol (DON) and zearalenone (ZEA) – may contaminate the food chain. FB1 is known for inhibiting de novo sphingolipid biosynthesis, DON effectively decreases protein synthesis inhibitor while ZEA can interact with estrogen receptors. There is increasing evidence that these substances may affect nervous system function as well.

In the present study, neuronal effects of *Fusarium* toxins were studied in subacute toxicological experiments.

Materials & Methods

♀, ♂ rats treated for 28 days via gavage with

- FB1 (50 and 500 µg/kg)
- DON (20 and 200 µg/kg)
- ZEA (20 and 200 µg/kg)

Behavioral tests

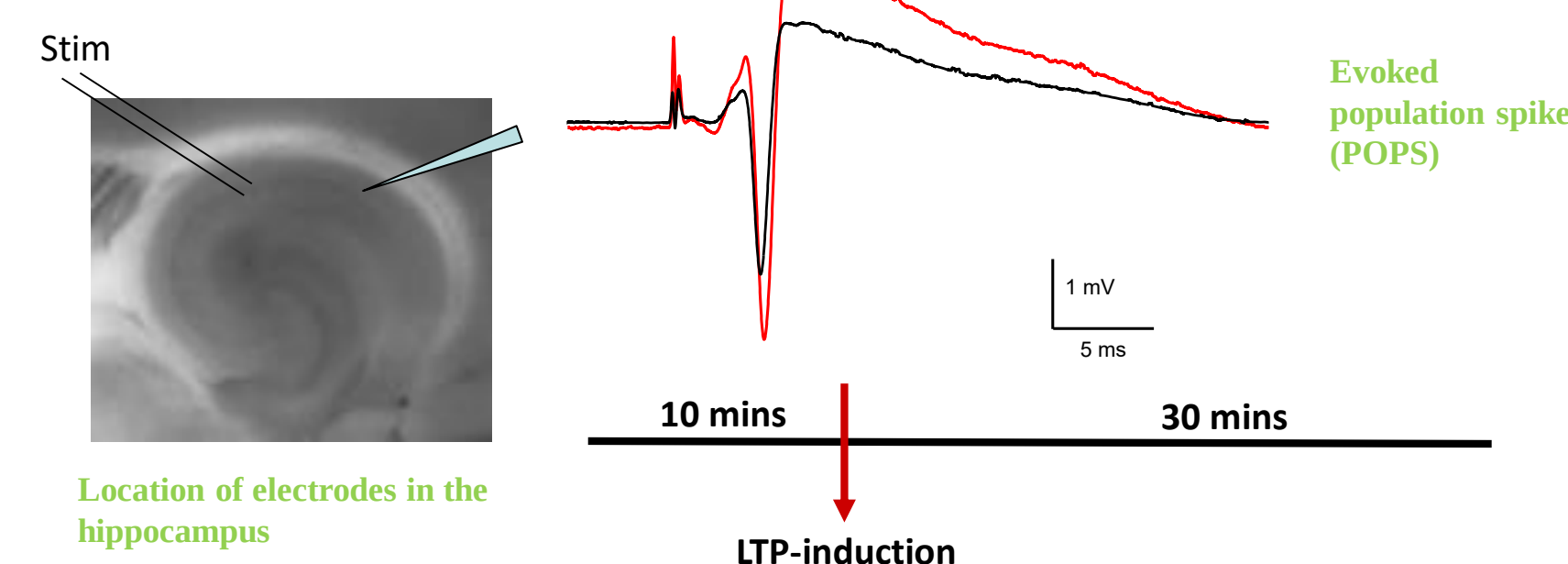
- 7♂ rats/treatment group with each toxin at lower dose
- **Elevated plus maze test**
duration: 6 min, location of rat recorded: open, closed arms and middle area
- **Forced swim test**
duration: 6 min, coded behavioral elements: climbing, floating, swimming

Sleep-wake pattern

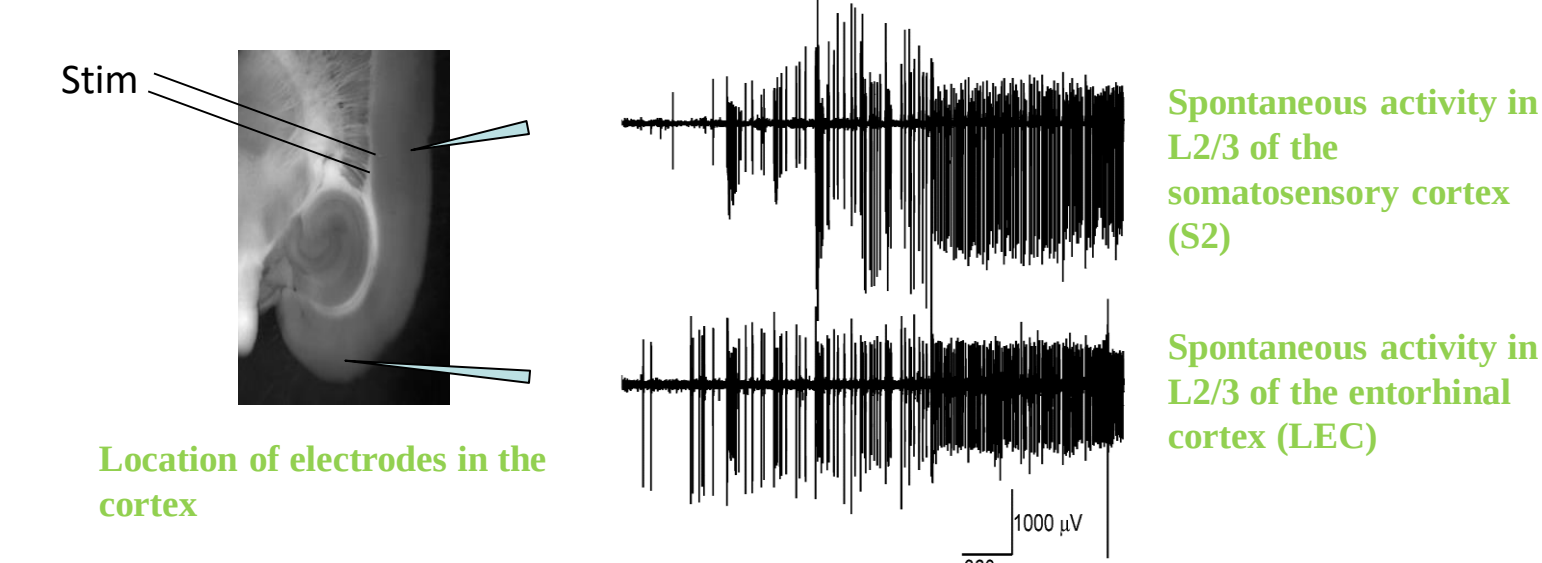
- 7♂ rats/treatment group with each toxin at lower dose
- EEG-electrodes over frontal, parietal cortex
- EMG electrode in neck muscle
- 12/12 h light-dark cycle
- 3*24 h recording
- identification of sleep stages with FFT power spectra in α , β , θ , δ range

Neuronal network excitability

- 400 µm thick brain slices of ♀, ♂ rats, treated with both doses (5/group)
- recording of electrically evoked and spontaneous field potentials
- long-term potentiation in the hippocampus (LTP, induced with a special theta-burst stimulus train - TBS)



- epileptiform activity in the entorhinal and somatosensory cortices (induced with magnesium-free ACSF – MFR)

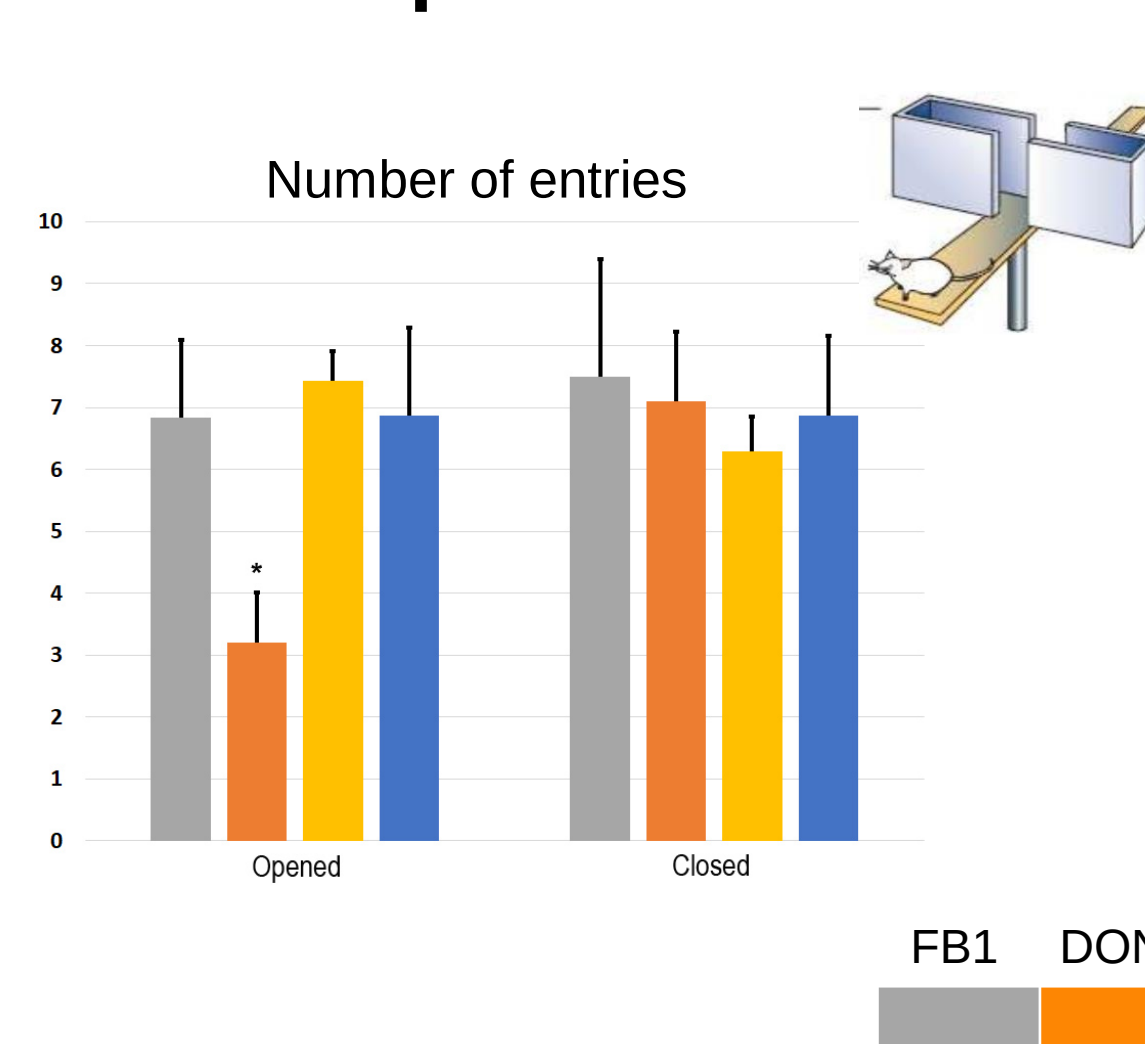


Statistical analysis: one-way ANOVA with Tukey post-hoc test or repeated-measures ANOVA
*: $p < 0.05$

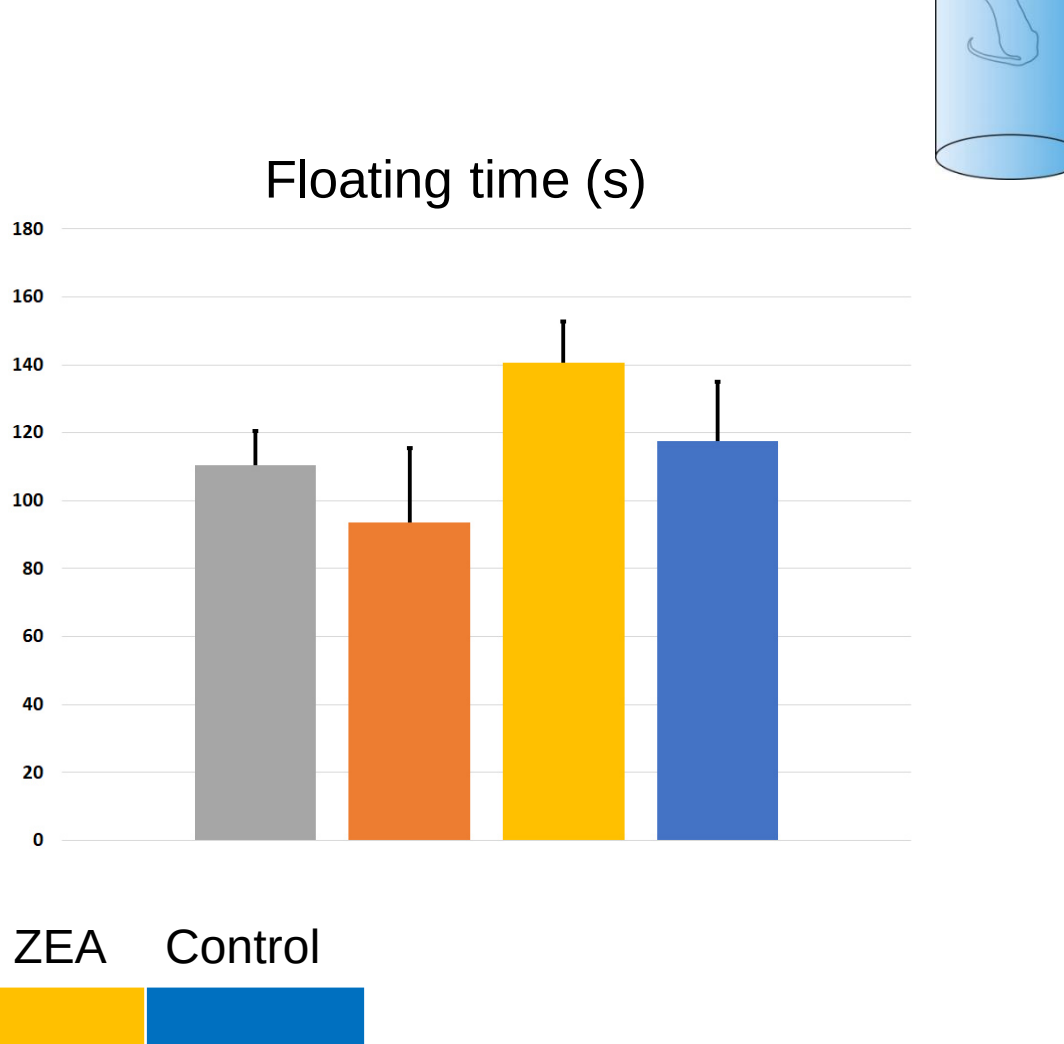
Results

Behavioral tests

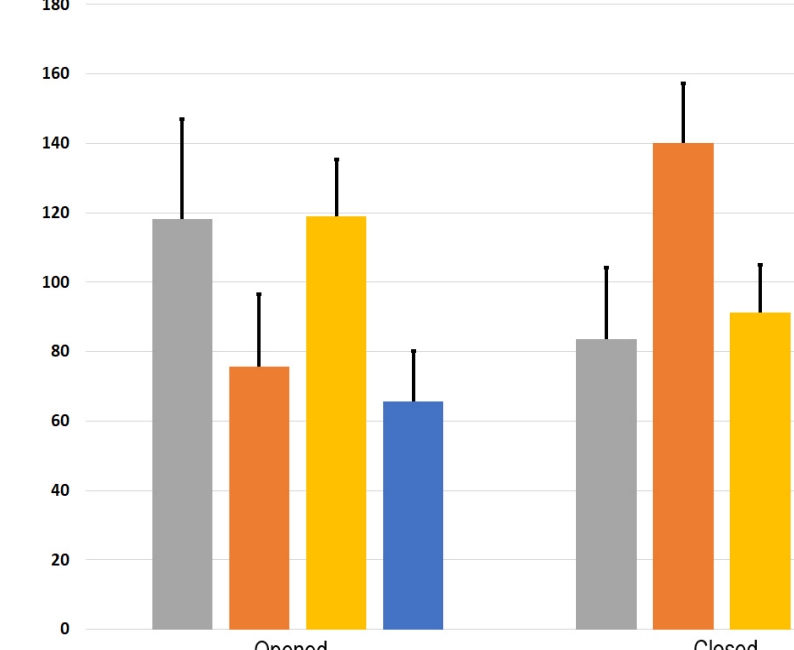
Elevated plus maze



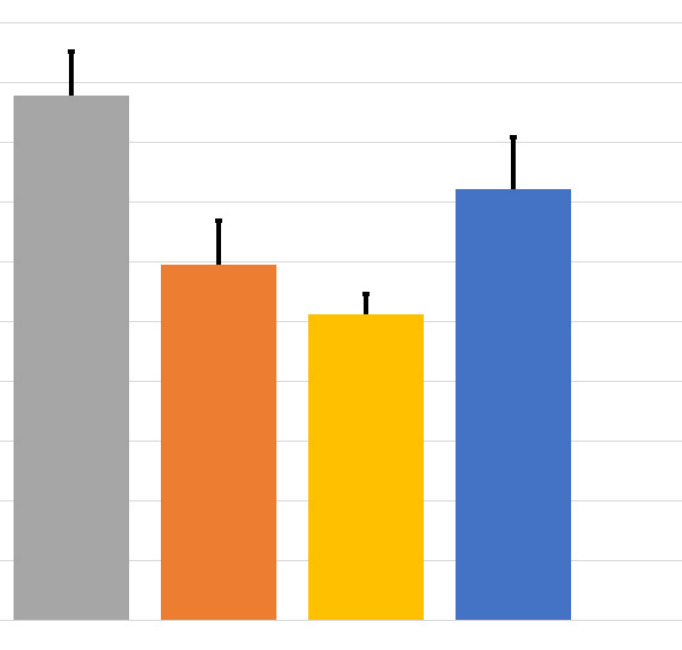
Forced swim test



Time spent in arms (s)



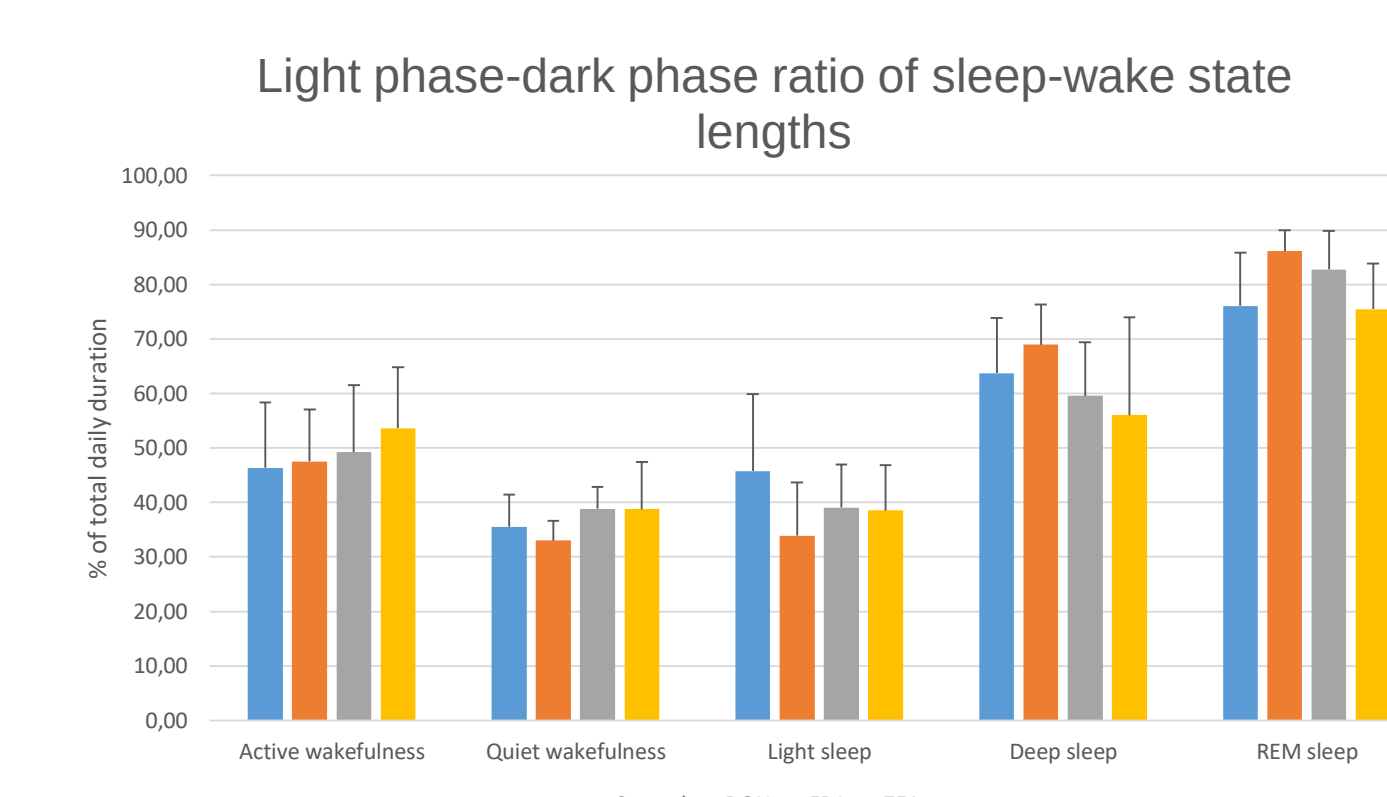
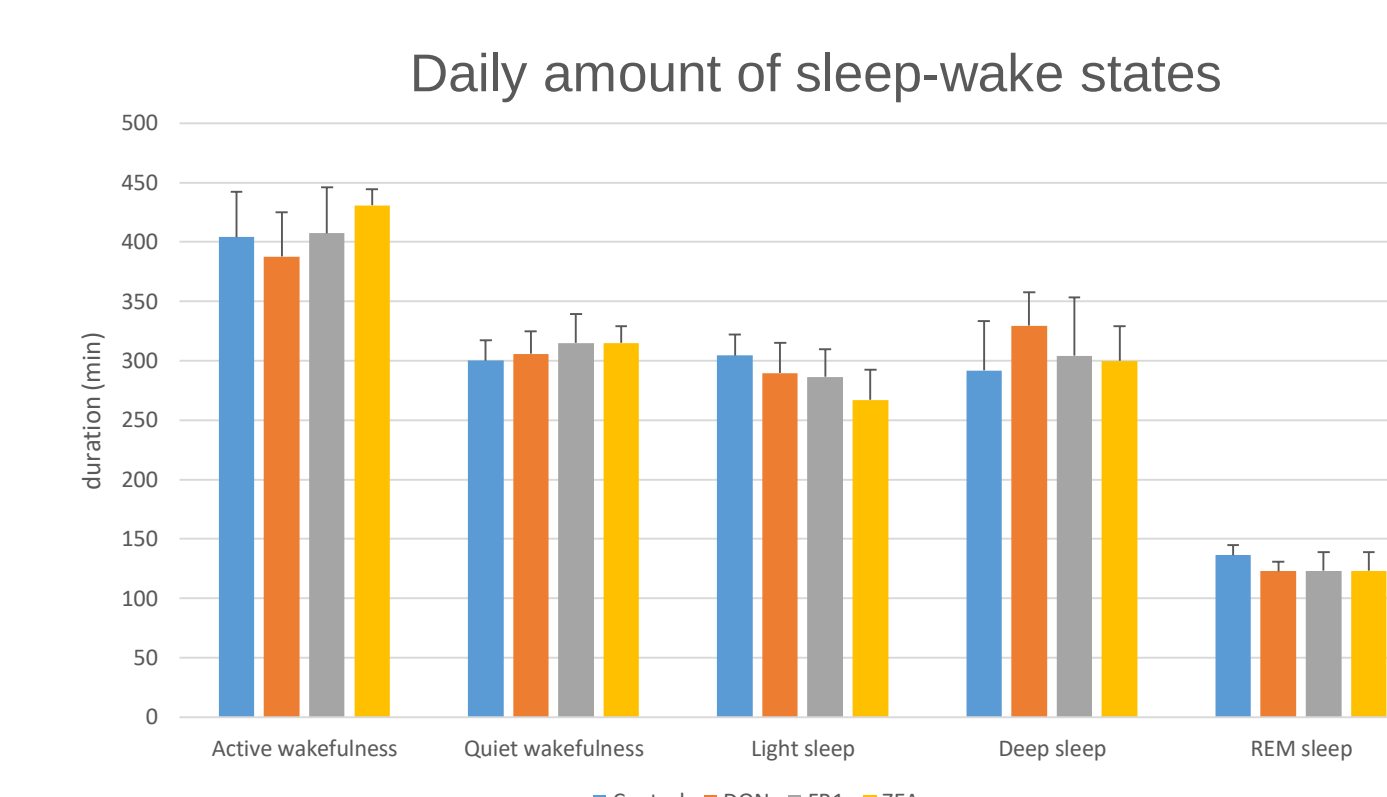
Climbing time (s)



DON decreased open arm entry number, indicating increased anxiety level.

ZEA had a tendency to increase the time spent floating, which is a marker of depression-like behavior.

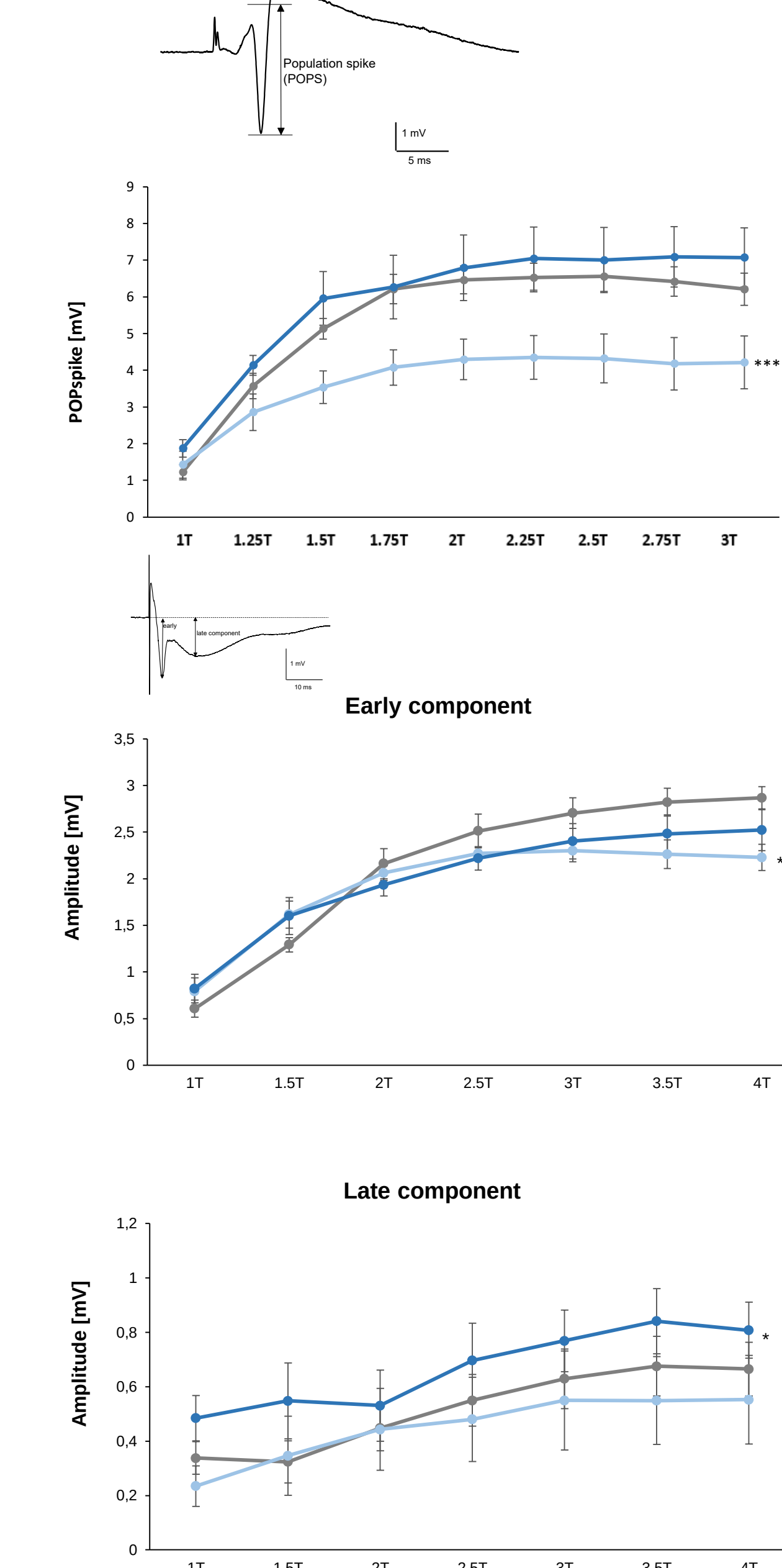
Sleep-wake pattern



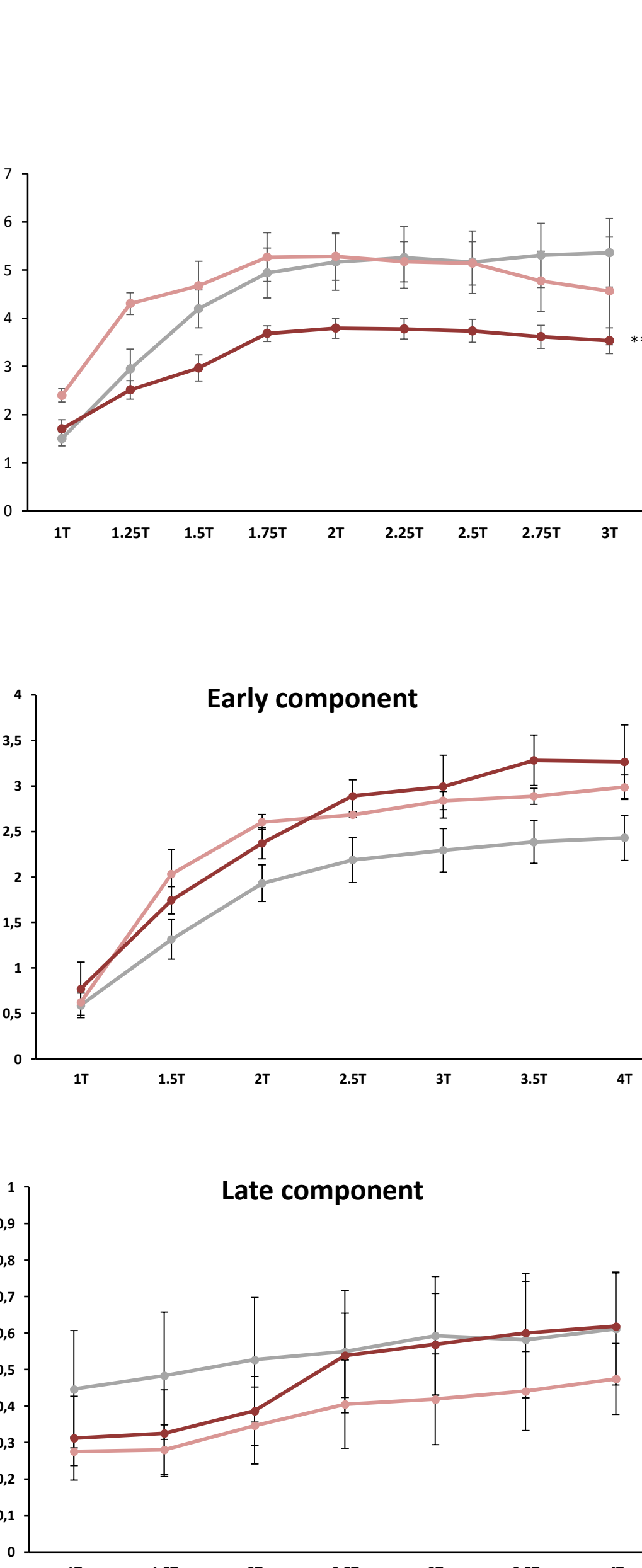
ZEA slightly decreased the time spent with light sleep, but none of the mycotoxins caused any significant change in the length and circadian distribution of wakefulness and sleep stages.

Neuronal network excitability

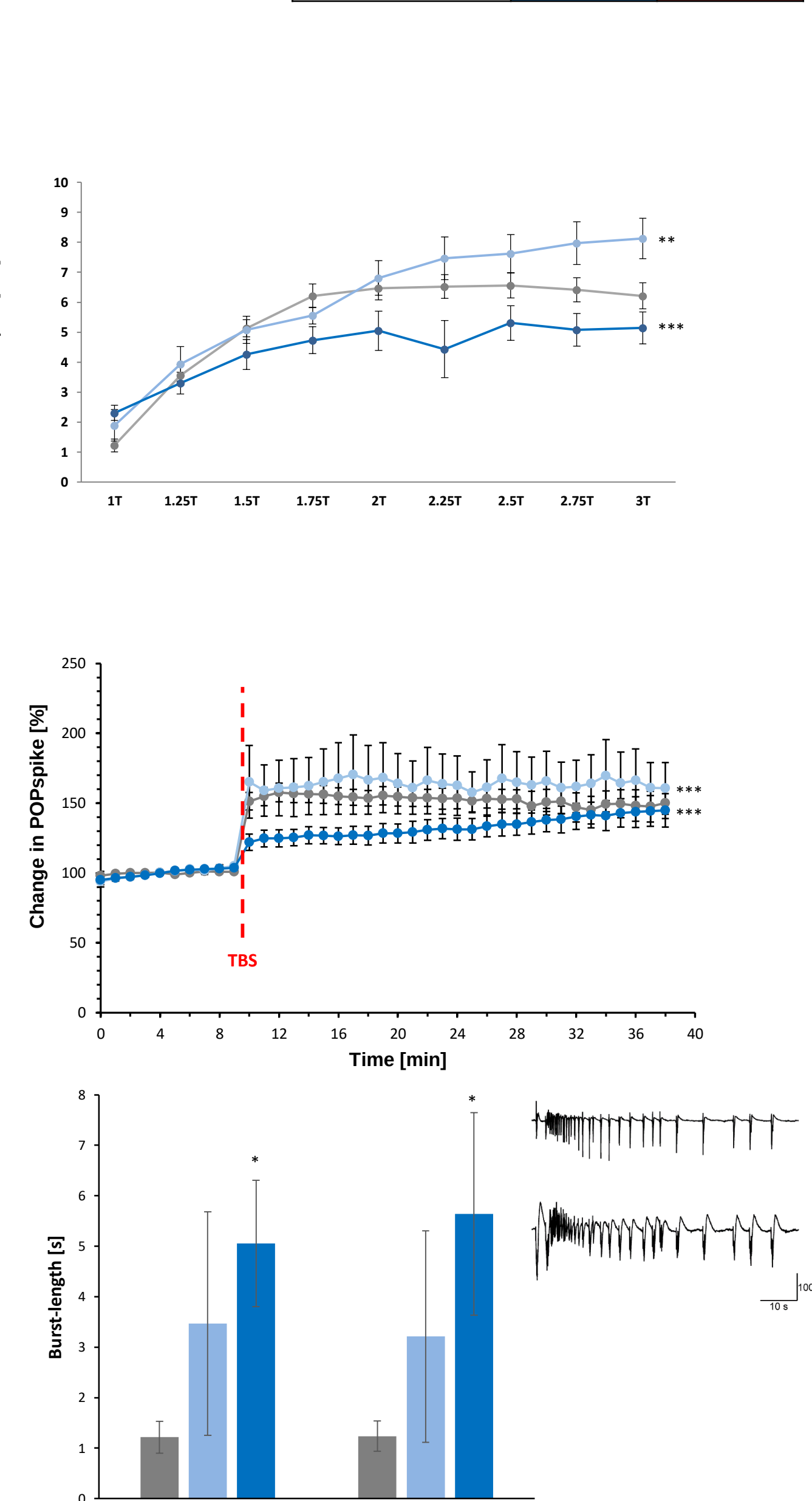
FB1



DON



ZEA



All three mycotoxins had variable effects on the excitability of neuronal networks in both hippocampus and entorhinal cortex; effects varied according to applied dose and sex of the rat. ZEA significantly modified the pattern of seizure-like events evoked with MFR in cortical slices of male rats. ZEA also modified the dynamics of the development of long-term potentiation in hippocampal slices of male rats.

Discussion

The current study aimed to examine the effects of 3 *Fusarium* toxins on the mammalian nervous system. A relatively realistic subchronic exposure type was applied, toxins were administered via oral gavage, using doses near to the NOEL values. Previous experiments indicated that the toxins cause changes activity of neurons in brain areas implicated in anxiety- and depression-related behaviors. DON and ZEA treatment indeed caused alterations in corresponding behavioral tests. Sleep-wake pattern was not significantly disrupted by the toxins, and subtle changes were detected in neuronal network functions like excitability, plasticity and seizure susceptibility using surviving brain slices.

To summarize, the three *Fusarium* toxins exert different effects on the nervous system, from the microcircuit to the behavioral level; severity of alterations may depend on the dose, sex and exact experimental endpoint.

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