



79th



International
Scientific
Conference of
the University
of Latvia

Positive allosteric modulator of sigma -1 receptor E1R alleviates generalised and chronic seizure severity

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Background

- Epilepsy affects more than 50 million people around the world.
- More than 1/3 of patients with epilepsy do not respond to treatment with antiepileptic drugs.

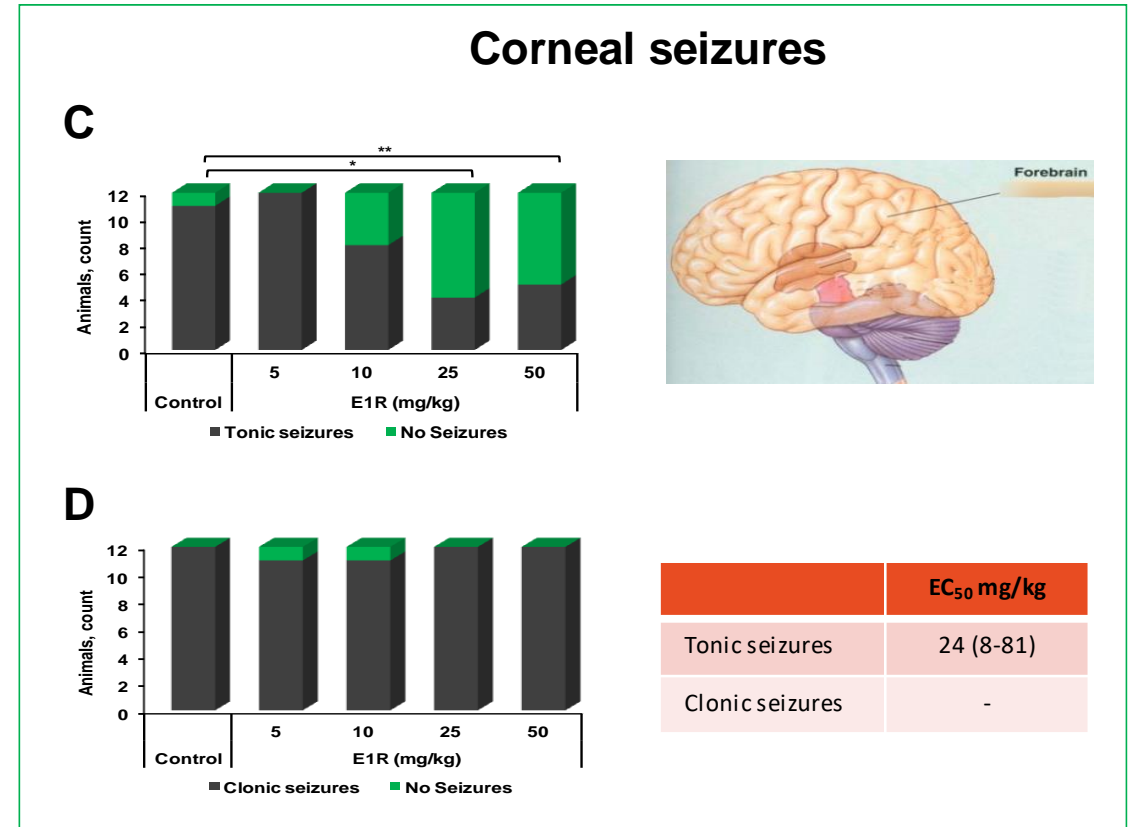
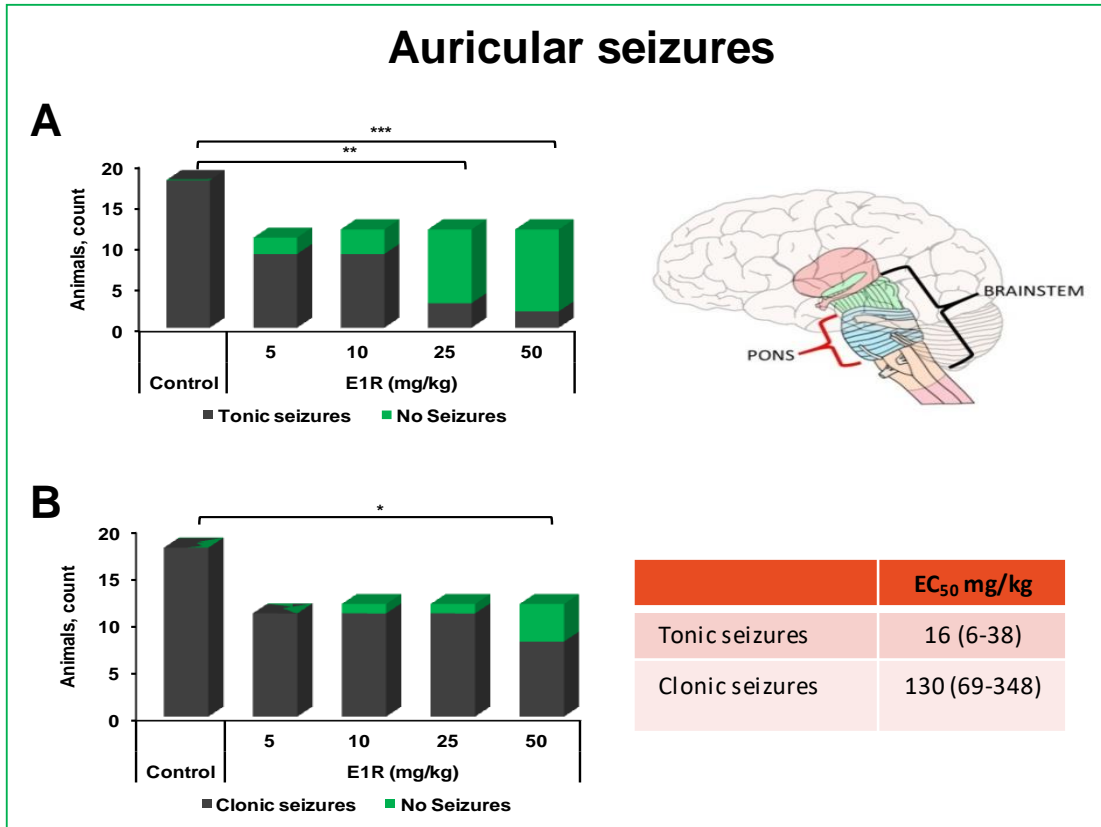
The aim of the present study was to investigate the efficacy of E1R in generalized and chronic seizure models.

Methods:



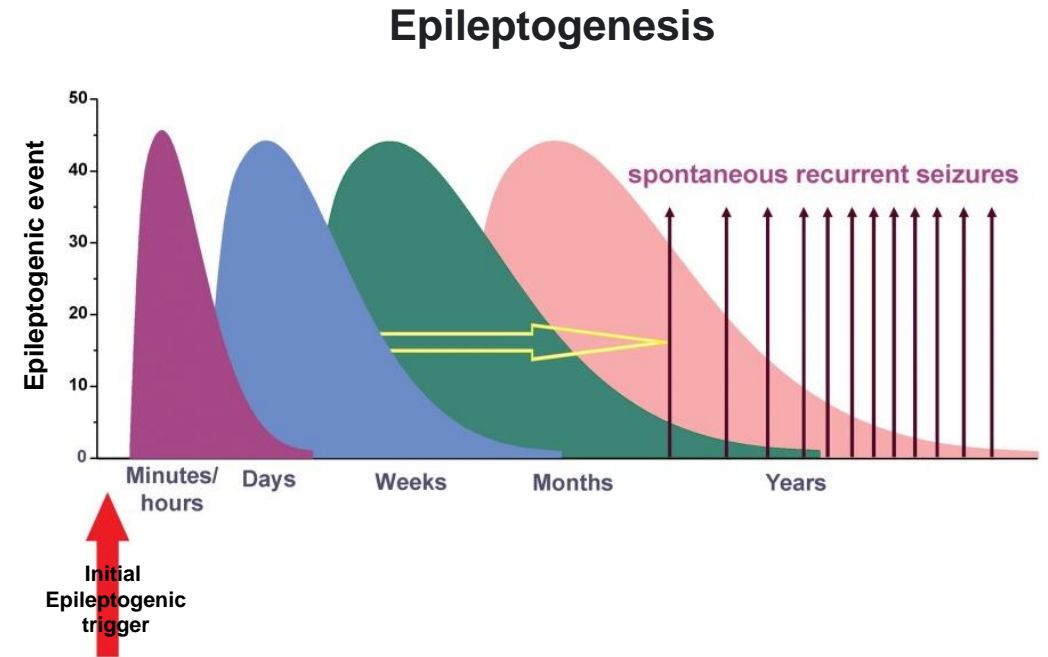
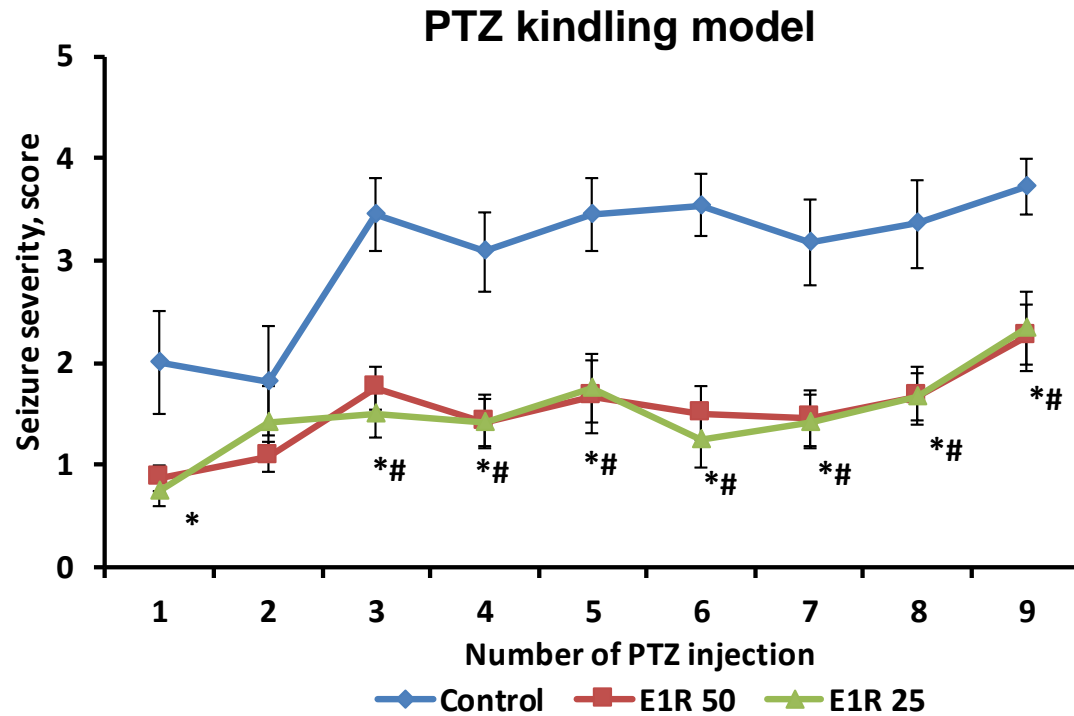
- The efficacy of E1R against generalized seizures of the tonic-clonic type was assessed in transcorneal and transauricular maximal electroshock-induced seizure (MES) tests.
- The anti-convulsive effect of E1R on chronic seizures during epileptogenesis was tested in the chronic pentylenetetrazole (PTZ) kindling model.

Anticonvulsant effect in MES models



Effect of E1R on tonic and clonic seizures in mice in the auricular and corneal maximal electroshock induced-seizures (MES) tests. Water (control) and E1R were administered p.o. at doses of 5, 10, 25, 50 mg/kg 60 min before MES.

E1R effect of epileptogenesis



Effect of E1R on PTZ-induced seizures in mice. PTZ (30 mg/kg) was injected every 48 hours (in total 9 injections).

Conclusions

- E1R exerts significant anti-convulsive activity against generalized tonic-clonic seizures and delays epileptogenesis.
- E1R is a promising drug candidate for treating a wide range of seizures.

Acknowledgements. This work was supported by grants from the State Education Development Agency of Latvia (Joint Ukraine-Latvia R&D project No. LV-UA/2020/1).