

CERTIFICATE OF ATTENDANCE

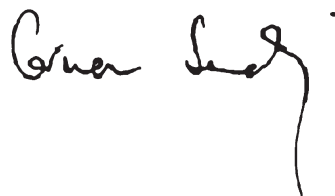
This is to certify that

Istvan Mihaly

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The effect of deep brain stimulation of the amygdala in the pilocarpine model of temporal lobe epilepsy



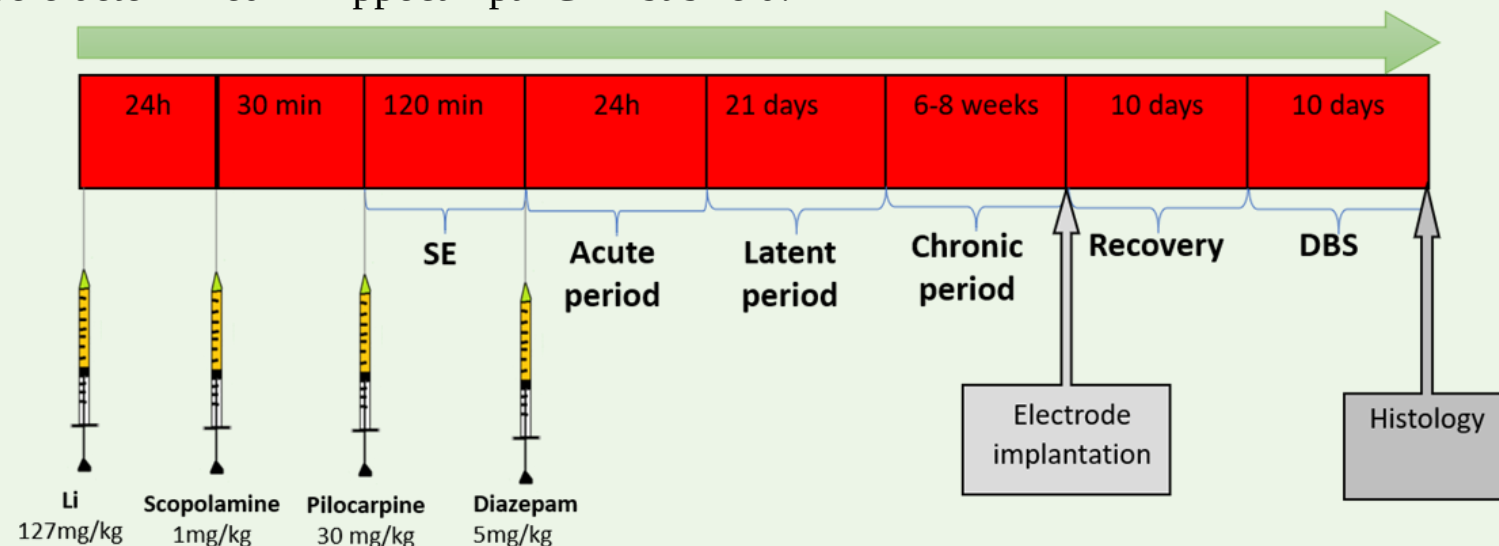
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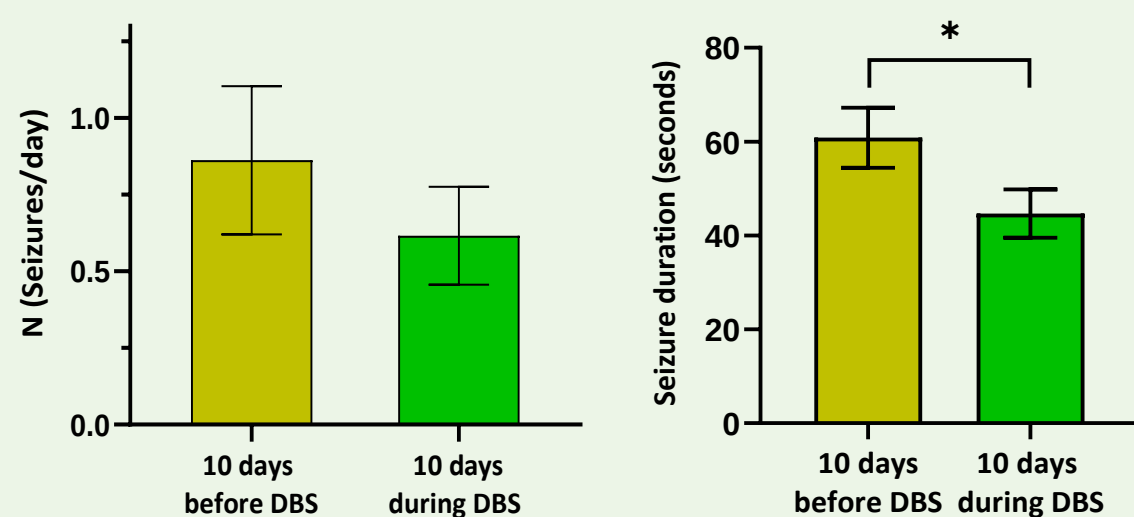
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Aims: Temporal-lobe epilepsy (TLE) is the most common type of drug-resistant epilepsy which calls for the development of new therapeutic methods such as deep-brain stimulation (DBS). The mechanism of action of DBS are not fully understood. In order to optimize DBS for best therapeutical results, we tried to characterize the effect of amygdala DBS in the pilocarpine model of TLE.

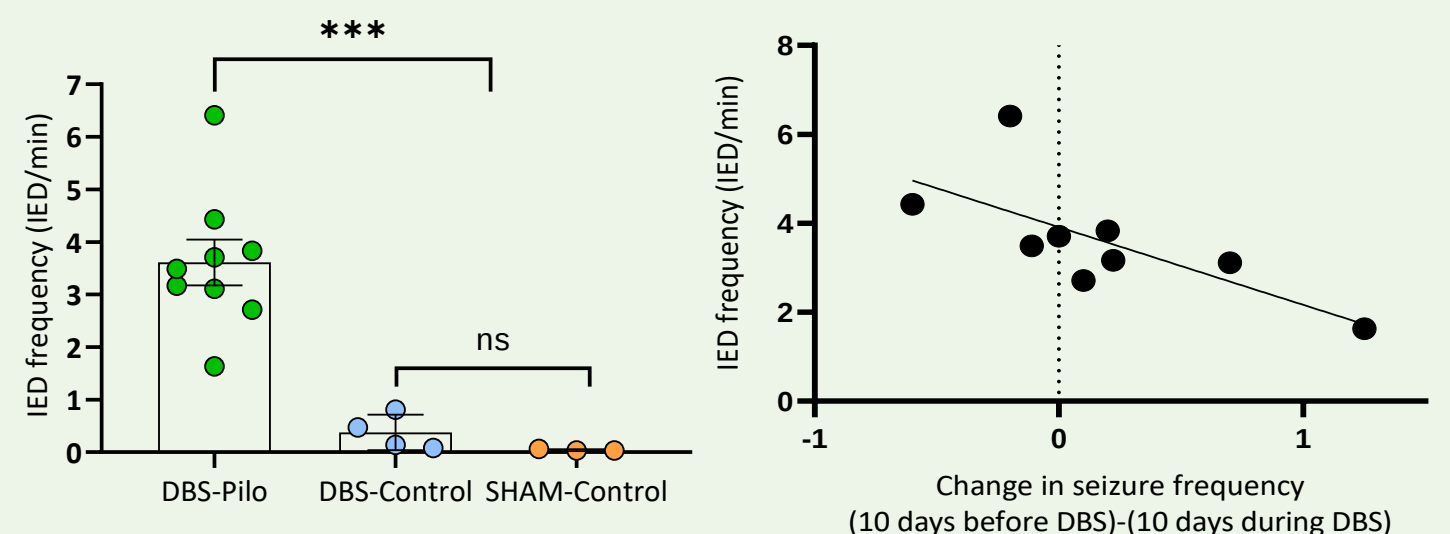
Methods: We induced status epilepticus with lithium-pilocarpine in male Wistar rats (Pilo). Afterwards, seizure patterns were determined based on continuous video recordings. After the appearance of spontaneous recurrent seizures, we inserted hippocampal recording electrodes and a stimulating electrode in the left basolateral amygdala of both Pilo and age matched control rats (N=7) (left). 10 Pilo (DBS-Pilo) and 4 control (DBS-Control) animals were stimulated daily for 10 days with 4 packages of 50 seconds trains (4Hz, 500mA, 0.1 ms, biphasic pulses, with 5-minute breaks between packages). Additional Pilo and control rats were recorded but not stimulated. Interictal electrical discharges (IEDs) from the EEG were analyzed offline. After euthanasia inhibitory interneurons were identified by immunolabeling for parvalbumin (PV), Y-neuropeptide (NPY), and nitric-oxide synthase (NOS) and their densities were determined in hippocampal CA1 subfield.



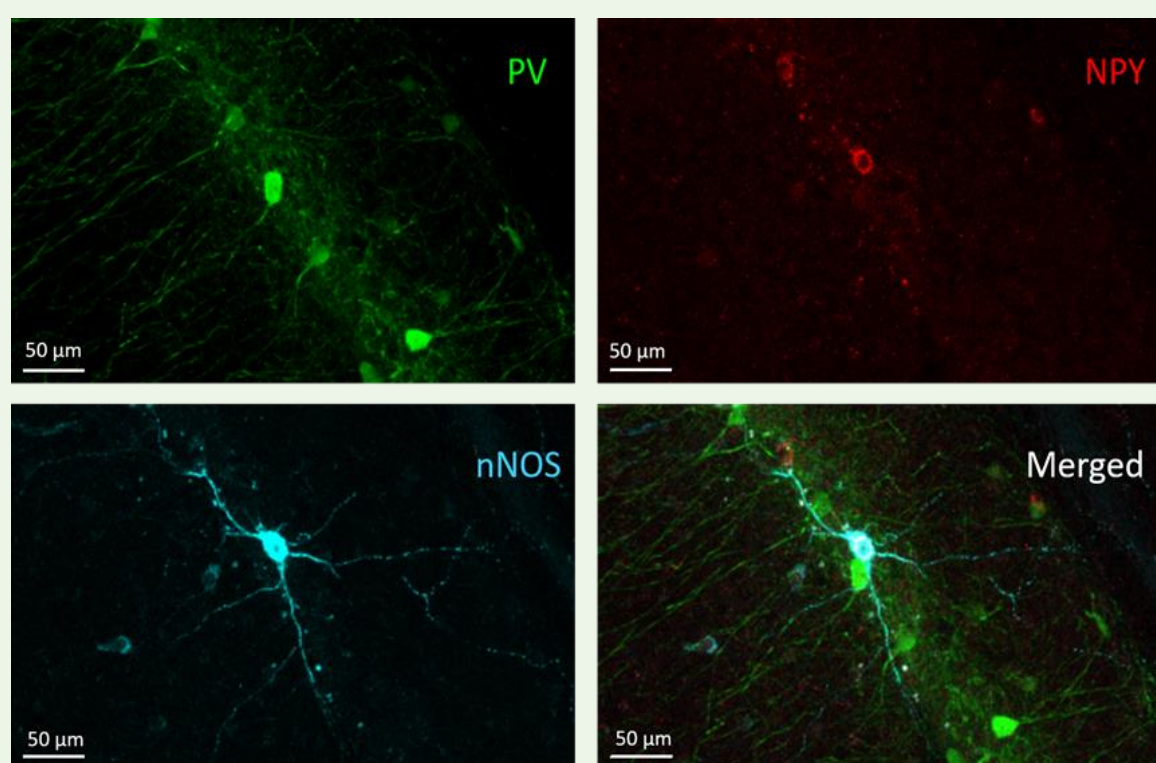
The average **number of seizures/day** decreased by 28.5% during DBS (left). The seizure **duration** was reduced by 23.5% (right).



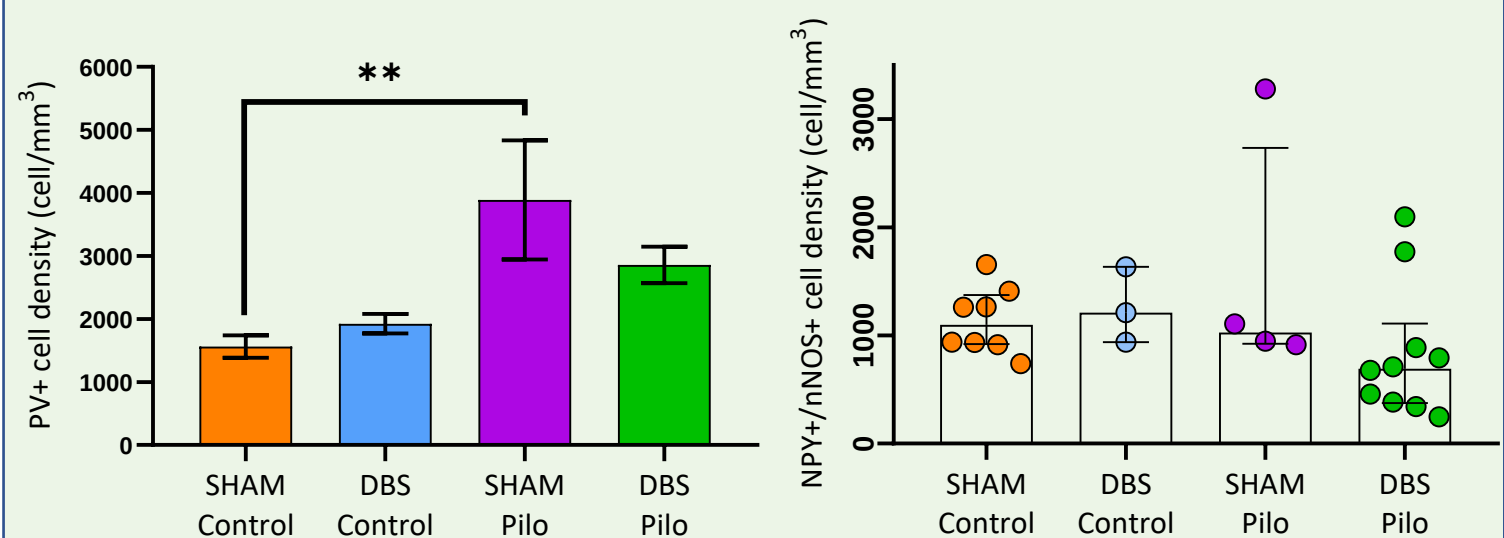
The mean **IED frequency (IED/min)** was significantly higher in DBS-Pilo group than in controls (left). The rate of decrease in seizure frequency (seizures/day) showed a significant **negative correlation** with the IED frequency (right).



Immunohistochemical identification of interneuron types. There are PV+ cells in the PV channel, but in the merged image PV signal is not superpositioned on the NPY+/nNOS+ signal, while the NPY and nNOS signal is superpositioned.



PV+ interneurons had a significantly **higher density** in the **SHAM-Pilo** group compared to the SHAM-Control group, while this difference was not present between the DBS-Pilo and DBS-Control groups (left). **No significant differences** were observed amongst **NPY+/nNOS+** interneuron densities (right).



Conclusion: DBS significantly reduced seizure frequency and duration; the rate of decrease was correlated with IED numbers. The higher IED numbers in epileptic animals may support their use as an epileptic marker. The return towards control values of PV+ cell density in treated epileptic animals may reflect a possible network normalizing effect of DBS.

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The Leica TCS-SP8 confocal microscope utilized in this work was provided by the Center for Advanced Medical and Pharmaceutical Research of the George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures (CCAMF).

The effect of deep brain stimulation of the amygdala in the pilocarpine model of temporal lobe epilepsy

Aim: to characterize the effect of amygdala deep brain stimulation (DBS) in a rodent model of temporal lobe epilepsy.

Methods: We induced status epilepticus with lithium-pilocarpine in male Wistar rats (Pilo). Afterwards seizure patterns were determined based on continuous video recordings. After the appearance of spontaneous recurrent seizures, we inserted hippocampal recording electrodes and a stimulating electrode in the left basolateral amygdala of both Pilo and age matched control rats (N=7). 10 Pilo (DBS-Pilo) and 4 control (DBS-Control) animals were stimulated daily for 10 days with 4 packages of 50 seconds trains. Additional Pilo and control rats were recorded but not stimulated. Interictal electrical discharges (IEDs) from the EEG were analyzed offline. After euthanasia inhibitory interneurons were identified by immunolabeling for parvalbumin (PV), Y-neuropeptide (NPY), and nitric-oxide synthase (NOS).

Results: The average number of seizures/day decreased by 28.5% during DBS. The seizure duration was reduced by 23.5%. The rate of decrease in seizures/day showed a significant negative correlation with the number of IED/minute. The mean IED/min was significantly higher in DBS-Pilo group than in controls. Compared to the non-treated Pilo group PV+ interneurons had a significantly lower density (similar to control groups) in the DBS-Pilo group.

Conclusions: DBS significantly reduced seizure frequency and duration; the rate of decrease was correlated with IED numbers. The higher IED numbers in epileptic animals may support their use as an epileptic marker. The return to control values of PV+ cell density in treated epileptic animals may reflect a possible network normalizing effect of DBS.