INTRODUCTION
Absence-type generalized seizures are particularly prevalent in children, often have a genetic origin, and are accompanied by neuropsychological and neurocognitive symptoms. The WAG/Rij rat is a well-known genetic model of absence seizure with age-dependent non-convulsive seizures characterized by spike-wave discharges (SWD) and neurobehavioral deficits. The aim of this study was to compare the efficacy of three antiepileptic substances: ethosuximide (ETX), valproate (VPA) and levetiracetam (LEV) on the number and the duration of SWD on EEG recordings. We also evaluated neuropsychological comorbidities in WAG/Rij rats.

MATERIAL & METHODS

SWD assessment: Six month old WAG/Rij rats (Charles River) were implanted with epidural electrodes placed over the fronto-parietal cortex. Cortical EEG signals were recorded by telemetry (EMKA Technologies) over 3 hours, immediately after administration of vehicle or antiepileptic drugs. The treatments were randomly assigned (2 to 5 rats received the same treatment per week). An absence seizure corresponds to spikes and waves of an amplitude at least twice the amplitude of baseline recording conditions and observed for more than 2 seconds.

Neurobehavioral assessment: Elevated Plus Maze test: The rats were left to explore a maze with two open arms and two closed arms with walls for 5 minutes. Sucrose number of SWD was measured over 24-hour and the percentage of sucrose preference was calculated (sucrose intake ×100/total intake).

RESULTS

SWD Assessment: ETX and VPA dose-dependently decreased the number of SWD. At high doses (200 mg/kg for ETX and 300 mg/kg for VPA), this was accompanied with a decrease of the duration of SWD (-41%) but no effects were observed on the duration or at lower doses.

VPA (100 mg/kg) showed a significant decrease of the number of SWD (-41%) but no effects were observed on the duration or at lower doses.

CONCLUSION
These data confirm the efficacy of ETX and VPA to antagonize SWD in WAG/Rij rats. In humans, ETX remains the gold standard treatment for this type of seizure, while VPA is mainly used when absence seizure is accompanied of tonico-clonic convulsions. LEV showed a moderate efficacy against SWD. Neurobehavioral deficits observed in these animals reinforce the translational value of this model. These results suggest that the strain of WAG/Rij rats may be particularly useful for evaluating absence seizure as well as comorbid neuropsychological deficits. This chronic genetic model has a good predictive validity for the evaluation of potential new treatments against absence seizure.