

## **P4.21.**

### **Doxycycline Increases Absence-like Epileptic Seizures in WAG/Rij Rats**

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Epileptic seizures might activate matrix metalloproteinases (MMPs) in the brain and increased MMP-9 activity have been found in a genetic model of generalized absence epilepsy (Wistar Albino Glaxo Rijswijk/WAG/Rij rats). In this study we investigated the effect of subantimicrobial doses of MMP inhibitor doxycycline on spike-wave-discharges (SWDs) in WAG/Rij rats. A single dose of 20 mg/kg doxycycline were injected intraperitoneally (i.p.) into WAG/Rij rats and number and duration of SWDs were measured for 4 hours. We found that 20 mg/kg doxycycline significantly increased the incidence and duration of SWDs compared to the preceding three-day average control level during the whole four-hour recording period. Doxycycline at similar dosage inhibits also inflammation, e.g. systemic injection of 10 mg/kg of doxycycline blocks the increase of pro-inflammatory cytokines. While the role of inflammation in absence epilepsy is not elucidated yet, we also investigated the effect of 10 mg/kg doxycycline on the number of SWDs. We found that 10 mg/kg doxycycline also increased the number of SWD but only between 30-90 min after i.p. injection. Our results indicate that while in many epilepsy models the overexpression of MMP-9 could deteriorate the behavioral seizures and its consequences, in case of absence seizures MMP-9 may exert beneficial effects.