Fingolimod shows antiepileptogenic and anti anxiety/depressive effects in Wag/Rij rats, a well established model of absence epilepsy and neuropsychiatric comorbidities

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Fingolimod (FTY720), a sphingosine-1-phosphate receptor (S1PR) modulator, was the first oral therapy approved by US Food and Drug Administration (FDA) and European Medicines Agency (EMA) for the treatment of relapsing-remitting multiple sclerosis[1]. To date, fingolimod has not been studied in epilepsy models; however, a recent study performed in the lithium-pilocarpine rat model of SE (status epilepticus) has shown the antiepileptogenic effects of fingolimod[2]. Moreover, epilepsy has been linked with behavioural, affective and cognitive disturbances. To date, co-morbidities are a rising problem in epilepsy and are frequently more harmful to patients than the seizures themselves [3].
Aim of the present study was to determine the potential antiepileptogenic and antiseizure effects of fingolimod, but also to investigate its effects on epilepsy comorbidity in WAG/Rij rats, a well-established genetic model of absence epilepsy, epileptogenesis, and neuropsychiatric comorbidity. Therefore, we have investigated the effects of some treatment paradigms (early-chronic; sub-chronic; acute) with fingolimod (1 and 3 mg/Kg), on absence-seizures development, seizures and psychiatric/neurologic comorbidity in WAG/Rij rats. Moreover, as recently reported it would seem that in this rat strain, at 6 and 13 months of age, there is cognitive impairment [4, 5]. In particular, the potential antiepileptogenic and antiseizure effects of fingolimod were tested by analysis of EEG recordings, whereas the effects of fingolimod in epilepsy comorbidity were evaluated in the following behavioural tests: elevated plus maze (EPM), open field test (OFT), forced swimming test (FST) and passive avoidance.
Our results have shown that, early-chronic fingolimod treatment (1 mg/Kg) significantly reduced the development of absence epilepsy and ameliorated anxiety/depressive like-behaviour in WAG/Rij rats. At odds, early-chronic treatment has not improved the cognitive performance in this rat strain. Both acute and sub-chronic treatments with fingolimod (1 and 3 mg/Kg) do not possess anti-absence properties and effects on animal behaviour. In conclusion, our results support the antiepileptogenic and anti anxiety/depressive effects of chronic fingolimod in WAG/Rij absence model; therefore, fingolimod could be a new therapeutic approach for the prevention of epileptogenesis and neuropsychiatric-comorbidity.

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