EFFECTS OF NON-COMPETITIVE AMPA RECEPTOR ANTAGONISTS INJECTED INTO SOME BRAIN AREAS OF WAG/RIJ RATS, AN ANIMAL MODEL OF GENERALIZED ABSENCE EPILEPSY

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Generalized absence seizures in humans are characterized by brief periods of behavioural arrest, inability to answer questions and occasional automatism. These seizures are accompanied by a characteristic electroencephalographic (EEG) pattern defined by 3-5 Hz spike and wave discharges (SWDs)[(1)]. Excessive glutamatergic neurotransmission is understood to be one of the primary pathological mechanisms behind the aetiology of numerous types of epilepsy[(2)]. The excitatory system seems to play an identical role in the two main kinds of epilepsy: convulsive or tonic-clonic generalized epilepsy and non-convulsive or absence epilepsy. Generally, glutamate agonists facilitate and antagonists reduce both convulsive and non-convulsive epilepsy[(3)]. CFM-2 [1-(4-aminophenyl)-3,5-dihydro-7,8-dimethoxy-4H-2,3-benzodiazepin-4-one] and THIQ-10c [N-acetyl-1-(4-chlorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline], are two non-competitive 2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl) propionic acid (AMPA) receptor antagonists, which demonstrated to antagonize generalized tonic-clonic seizures in different animal models[(4)]. We have evaluated the effects of such compounds in a genetic animal model of absence epilepsy, the WAG/Rij rat. Animals were focally microinjected into specific brain areas of the cortico-thalamic circuit in order to evaluate the effects of these compounds on the number and duration of epileptic spike-wave discharges (SWDs) and better characterize the role of AMPA neurotransmission in this animal model. The focal microinjection of the two AMPA antagonists into some thalamic nuclei (ventralis posteromedialis (VPM), reticularis (NRT), ventralis posterolateralis (VPL) and the primary somatosensory forelimb region (S1FL) was, generally, not able to significantly modify the occurrence of SWDs. Whereas, both compounds were able to reduce the number and duration of SWDs dose-dependently when microinjected into the peri-oral region of the primary somatosensory cortex (S1po). These findings suggest that AMPA receptor antagonists might play a role in absence epilepsies and that it might depend on the involvement of specific neuronal areas.

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