

Influence of flavonoids from Georgian endemic grape species "Saperavi" on brain disfunction induced by kainic acid-status epilepticus in laboratory rats.

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Epilepsy is a chronic neurological disease, which affects roughly 1% of the human population. The development of an epileptic network is associated with a diversity of plastic changes. These changes functionally affect different system levels, resulting in epilepsy-related cognitive impairment and psychiatric comorbidities. In most cases, the epileptogenic region is found in the hippocampus and evidence indicates that glutamate excitotoxicity is involved in epilepsy-induced neurodegeneration: excessive glutamate overactivates Ca^{2+} -permeable and the resulting imbalance in intracellular Ca^{2+} causes the activation of lethal signalling pathways ending in neuronal death. Ca^{2+} influx include the activation of Ca^{2+} -dependent enzymes, and generation of reactive oxygen species (ROS) (Wang et al., 2005). Some signs of induction of inflammatory mediators after seizures have also been detected in the developing brain (Rizzi et al., 2003). Earlier in biochemical experiments we have found that flavonoids from the Saperavi grapes (FSG) effectively prevented age-related increase of quantity of malondialdehyde (final product of lipid oxidation) in the brain of adult rats, significantly improved age-related spatial memory decline and efficiently corrected scopolamine-induced memory disturbance in young ones (Doreulee et.al, 2012 SfN). In the present study behavioral experiments were performed to investigate the influence of FSG on spatial memory deficit associated with kainic acid-induced status epilepticus (KA-SE) in laboratory rats.

Animal model of epilepsy were induced by single intraperitoneal injection of kainic acid (KA) (15mg/kg) in 8-10 weeks old rats. Behavioral changes associated with epilepsy were recorded in the open-field, T-maze and passive avoidance tasks. The effects of FSG on KA-SE induced behavioral changes were monitored after supplementation of rats with FSG (8 days 25mg/kg, daily). FSG led to significant reversals of KA-SE-induced spatial memory decline that was accompanied by massive reduction of the total number of neurons of the hippocampus shown by hematoxylin-eosine staining and significant decrease in number of glutamic acid decarboxylase (GAD)-positive neurons demonstrated by anti-GAD65/67 antibodies in immunocytochemical experiments. The anti-amnesic effects of the flavonoid extract from Saperavi grapes compared to other antioxidant flavonoid – quercetin (50mg/kg) was more pronounced. In open field experiments no significant changes of emotional state were detected in the flavonoid-fed rats.

In conclusion, we suggest that dietary flavonoids from the Saperavi grapes have beneficial effect on hippocampal-related plasticity.

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