BENEFICIAL EFFECT OF KETONE SUPPLEMENTS ON ABSENCE-LIKE EPILEPTIC ACTIVITY AND ANXIETY-LIKE BEHAVIOR IN WAG/RIJ RATS

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Ketone supplementation-evoked nutritional ketosis may be beneficial in several central nervous system diseases including epilepsy. The focus of this study was to determine the effects of ketone supplementation on anxiety-related behavior and absence-like epileptic activity in genetically absence epileptic Wistar Albino Glaxo/Rijswijk (WAG/Rij) rats. In the first part of the study, we tested exogenous ketone supplements administered sub-chronically (7 days, normal food with daily intragastric gavage bolus) followed by assessment of anxiety measures on elevated plus maze (EPM). The groups included standard diet (SD) or SD + ketone supplementation (2.5 g/kg/day). Ketone ester (KE; 1,3-butanediol-acetoacetate diester), beta-hydroxybutyrate-mineral salt (KS), and KS + medium chain triglyceride (KSMCT) were used as ketone supplements. The results revealed that KSMCT reduced anxiety on EPM as measured by less entries to closed arms and more time spent in open arms. In the second part of the study, we tested the effects of sub-chronically applied exogenous ketone supplements (KE, 2.5 g/kg/day; KSMCT, 2.5 g/kg/day; intragastric gavage) on absence epileptic seizures in WAG/Rij rats. We demonstrated that the number of spike-wave discharges (SWDs)significantly decreased after ketone supplement treatments between 3rd and 7th days of gavage. Moreover, blood beta-hydroxybutyrate levels were significantly increased in both parts of the study after ketone supplement gavage. Our data indicate that sub-chronic ketone supplementation not only elevated blood beta-hydroxybutyrate levels, but also reduced anxiety-related behavior and absence-like epileptic activity in WAG/Rij rats.