

## INTESTINAL INFLAMMATION INCREASES CONVULSANT ACTIVITY AND REDUCES ANTIEPILEPTIC DRUG EFFICACY IN A MOUSE MODEL OF EPILEPSY

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**Introduction:**  $\alpha$ -Lactalbumin (ALAC) is the major protein component of bovine milk and possesses many pharmacological functions such as antioxidant, hypolipidemic and hypoallergenic. It was previously reported that ALAC exerts significant protective activity against seizures in animal models and part of its effects are mediated by the inhibition of NMDA receptors through the glycine binding site. Recently, several studies have shown a bidirectional communication between the brain and the gut microbiota. Aim of this study was to evaluate whether ALAC would be able to reduce intestinal inflammation induced by dextran sulphate sodium (DSS) and if this action could reduce seizures in the pentylenetetrazol (PTZ) model in BALB/c mice.

**Material and methods:** Colitis was induced in mice by administering DSS (4%, wt:vol) in drinking water ad libitum for 6 days, followed by DSS-free water up to day 13. Drug treatments as follows were started at day 3: ALAC (375mg/kg), Valproic Acid (600 mg/kg), Sodium Butyrate (100 mg/kg) and Mesalazine (15mg/kg). On day 14th, mice were tested for PTZ susceptibility and samples were collected for intestinal analysis of inflammation and damage.

**Results:** ALAC treatment reduced colitis symptoms and colon damage and significantly decreased polymorphonuclear cell infiltration scores compared to the DSS group and other groups and in western blot analysis there was a reduction of inflammatory markers (COX-2, iNOS and NF $\kappa$ B). Moreover, ALAC treatment restores levels of propionic and butyric acid in stool samples. DSS-dependent intestinal inflammation significantly decreases PTZ seizure threshold and ALAC treatment completely prevents this phenomenon.

**Discussion and conclusions:** Our data support the concept that intestinal inflammation can predispose to seizures and that ALAC, improving intestinal inflammation, has antiepileptic effects also through this mechanism.