

THE THALAMIC RETICULAR NUCLEUS IS ACTIVATED BY CORTICAL SPREADING DEPRESSION IN FREELY MOVING RATS: PREVENTION BY ACUTE VALPROATE

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Aim: The present study is designed to investigate the behavioral alterations induced by cortical spreading depression (CSD), in freely moving rats and accompanying activation of certain subcortical brain structures along with TRN.

Methods: CSD's effects on behavioral parameters were recorded by using a combination of an automated behavioral analysis system and a video camera in freely moving rats. Neuronal activity was also acquired during CSD. The effects of acute valproate administration on behavioral parameters and c-fos activation were evaluated.

Results: CSD significantly decreased locomotor activity, and induced freezing behavior and immobility in consciously behaving rats. Valproate pretreatment decreased the duration of CSD-induced freezing episodes and reversed the CSD-induced reduction in locomotor activity. CSD significantly stimulated c-fos expression in trigeminal nucleus caudalis (TNC), amygdala and thalamic reticular nucleus (TRN) ipsilaterally. The c-fos activation was prominent in the visual sector of TRN and not detected in somatosensorial and auditory TRN sectors. Electrophysiological recordings revealed the propagation of SD into the TRN. Whereas acute valproate administration did not alter the electrophysiological properties of SD in the cortex, it significantly blocked CSD induced c-fos expression in TNC and TRN, but not in amygdala.

Conclusions: Multiple CSDs activate trigeminal pain nucleus in the brainstem and reticular nucleus in the thalamus in freely moving rats. Anti-migraine action of valproate may also include TRN among other sites in the brain. TRN involvement during CSD in conscious and behaving rats is a novel finding that may have mechanistic and therapeutic implications as a new target in migraine.