

CGRP RECEPTOR ANTAGONISTS ATTENUATE PAIN BEHAVIOR INDUCED BY CORTICAL SPREADING DEPRESSION IN FREELY MOVING RATS

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Aim: Cortical spreading depression (CSD) is implicated in migraine. In this study, the effect of CSD on pain and anxiety behavior in freely moving rats was investigated. In addition, the effect of CGRP receptor antagonist (MK-8825) on CSD induced behavior, and c-fos activation pattern in certain brain structures were evaluated to understand pain mechanisms.

Methods: CSD was performed by topical KCl in awake rat and basal pain thresholds to mechanical and cold allodynia were evaluated. Rats were given either saline or CGRP receptor antagonist 30 or 100 mg/kg. After CSD induction, spontaneous behavior, ultrasonic vocalization was recorded; anxiety tested by elevated plus maze and mechanical and cold allodynia were evaluated. C-fos immunohistochemistry was performed to brain sections. **Results:** MK-8825 reversed CSD induced freezing, grooming, head shake and wet dog shake behavior. MK-8825 also increased mechanical and cold allodynia thresholds. MK-8825 reduced c-fos positive cell number in ipsilateral trigeminal nucleus caudalis (TNC) and thalamic reticular nucleus.

Conclusions: CGRP receptor antagonists dose dependently attenuated CSD induced pain response. Besides blocking central transmission at TNC, CGRP receptor antagonists may also exert their effect on thalamic reticular nucleus.