Motor function changes after centrally or peripherally administered kynurenic acid

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Introduction: Data suggest that NMDA receptors play an important role in pain-induced responses, and can also influence motor behavior primarily at spinal level. The goal of this study was to reveal the motor effects of spinally and perineurally applied endogenous NMDA-antagonist kynurenic acid (KYNA).

Methods: Chronic intrathecal catheterization was performed in ketamine-xylazine anesthesia in one group of Wistar rats. Motor behavior (placing reflex, paw withdrawal behavior) and thermal pain threshold were determined before and after KYNA (10-100 µg).

The next two groups of Wistar rats were involved in electromyographic (EMG) or electroneurographic (ENG) recording studies. Wistar rats were anesthetized with ketamine-xylazine, and facial (motor) nerve at both sides was exposed at buccal level. The nerve was wrapped around unipolar wire electrode, and electrically stimulated (Fig. 1.). Motor responses of whisker muscles were recorded with unipolar needle electrodes placed into the whisker area of the rats. The sciatic (mixed) nerve activity was investigated in other group of rats. The proximal end of nerve (near to the hip) was electrically stimulated, and the nerve activities were registered from the distal end of the nerve (Fig. 2.). After baseline measurements KYNA (100 µg) was injected in the perineural sack, and repeated responses were detected for 30 min. The amplitude changes in percentage were analyzed. Lidocain was used as positive control.

Fig. 1.

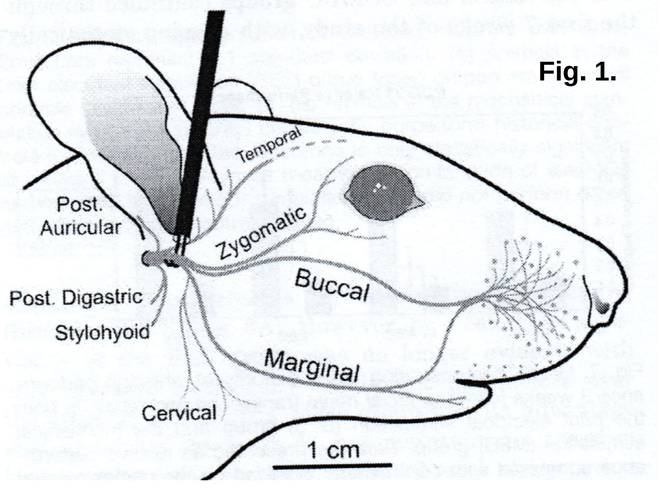
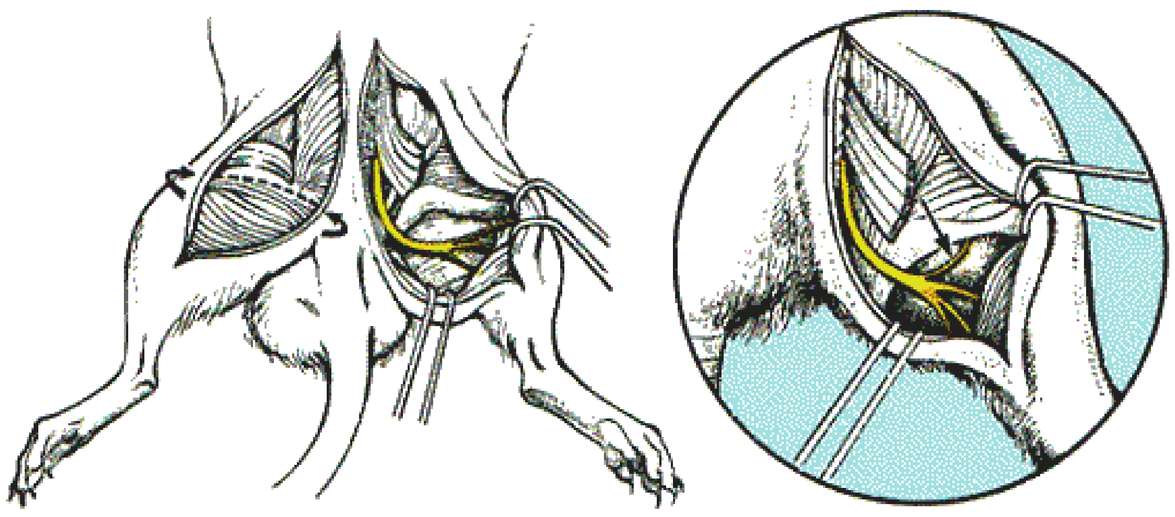


Fig. 2.



Results: Intrathecal administration of KYNA caused dose-dependent antinociception (Fig. 3.) and motor impairment (Figs. 4-5.), and the largest dose caused a prolonged paralysis at both sides up to 106 ± 5 min. Regarding the EMG or ENG activities, the single stimulus produced a visible whisker/limb movements accompanied with action potentials (AP) (Fig. 6.). Injection of a vehicle did not produce significant changes in amplitudes of APs (Fig. 7.). Lidocain evoked dose-dependent decrease in the amplitude of APs (Figs. 7-8.). In contrast a high dose of KYNA (100 µg) did not cause any effects on these nerves.

Fig. 3.

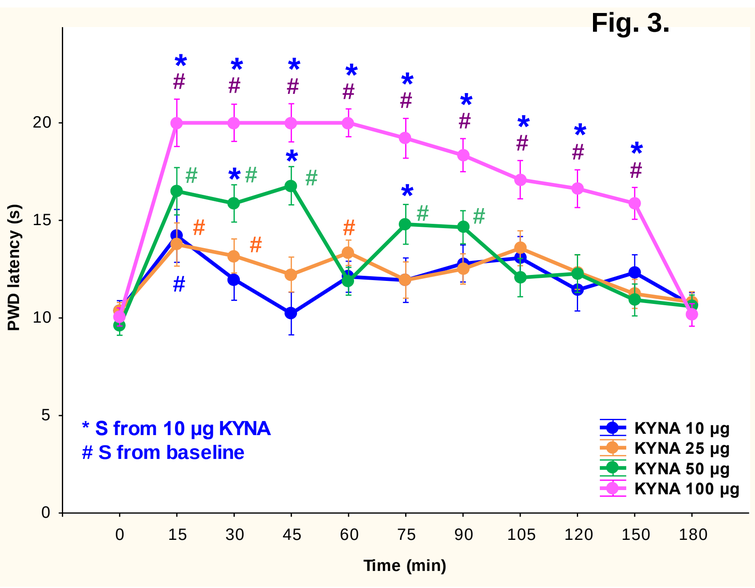


Fig. 4.

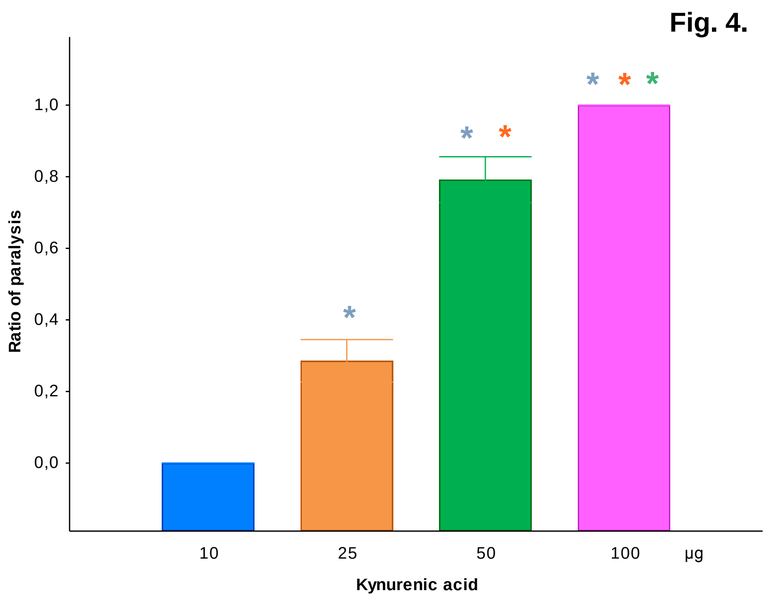


Fig. 5.

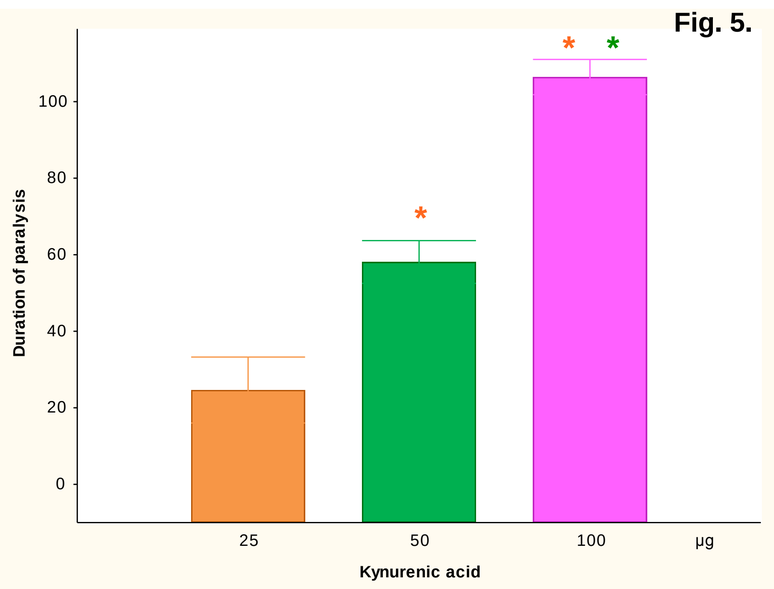


Fig. 6.

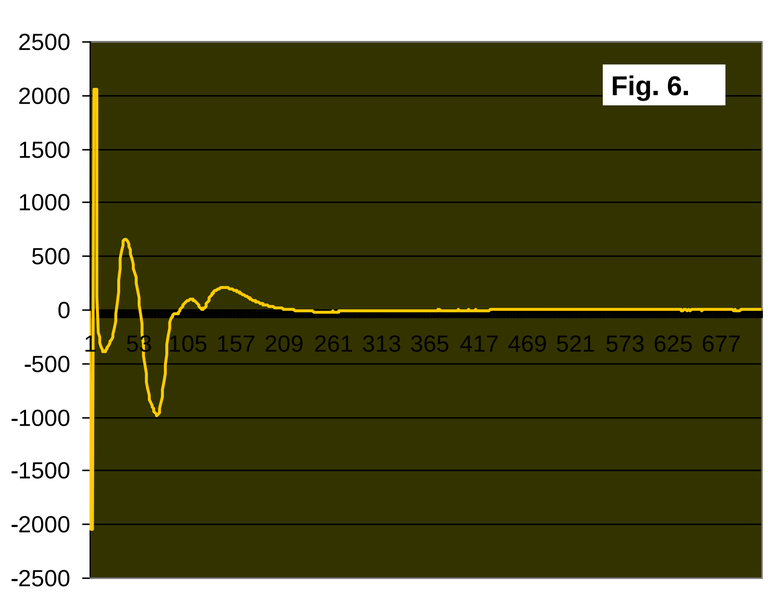


Fig. 7.

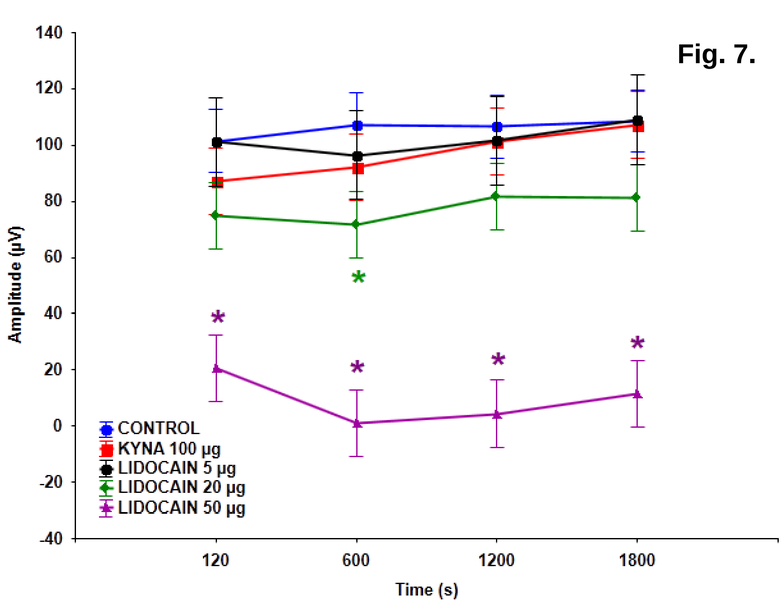
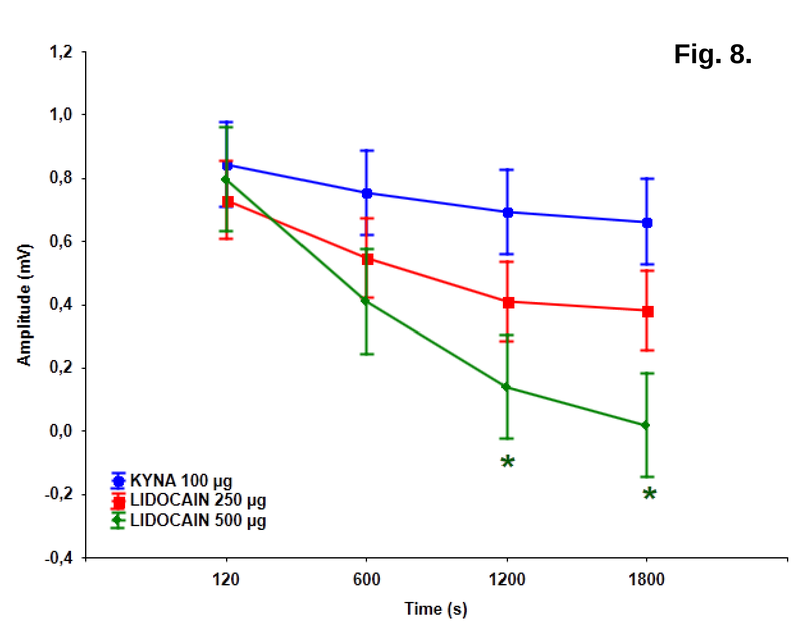


Fig. 8.



Conclusion: Our results showed that spinal KYNA treatment caused dose-dependent antinociception and motor paralysis. In contrast, it had no effect on the peripheral nerve activity, suggesting that inhibition of voltage gated sodium channels do not have role in the anesthetic effect of KYNA at spinal level.

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