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Suppression of hyperexcitability of trigeminal nociceptive neurons associated with inflammatory hyperalgesia following systemic administration of lutein via inhibition of cyclooxygenase-2 cascade signaling

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Abstract

Introduction: Lutein is a dietary constituent known to inhibit inflammation; however, its effect on nociceptive neuron-associated hyperalgesia remains to be determined. The present study therefore investigated under in vivo conditions whether administration of lutein attenuates the inflammation-induced hyperexcitability of trigeminal spinal nucleus caudalis (SpVc) neurons that is associated with mechanical hyperalgesia.

Results: Complete Freund's adjuvant (CFA) was injected into the whisker pads of rats to induce inflammation, and then mechanical stimulation was applied to the orofacial area to assess the threshold of escape. The mechanical threshold was significantly lower in inflamed rats compared to uninjected naïve rats, and this lowered threshold was returned to control levels by 3 days after administration of lutein (10 mg/Kg, i.p.) Also the lutein administration, inflammation-induced thickness of edema was returned to control levels. The mean increased number of cyclooxygenase-2 (Cox-2)-immunoreactive cells in the whisker pads of inflamed rats was also returned to control levels by administration with lutein. The mean discharge frequency of SpVc wide-dynamic range (WDR) neurons to both non-noxious and noxious mechanical stimuli in inflamed rats was significantly decreased after lutein administration. In addition, the increased mean spontaneous discharge of SpVc WDR in inflamed rats was significantly decreased after lutein administration. Similarly, lutein significantly diminished noxious pinch-evoked mean after discharge frequency and occurrence in inflamed rats. Finally, lutein restored the expanded mean size of the receptive field in inflamed rats to control levels.

Conclusion: These results together suggest that administration of lutein attenuates inflammatory hyperalgesia associated with hyperexcitability of nociceptive SpVc WDR neurons via inhibition of the peripheral Cox-2 signaling cascade. These findings support the proposed potential of lutein as a therapeutic agent in complementary alternative medicine strategies for preventing inflammatory mechanical hyperalgesia.

ハイライト:ブロッコリーやホウレンソウに含まれる食品成分であるルテインが、炎症組織で産生されるプロスタグランジン合成酵素であるシクロオキシゲナーゼ2の合成を阻害することにより、炎症性浮腫と炎症性痛覚過敏を抑制することが、行動学・免疫組織化学・電気生理学的手法により判明した。これにより、食品に含まれるルテインの摂取が、関節炎等の炎症に伴う疼痛などの症状の緩和を行う非ステロイド抗炎症薬(NSAIDs)の代わりとして奏効する可能性が示唆された。