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Resveratrol suppresses nociceptive jaw-opening reflex *via* $5HT_3$ receptor-mediated GABAergic inhibition

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ABSTRACT

Systemic administration of the dietary constituent, resveratrol, was previously shown to inhibit the nociceptive jaw-opening reflex (JOR) *via* the endogenous opioid system. The present study investigated whether resveratrol could similarly affect the JOR under *in vivo* conditions *via* $5HT_3$ receptor-mediated GABAergic inhibition. We used electrical stimulation of the tongue in pentobarbital-anesthetized rats to evoke the JOR, which was recorded as the anterior belly of the digastric muscle electromyograms (dEMG). Intravenous administration of resveratrol (2 mg/kg) reduced the dEMG amplitude in response to three times the determined threshold electrical stimulation, with maximum inhibition reached within approximately 10 min. These inhibitory effects on the JOR were reversible to control levels after approximately 20 min. Pretreatment of rats with either $5HT_3$ receptor antagonist, ondansetron (0.25–1 mg/kg, i.p.), or $GABA_A$ receptor antagonist, bicuculline (0.5–1 mg/kg, i.p.), significantly and dose-dependently attenuated the inhibitory effects of resveratrol on dEMG amplitude compared with untreated controls. These findings suggest that resveratrol also attenuates the nociceptive JOR *via* $5HT_3$ receptor-mediated GABAergic inhibition. The present study therefore provides new insight into a possible mechanism underlying resveratrol-induced trigeminal antinociception *via* the descending pain control system and highlights a potential therapeutic agent for complementary alternative medicine.

ハイライト：これまでに赤ワインの成分で知られるレスベラトロールの抑制効果は内因性疼痛抑制系の中のオピオイド受容体を介して開口反射を抑制される可能性が示唆されておりましたが、詳細なメカニズムは不明でした。今回我々は、侵害受容性開口反射を用いて「レスベラトロール」が、三叉神経脊髄路核内の5HT3受容体の活性化を介するGABA作動性抑制ニューロンを介して疼痛緩和効果を発揮することを解明し、補完代替医療に応用できる可能性を指摘致しました。