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Cannabidiol, a non-psychotropic component of cannabis, attenuates vomiting and nausea-like behaviour via indirect agonism of 5-HT(1A) somatodendritic autoreceptors in the dorsal raphe nucleus.

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Abstract

BACKGROUND AND PURPOSE: To evaluate the hypothesis that activation of somatodendritic 5-HT(1A) autoreceptors in the dorsal raphe nucleus (DRN) produces the anti-emetic/anti-nausea effects of **cannabidiol** (CBD), a primary non-psychoactive cannabinoid found in **cannabis**.

EXPERIMENTAL APPROACH: The potential of systemic and intra-DRN administration of 5-HT(1A) receptor antagonists, WAY100135 or WAY100635, to prevent the anti-emetic effect of CBD in shrews (*Suncus murinus*) and the anti-nausea-like effects of CBD (conditioned gaping) in rats were evaluated. Also, the ability of intra-DRN administration of CBD to produce anti-nausea-like effects (and reversal by systemic WAY100635) was assessed. In vitro studies evaluated the potential of CBD to directly target 5-HT(1A) receptors and to modify the ability of the 5-HT(1A) agonist, 8-OH-DPAT, to stimulate [(35) S]GTPγS binding in rat brainstem membranes.

KEY RESULTS: CBD suppressed nicotine-, lithium chloride (LiCl)- and cisplatin (20 mg·kg⁻¹), but not 40 mg·kg⁻¹)-induced vomiting in the *S. murinus* and LiCl-induced conditioned gaping in rats. Anti-emetic and anti-nausea-like effects of CBD were suppressed by WAY100135 and the latter by WAY100635. When administered to the DRN: (i) WAY100635 reversed anti-nausea-like effects of systemic CBD, and (ii) CBD suppressed nausea-like effects, an effect that was reversed by systemic WAY100635. CBD also displayed significant potency (in a bell-shaped dose-response curve) at enhancing the ability of 8-OH-DPAT to stimulate [(35) S]GTPγS binding to rat brainstem membranes in vitro. Systemically administered CBD and 8-OH-DPAT synergistically suppressed LiCl-induced conditioned gaping.

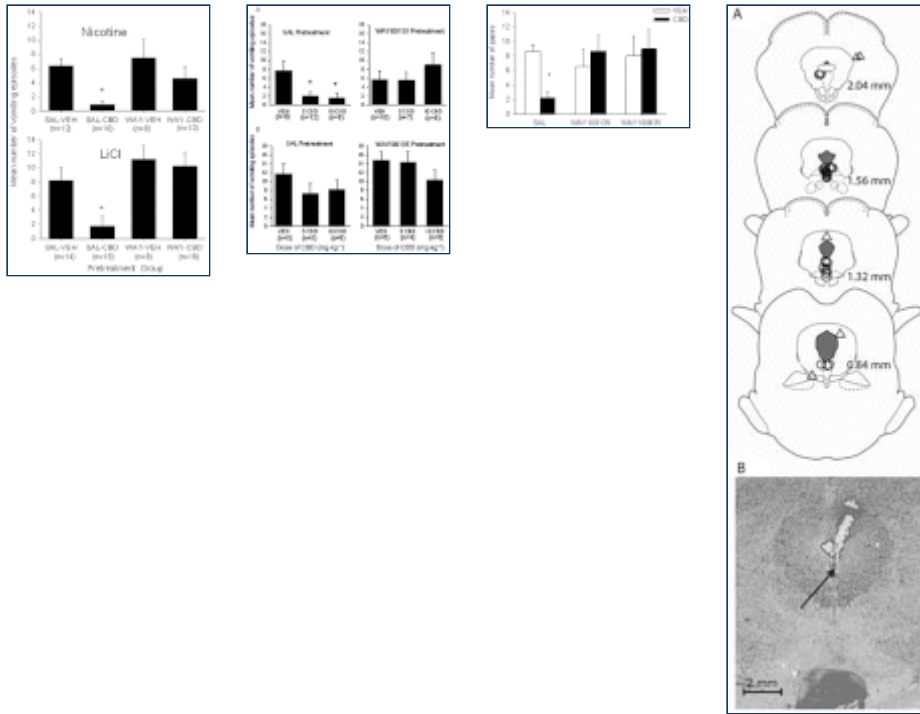
CONCLUSIONS AND IMPLICATIONS: These results suggest that CBD produced its anti-emetic/anti-nausea effects by indirect activation of the somatodendritic 5-HT(1A) autoreceptors in the DRN.

LINKED ARTICLES: This article is part of a themed section on Cannabinoids in Biology and Medicine. To view the other articles in this section visit <http://dx.doi.org/10.1111/bph.2012.165.issue-8>. To view Part I of Cannabinoids in Biology and Medicine visit <http://dx.doi.org/10.1111/bph.2011.163.issue-7>.

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