CBD: broncho-spasm, asthma, COPD

Pulm Pharmacol Ther. 2013 Jun;26(3):373-9. doi: 10.1016/j.pupt.2013.02.002. Epub 2013 Feb 18.

The effects of cannabidiol on the antigen-induced contraction of airways smooth muscle in the guinea-pig.

Dudášová A[1], Keir SD, Parsons ME, Molleman A, Page CP.

Abstract

(-)-Δ(9)-Tetrahydrocannabinol has been demonstrated to have beneficial effects in the airways, but its psychoactive effects preclude its therapeutic use for the treatment of airways diseases. In the present study we have investigated the effects of (-)-cannabidiol, a non-psychoactive component of cannabis for its actions on bronchial smooth muscle in vitro and in vivo. Guinea-pig bronchial smooth muscle contractions induced by exogenously applied spasmogens were measured isometrically. In addition, contractile responses of bronchial smooth muscle from ovalbumin-sensitized guinea-pigs were investigated in the absence or presence of (-)-cannabidiol. Furthermore, the effect of (-)-cannabidiol against ovalbumin-induced airway obstruction was investigated in vivo in ovalbumin-sensitized guinea-pigs. (-)-Cannabidiol did not influence the bronchial smooth muscle contraction induced by carbachol, histamine or neurokinin A. In contrast, (-)-cannabidiol inhibited anandamide- and virodhamine-induced responses of isolated bronchi. A fatty acid amide hydrolase inhibitor, phenylmethanesulfonyl fluoride reversed the inhibitory effect of (-)-cannabidiol on anandamide-induced contractions. In addition, (-)-cannabidiol inhibited the contractile response of bronchi obtained from allergic guinea-pigs induced by ovalbumin. In vivo, (-)-cannabidiol reduced ovalbumin-induced airway obstruction. In conclusion, our results suggest that cannabidiol can influence antigen-induced airway smooth muscle tone suggesting that this molecule may have beneficial effects in the treatment of obstructive airway disorders.

PMID:
23428645
DOI:
10.1016/j.pupt.2013.02.002

CBD: lung injury / inflammation

Eur J Pharmacol. 2012 Mar 5;678(1-3):78-85. doi:10.1016/j.ejphar.2011.12.043.Epub 2012Jan12.

Cannabidiol, a non-psychotropic plant-derived cannabinoid, decreases inflammation in a murine model of acute lung injury: role for the adenosine A(2A) receptor.

Ribeiro A[1], Ferraz-de-Paula V, Pinheiro ML, Vitoretti LB, Mariano-Souza DP, Quinteiro-Filho WM, Akamine AT, Almeida VI, Quevedo J, Dal-Pizzol F, Hallak JE, Zuardi AW, Crippa JA, Palermo-Neto J.

Abstract

Acute lung injury is an inflammatory condition for which treatment is mainly supportive because effective therapies have not been developed. Cannabidiol, a non-psychotropic cannabinoid component of marijuana (Cannabis sativa), has potent immunosuppressive and anti-inflammatory properties. Therefore, we investigated the possible anti-inflammatory effect of cannabidiol in a murine model of acute lung injury. Analysis of total inflammatory cells and differential in bronchoalveolar lavage fluid was used to characterize leukocyte migration into the lungs; myeloperoxidase activity of lung tissue and albumin concentration in the bronchoalveolar lavage fluid were analyzed by colorimetric assays; cytokine/chemokine production in the bronchoalveolar lavage fluid was also analyzed by Cytometric Bead Arrays and Enzyme-Linked Immunosorbent Assay (ELISA). A single dose of cannabidiol (20mg/kg) administered prior to the induction of LPS (lipopolysaccharide)-induced acute lung injury decreases leukocyte (specifically neutrophil) migration into the lungs, albumin concentration in the bronchoalveolar lavage fluid, myeloperoxidase activity in the lung tissue, and production of pro-inflammatory cytokines (TNF and IL-6) and chemokines (MCP-1 and MIP-2) 1, 2, and 4days after the induction of LPS-induced acute lung injury. Additionally, adenosine A(2A) receptor is involved in the anti-inflammatory effects of cannabidiol on LPS-induced acute lung injury because ZM241385 (4-(2-[7-Amino-2-(2-furyl)[1,2,4]triazolo[2,3-a][1,3,5]triazin-5-ylamino]ethyl)phenol) (a highly selective antagonist of adenosine A(2A) receptor) abrogated all of the anti-inflammatory effects of cannabidiol previously described. Thus, we show that cannabidiol has anti-inflammatory effects in a murine model of acute lung injury and that this effect is most likely associated with an increase in the extracellular adenosine offer and signaling through adenosine A(2A) receptor.

PMID:22265864DOI:10.1016/j.ejphar.2011.12.043[Indexed for MEDLINE]Free full text

CBD: “Heart Attack” Prevention and Recovery

Am J Physiol Heart Circ Physiol. 2007 Dec;293(6):H3602-7. Epub 2007 Sep 21.

Cannabidiol, a nonpsychoactive Cannabis constituent, protects against myocardial ischemic reperfusion injury.

Durst R[1], Danenberg H, Gallily R, Mechoulam R, Meir K, Grad E, Beeri R, Pugatsch T, Tarsish E, Lotan C.

Author information

Abstract

Cannabidiol (CBD) is a major, nonpsychoactive Cannabis constituent with anti-inflammatory activity mediated by enhancing adenosine signaling. Inasmuch as adenosine receptors are promising pharmaceutical targets for ischemic heart diseases, we tested the effect of CBD on ischemic rat hearts. For the in vivo studies, the left anterior descending coronary artery was transiently ligated for 30 min, and the rats were treated for 7 days with CBD (5 mg/kg ip) or vehicle. Cardiac function was studied by echocardiography. Infarcts were examined morphometrically and histologically. For ex vivo evaluation, CBD was administered 24 and 1 h before the animals were killed, and hearts were harvested for physiological measurements. In vivo studies showed preservation of shortening fraction in CBD-treated animals: from 48 +/- 8 to 39 +/- 8% and from 44 +/- 5 to 32 +/- 9% in CBD-treated and control rats, respectively (n = 14, P < 0.05). Infarct size was reduced by 66% in CBD-treated animals, despite nearly identical areas at risk (9.6 +/- 3.9 and 28.2 +/- 7.0% in CBD and controls, respectively, P < 0.001) and granulation tissue proportion as assessed qualitatively. Infarcts in CBD-treated animals were associated with reduced myocardial inflammation and reduced IL-6 levels (254 +/- 22 and 2,812 +/- 500 pg/ml in CBD and control rats, respectively, P < 0.01). In isolated hearts, no significant difference in infarct size, left ventricular developed pressures during ischemia and reperfusion, or coronary flow could be detected between CBD-treated and control hearts. Our study shows that CBD induces a substantial in vivo cardioprotective effect from ischemia that is not observed ex vivo. Inasmuch as CBD has previously been administered to humans without causing side effects, it may represent a promising novel treatment for myocardial ischemia.

PMID:17890433DOI:10.1152/ajpheart.00098.2007[Indexed for MEDLINE]
Free full text

CBD: cardiomyopathy / mitochondria

Mol Med. 2015 Jan 6;21:38-45. doi: 10.2119/molmed.2014.00261.

Cannabidiol Protects against Doxorubicin-Induced Cardiomyopathy by Modulating Mitochondrial Function and Biogenesis.

Hao E1,2, Mukhopadhyay P1, Cao Z1, Erdélyi K1, Holovac E1, Liaudet L3, Lee WS1,4, Haskó G5, Mechoulam R6, Pacher P1.
Author information

Abstract
Doxorubicin (DOX) is a widely used, potent chemotherapeutic agent; however, its clinical application is limited because of its dose-dependent cardiotoxicity. DOX's cardiotoxicity involves increased oxidative/nitrative stress, impaired mitochondrial function in cardiomyocytes/endothelial cells and cell death. Cannabidiol (CBD) is a nonpsychotropic constituent of marijuana, which is well tolerated in humans, with antioxidant, antiinflammatory and recently discovered antitumor properties. We aimed to explore the effects of CBD in a well-established mouse model of DOX-induced cardiomyopathy. DOX-induced cardiomyopathy was characterized by increased myocardial injury (elevated serum creatine kinase and lactate dehydrogenase levels), myocardial oxidative and nitrative stress (decreased total glutathione content and glutathione peroxidase 1 activity, increased lipid peroxidation, 3-nitrotyrosine formation and expression of inducible nitric oxide synthase mRNA), myocardial cell death (apoptotic and poly[ADP]-ribose polymerase 1 [PARP]-dependent) and cardiac dysfunction (decline in ejection fraction and left ventricular fractional shortening). DOX also impaired myocardial mitochondrial biogenesis (decreased mitochondrial copy number, mRNA expression of peroxisome proliferator-activated receptor γ coactivator 1-alpha, peroxisome proliferator-activated receptor alpha, estrogen-related receptor alpha), reduced mitochondrial function (attenuated complex I and II activities) and decreased myocardial expression of uncoupling protein 2 and 3 and medium-chain acyl-CoA dehydrogenase mRNA. Treatment with CBD markedly improved DOX-induced cardiac dysfunction, oxidative/nitrative stress and cell death. CBD also enhanced the DOX-induced impaired cardiac mitochondrial function and biogenesis. These data suggest that CBD may represent a novel cardioprotective strategy against DOX-induced cardiotoxicity, and the above-described effects on mitochondrial function and biogenesis may contribute to its beneficial properties described in numerous other models of tissue injury.

PMID:
25569804
PMCID:

PMC4461586
DOI:
10.2119/molmed.2014.00261
[Indexed for MEDLINE]
Free PMC Article

CBD: myocarditis and autoimmune

Mol Med. 2016 Sep;22:136-146. doi: 10.2119/molmed.2016.00007. Epub 2016 Jan 8.

Cannabidiol Limits T Cell-Mediated Chronic Autoimmune Myocarditis: Implications to Autoimmune Disorders and Organ Transplantation.

Lee WS1,2, Erdelyi K1, Matyas C1,3, Mukhopadhyay P1, Varga ZV1, Liaudet L4, Haskú G5, Čiháková D6, Mechoulam R7, Pacher P1.
Author information

Abstract
Myocarditis is a major cause of heart failure and sudden cardiac death in young adults and adolescents. Many cases of myocarditis are associated with autoimmune processes in which cardiac myosin is a major autoantigen. Conventional immunosuppressive therapies often provide unsatisfactory results and are associated with adverse toxicities during the treatment of autoimmune myocarditis. Cannabidiol (CBD) is a nonpsychoactive constituent of marijuana that exerts antiinflammatory effects independent of classical cannabinoid receptors. Recently, 80 clinical trials have investigated the effects of CBD in various diseases from inflammatory bowel disease to graft versus host disease. CBD-based formulations are used for the management of multiple sclerosis in numerous countries, and CBD also received U.S. Food and Drug Administration approval for the treatment of refractory childhood epilepsy and glioblastoma multiforme. Herein, using a well-established mouse model of experimental autoimmune myocarditis (EAM) induced by immunization with cardiac myosin emmulsified in adjuvant resulting in T cell-mediated inflammation, cardiomyocyte cell death, fibrosis and myocardial dysfunction, we studied the potential beneficial effects of CBD. EAM was characterized by marked myocardial T-cell infiltration, profound inflammatory response and fibrosis (measured by quantitative real-time polymerase chain reaction, histology and immunohistochemistry analyses) accompanied by marked attenuation of both systolic and diastolic cardiac functions measured with a pressure-volume conductance catheter technique. Chronic treatment with CBD largely attenuated the CD3+ and CD4+ T cell-mediated inflammatory response and injury, myocardial fibrosis and cardiac dysfunction in mice. In conclusion, CBD may represent a promising novel treatment for managing autoimmune myocarditis and possibly other autoimmune disorders and organ transplantation.

PMID:
26772776
PMCID:
PMC5004721
DOI:
10.2119/molmed.2016.00007
Free PMC Article

CBD: cardio

J Am Coll Cardiol. 2010 Dec 14;56(25):2115-25. doi: 10.1016/j.jacc.2010.07.033.

Cannabidiol attenuates cardiac dysfunction, oxidative stress, fibrosis, and inflammatory and cell death signaling pathways in diabetic cardiomyopathy.

Rajesh M1, Mukhopadhyay P, Bátkai S, Patel V, Saito K, Matsumoto S, Kashiwaya Y, Horváth B, Mukhopadhyay B, Becker L, Haskó G, Liaudet L, Wink DA, Veves A, Mechoulam R, Pacher P.

Author information

Abstract

OBJECTIVES:

In this study, we have investigated the effects of cannabidiol (CBD) on myocardial dysfunction, inflammation, oxidative/nitrative stress, cell death, and interrelated signaling pathways, using a mouse model of type I diabetic cardiomyopathy and primary human cardiomyocytes exposed to high glucose.

BACKGROUND:

Cannabidiol, the most abundant nonpsychoactive constituent of Cannabis sativa (marijuana) plant, exerts anti-inflammatory effects in various disease models and alleviates pain and spasticity associated with multiple sclerosis in humans.

METHODS:

Left ventricular function was measured by the pressure-volume system. Oxidative stress, cell death, and fibrosis markers were evaluated by molecular biology/biochemical techniques, electron spin resonance spectroscopy, and flow cytometry.

RESULTS:

Diabetic cardiomyopathy was characterized by declined diastolic and systolic myocardial performance associated with increased oxidative-nitrative stress, nuclear factor-κB and mitogen-activated protein kinase (c-Jun N-terminal kinase, p-38, p38α) activation, enhanced expression of adhesion molecules (intercellular adhesion molecule-1, vascular cell adhesion molecule-1), tumor necrosis factor-α, markers of fibrosis (transforming growth factor-β, connective tissue growth factor, fibronectin, collagen-1, matrix metalloproteinase-2 and -9), enhanced cell death (caspase 3/7 and poly[adenosine diphosphate-ribose] polymerase activity, chromatin fragmentation, and terminal deoxynucleotidyl transferase dUTP nick end labeling), and diminished Akt phosphorylation. Remarkably, CBD attenuated myocardial dysfunction, cardiac fibrosis, oxidative/nitrative stress, inflammation, cell death, and interrelated signaling pathways. Furthermore, CBD also attenuated the high glucose-induced increased reactive oxygen species generation, nuclear factor-κB activation, and cell death in primary human

cardiomyocytes.
CONCLUSIONS:
Collectively, these results coupled with the excellent safety and tolerability profile of CBD in humans, strongly suggest that it may have great therapeutic potential in the treatment of diabetic complications, and perhaps other cardiovascular disorders, by attenuating oxidative/nitrative stress, inflammation, cell death and fibrosis.

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21144973
PMCID:
PMC3026637
DOI:
10.1016/j.jacc.2010.07.033
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Free PMC Article

CYMENE: (a terpene prevalent in PoP tablets) vasorelaxant

ScientificWorldJournal. 2015;2015:458080. doi: 10.1155/2015/458080. Epub 2015 Jan 15.

The vasorelaxant effect of p-cymene in rat aorta involves potassium channels.

Silva MT1, Ribeiro FP1, Medeiros MA1, Sampaio PA2, Silva YM2, Silva MT2, Quintans JS3, Quintans-Júnior LJ3, Ribeiro LA4.
Author information

Abstract
The monoterpenes are the main constituents of most essential oils and p-cymene is a monoterpene commonly found in various species of aromatic herbs, which has been reported for anti-inflammatory, antinociceptive, and antimicrobial activities. However, there is no report concerning its pharmacological activity on the vascular smooth muscle. The aim of current work was to investigate the effects of p-cymene in isolated rat aorta and also study its mechanism of action. In this work, we show that p-cymene has a relaxant effect, in a dose-dependent way, on the vascular smooth muscle, regardless of the presence of the endothelium. Using a nonselective potassium channel blocker, the CsCl, the relaxant effect of p-cymene was attenuated. In the presence of more selective potassium channels blockers, such as TEA or 4-AP, no change in the relaxant effect of p-cymene was evidenced, indicating that BKCa and KV channels are not involved in that relaxant effect. However, in the presence of glibenclamide or BaCl2, KATP and Kir blockers, respectively, the relaxant effect of p-cymene was attenuated. The data presented indicate that p-cymene has a relaxing effect on rat aorta, regardless of the endothelium, but with the participation of the KATP and Kir channels.

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25667938
PMCID:
PMC4312567
DOI:
10.1155/2015/458080
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Free PMC Article

Cardioprotective effect of cannabidiol in rats exposed to doxorubicin toxicity.

Fouad AA, Albuali WH, Al-Mulhim AS, Jresat I.
Environ Toxicol Pharmacol. 2013 Sep;36(2):347-57. doi: 10.1016/j.etap.2013.04.018. Epub 2013 May 10.
PMID:
23721741
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Cannabinoids, inflammation, and fibrosis.

Zurier RB, Burstein SH.
FASEB J. 2016 Nov;30(11):3682-3689. Epub 2016 Jul 19. Review.
PMID:
27435265
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Is the cardiovascular system a therapeutic target for cannabidiol?

Stanley CP, Hind WH, O'Sullivan SE.
Br J Clin Pharmacol. 2013 Feb;75(2):313-22. doi: 10.1111/j.1365-2125.2012.04351.x. Review.

CBD: HR and BP

“A Systematic Review and Meta-Analysis of the Haemodynamic Effects of Cannabidiol.”

https://www.ncbi.nlm.nih.gov/pubmed/28286481 Front Pharmacol. 2017 Feb 24;8:81. doi: 10.3389/fphar.2017.00081. eCollection

Abstract Despite cannabidiol (CBD) having numerous cardiovascular effects *in vitro*, its haemodynamic effects *in vivo* are unclear. Nonetheless, the clinical use of CBD (Epidiolex) is becoming more widespread. The aim of this systematic review was to establish whether CBD is associated with changes in haemodynamics *in vivo*. Twenty-five studies that assessed the haemodynamic effects of CBD (from PubMed, Medline and EMBASE) were systematically reviewed and meta-analyzed. Data on blood pressure (BP), heart rate (HR), and blood flow (BF) were extracted and analyzed using random effects models. Twenty-two publications assessed BP and HR among 6 species (BP n = 344 and HR n = 395), and 5 publications assessed BF in 3 species (n = 56) after acute dosing of CBD. Chronic dosing was assessed in 4 publications in 3 species (total subjects BP, n = 6; HR, n = 27; BF, n = 3). Acute CBD dosing had no effect on BP or HR under control conditions. Similarly, chronic dosing with CBD had no effect on HR. In models of stress, acute CBD administration significantly reduced the increase in BP and HR induced by stress (BP, mean difference (MD) -3.54, 95% CI -5.19, -1.9, $p < 0.0001$; HR, MD -16.23, 95% CI -26.44, -6.02, $p = 0.002$). In mouse models of stroke, CBD significantly increased cerebral blood flow (CBF, standardized mean difference (SMD) 1.62, 95% CI 0.41, 2.83, $p = 0.009$). Heterogeneity among the studies was present, there was no publication bias except in HR of control and stressful conditions after acute CBD dosing, and median study quality was 5 out of 9 (ranging from 1 to 8). From the limited data available, we conclude that acute and chronic administration of CBD had no effect on BP or HR under control conditions, but reduces BP and HR in stressful conditions, and increases cerebral blood flow (CBF) in mouse models of stroke. Further studies are required to fully understand the potential haemodynamic effects of CBD in humans under normal and pathological conditions.

CBD: Stroke / Cardiac Events / Neuroprotective

High-Dose Cannabidiol Induced Hypotension after Global Hypoxia-Ischemia in Piglets

Garberg H.T.a, b · Solberg R.a · Barlinn J.a · Martinez-Orgado J.d · Løberg E.-M.b, c · Saugstad O.D.a, b

Author affiliations

Keywords: Newborn piglet Cannabidiol Side effects Neuroprotection Neonatal hypoxia-ischemiaHypoxic-ischemic brain injury Neonatal hemodynamics Hypotension

Neonatology 2017;112:143-149

https://doi.org/10.1159/000471786

Abstract

Background: Cannabidiol (CBD) is considered a promising neuroprotectant after perinatal hypoxia-ischemia (HI). We have previously studied the effects of CBD 1 mg/kg in the early phase after global HI in piglets. In contrast to prior studies, we found no evidence of neuroprotection and hypothesized that higher doses might be required to demonstrate efficacy in this animal model. Objective: To assess the safety and potential neuroprotective effects of high-dose CBD. Methods: Anesthetized newborn piglets underwent global HI by ventilation with 8% O2 until the point of severe metabolic acidosis (base excess -20 mmol/L) and/or hypotension (mean arterial blood pressure ≤20 mm Hg). Piglets were randomized to intravenous treatment with vehicle (n = 9) or CBD (n = 13). The starting dose, CBD 50 mg/kg, was reduced if adverse effects occurred. The piglets were euthanized 9.5 h after HI and tissue was collected for analysis. Results: CBD 50 mg/kg (n = 4) induced significant hypotension in 2 out of 4 piglets, and 1 out of 4 piglets suffered a fatal cardiac arrest. CBD 25 mg/kg (n = 4) induced significant hypotension in 1 out of 4 piglets, while 10 mg/kg (n = 5) was well tolerated. A significant negative correlation between the plasma concentration of CBD and hypotension during drug infusion was observed ($p < 0.005$). Neuroprotective effects were evaluated in piglets that did not display significant hypotension (n = 9) and CBD did not alter the degree of neuronal damage as measured by a neuropathology score, levels of the astrocytic marker S100B in CSF, magnetic resonance spectroscopy markers (Lac/NAA and Glu/NAA ratios), or plasma troponin

T. Conclusions: High-dose CBD can induce severe hypotension and did not offer neuroprotection in the early phase after global HI in piglets.

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Short Communication
Free Access

CBD: Calcium Channel / PPARg Vasorelaxant

Eur J Pharmacol. 2009 Jun 10;612(1-3):61-8. doi: 10.1016/j.ejphar.2009.03.010. Epub 2009 Mar 11.

Time-dependent vascular actions of cannabidiol in the rat aorta.

O'Sullivan SE[1], Sun Y, Bennett AJ, Randall MD, Kendall DA. **Author information**

Abstract

We have shown that the major active agent of Cannabis sativa, Delta(9)-tetrahydrocannabinol, activates peroxisome proliferator-activated receptor gamma [PPARgamma, O'Sullivan, S.E., Tarling, E.J., Bennett, A.J., Kendall, D.A., Randall, M.D., 2005c. Novel time-dependent vascular actions of delta9-tetrahydrocannabinol mediated by peroxisome proliferator-activated receptor gamma. Biochem. Biophys. Res. Commun. 337, 824-831]. The aim of the present study was to investigate whether another pharmacologically active phytocannabinoid, cannabidiol, similarly activates PPARgamma. Functional vascular studies were carried out in rat aortae in vitro by myography. PPARgamma activation was investigated using reporter gene assays, a PPARgamma competition-binding assay and an adipogenesis assay. Cannabidiol caused time-dependent (over 2 h) vasorelaxation of pre-constricted aortae, sensitive to PPARgamma antagonism (GW9662, 1 microM) and super oxide dismutase inhibition. The vascular effects of cannabidiol were not affected by endothelial denudation, nitric oxide synthase inhibition, pertussis toxin, cannabinoid CB1 or cannabinoid CB2 receptor antagonism, or capsaicin pre-treatment. When aortae were contracted with U46619 in a Ca2+-free buffer, vasorelaxation to cannabidiol was substantially reduced. Furthermore, cannabidiol (1-30 microM) inhibited the contractile response to the re-introduction of Ca2+. In a reporter gene assay, cannabidiol increased the transcriptional activity of PPARgamma. Cannabidiol was also found to bind to PPARgamma and stimulate the differentiation of 3T3-L1 fibroblasts into adipocytes, a PPARgamma-mediated response. These results show that cannabidiol binds to and activates PPARgamma, which partially underlies the time-dependent vascular effects of cannabidiol. However, cannabidiol-induced vasorelaxation in the rat isolated aorta appears to be largely due to calcium channel inhibition.

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CBD: prevents stroke

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Cannabidiol prevents cerebral infarction via a serotonergic 5-hydroxytryptamine1A receptor-dependent mechanism.

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Abstract

BACKGROUND AND PURPOSE:
Cannabidiol has been reported to be a neuroprotectant, but the neuroprotective mechanism of cannabidiol remains unclear. We studied the neuroprotective mechanism of cannabidiol in 4-hour middle cerebral artery (MCA) occlusion mice.

METHODS:
Male MCA occluded mice were treated with cannabidiol, abnormal cannabidiol, anandamide, methanandamide, cannabidiol plus capsazepine, and cannabidiol plus WAY100135 before and 3 hours after MCA occlusion. The infarct size was determined after 24 hours (2,3,5-triphenyltetrazolium chloride staining). Cerebral blood flow (CBF) was measured at, before and 1, 2, 3, and 4 hours after MCA occlusion.

RESULTS:
Cannabidiol significantly reduced the infarct volume induced by MCA occlusion in a bell-shaped curve. Similarly, abnormal cannabidiol but not anandamide or methanandamide reduced the infarct volume. Moreover, the neuroprotective effect of cannabidiol was inhibited by WAY100135, a serotonin 5-hydroxytriptamine1A (5-HT1A) receptor antagonist but not capsazepine a vanilloid receptor antagonist. Cannabidiol increased CBF to the cortex, and the CBF was partly inhibited by WAY100135 in mice subjected to MCA occlusion.

CONCLUSIONS:
Cannabidiol and abnormal cannabidiol reduced the infarct volume. Furthermore, the neuroprotective effect of cannabidiol was inhibited by WAY100135 but not capsazepine, and the CBF increased by cannabidiol was partially reversed by WAY100135. These results suggested that the neuroprotective effect of cannabidiol may be related to the increase in CBF through the serotonergic 5-HT1A receptor.
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