LE CANNABIDIOL (CBD) POUR L'ANXIÉTÉ, QU'EN DISENT LES ÉVIDENCES?

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leSoleil

JE CONTRIBUE

Recherche

30 septembre 2018 16h21

Le cannabidiol, nouvel eldorado

LA PRESSE

ACTUALITÉS | INTERNATIONAL | DÉBATS | AFFAIRES | SPORTS | AUTO | ARTS | CINÉMA | SOCIÉTÉ | GOURMAND | VOYAGE

National | Politique | Grand Montréal | Régional | Justice et faits divers | Santé | Éducation | Enquêtes | Insolite

Hemprove: de l'huile de CBD douteuse

LA PRESSE+

DÉCOUVREZ LA PRESSE+ | CE DONT VOUS AVEZ BESOIN | ÉTAPES D'INSTALLATION

CANNABIS

LE *BUZZ* DU CBD

Coca-Cola ne cache pas son intérêt pour la substance, qui se vend plus vite qu'elle n'arrive sur les rayons de la SQDC. Consommé sous forme de gélules, d'huile ou en cocktail, le cannabidiol – ou CBD – est censé soigner les petits et grands bobos du corps et du cerveau. Notre journaliste a testé cette molécule issue du cannabis pendant trois semaines, sous la supervision d'une infirmière praticienne.

UN DOSSIER DE TRISTAN PÉLOQUIN

TRISTAN PÉLOQUIN
LA PRESSE

INFO

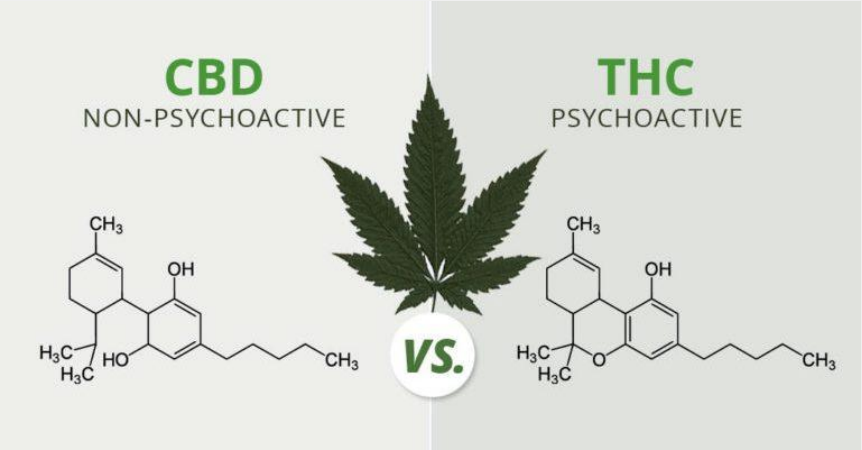
À la une | En continu | ICI RDI | Vidéos | Dossiers | Internati

ACCUEIL | INFO | ÉCONOMIE | SANTÉ

Les détaillants de cannabis peinent à garder le cannabidiol sur leurs tablettes

Le CBD

- Extrait en 1940
- Substance non psychoactive du cannabis
- Neuromodulateur du système endocannabinoid
- Action sur différents récepteurs:
  - Récepteur de type 1 vanilloid
  - **Récepteur 5-HT1A**
  - Signal de l'adénosine



Les troubles anxieux au Canada

- Plus de 3 millions de Canadien sont atteints de troubles anxieux (11.6%)
- 64.9% ont consulté un omnipraticien
- 93 % ont déjà pris des médicaments sous ordonnance

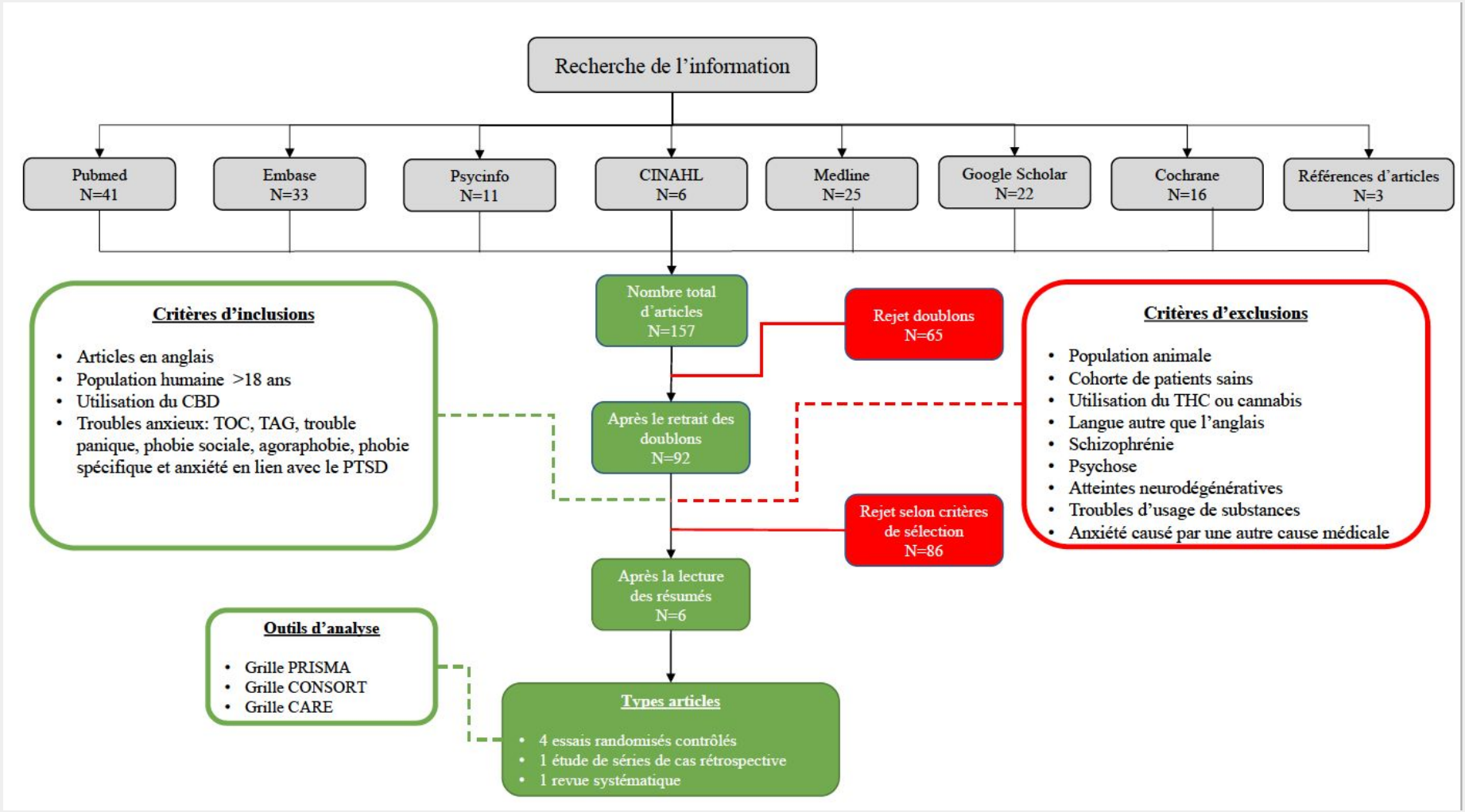
Chez les patients souffrants de troubles anxieux, est-ce que l'usage de cannabidiol efficace pour réduire l'anxiété?

P	• Chez les patients atteints de troubles anxieux
I	• L'utilisation cannabidiol (CBD)
C	• Autres méthodes pharmacologiques, aucun traitement ou placebo
O	• L'efficacité

Méthodologie

Bases de données
○ Pubmed ○ Embase ○ PsycInfo ○ CINAHL ○ Cochrane ○ Medline ○ Google scholar ○ EBM review o Autres références articles

Mots clés MeSH/ Termes libres
○ Cannabidiol ○ CBD ○ Cannabidiolum ○ Anxiety disorders ○ Anxiety ○ humans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Embase N=33
Psycinfo N=11
CINAHL N=6
Medline N=25
Google Scholar N=22
Cochrane N=16
Références d'articles N=3
Nombre total d'articles N=157
Rejet doublons N=65
Critères d'inclusions
Articles en anglais
Population humaine >18 ans
Utilisation du CBD
Troubles anxieux: TOC, TAG, trouble panique, phobie sociale, agoraphobie, phobie spécifique et anxiété en lien avec le PTSD
Après le retrait des doublons N=92
Critères d'exclusions
Population animale
Cohorte de patients sains
Utilisation du THC ou cannabis
Langue autre que l'anglais
Schizophrénie
Psychose
Atteintes neurodégénératives
Troubles d'usage de substances
Anxiété causé par une autre cause médicale
Rejet selon critères de sélection N=86
Après la lecture des résumés N=6
Outils d'analyse
Grille PRISMA
Grille CONSORT
Grille CARE
Types articles
4 essais randomisés contrôlés
1 étude de séries de cas rétrospective
1 revue systématique

	Article 1	*Article 2*	*Article 3*	*Article 4*	*Article 5*	*Article 6*
Titre	Cannabidiol Reduces the Anxiety Induced by Simulated Public Speaking in Treatment-Naïve Social Phobia Patients	The effects of cannabidiol on persecutory ideation and anxiety in a high trait paranoid group	Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report.	Cannabidiol in Anxiety and Sleep: A Large Case Series	Use of cannabidiol in anxiety and anxiety-related disorders	Anxiolytic Effects of Repeated Cannabidiol Treatment in Teenagers with Social Anxiety Disorders
Site de l'Étude	Sao Paulo, Brésil	Oxford, Royaume-Uni	Sao Paulo, Brésil	Fort Collins, Etats-Unis	Samford, Royaume-Uni	Osaka, Japon
Année de publication	2011	2018	2011	2019	2019	2019
Type de devis	Essai clinique randomisé à double insu	Essai clinique randomisé à double insu	Essai clinique randomisé transversale à double insu	Étude de série de cas rétrospective	Revue systématique	Essai clinique randomisé à double insu
Population à l'étude	Total de 36 patients : 24 atteints de phobie sociale (12 dans le groupe CBD et 12 dans le groupe placebo) et 12 sujets sains.	Total de 32 participants : 16 dans le groupe CBD et 16 dans le groupe placebo	Total de 10 hommes droitier atteint de phobie sociale	Total de 72 patients : 47 atteint de plainte primaire d'anxiété et 25 avec troubles du sommeil	8 études au total : 6 essais contrôlés randomisés, 1série de cas et 1 étude de cas	40 patients Japonais de 18-19 ans atteint de trouble anxiété sociale (SAD) répartit en 2 groupes: 20 dans le groupe placebo Et 20 dans le groupe CBD dont 3 refus traitement, car ils n'aimaient pas la senteur ou le goût. Au final, 17 participants dans le groupe CBD
Type de trouble anxieux	Phobie sociale	Traits paranoïdes	Phobie sociale	Troubles anxieux et troubles du sommeil	1 volontaire sain, 1 trouble anxieux généralisé, 1 anxiété en lien avec PTSD et 5 phobies sociales	Trouble d'anxiété sociale
Niveau d'évidence	Modéré	Modéré	Faible à modéré	Faible	Modéré	Modéré

Tableau 1 : Sommaire des articles

	Article 1	*Article 2*	*Article 3*	*Article 4*	*Article 5*	*Article 6*
Type instrument utilisé	*Visual analogue mood scale* (VAMS) *Negative Self-statement scale* (SSPS-N)	*Negative Self-statement scale* (SSPS-N) *Beck's anxiety inventory* (BAI)	*Visual analogue mood scale* (VAMS)	*Hamilton Anxiety Rating Scale* (HAM-A) *Pittsburg Sleep Quality Index* (PSQI)	*Visual Analogue Mood Scale* (VAMS) *Hamilton Anxiety Rating Scale;* (HAM-A) *Screen for Anxiety-Related Disorders* (SCARED)	*Fear of Negative Evaluation Questionnaire (FNE)* *Liebowitz Social Anxiety Scale (LSAS)*
Principaux résultats	Pour le VAMS : Le CBD montre un niveau d'anxiété inférieur (p=0.012) à la prise de parole Pour le SSPS-N : Le CBD a un impact positif à la phase anticipatoire (p = 0.043) et à la prise de parole (p = 0.001)	Au SSPS-N; aucune différence statistiquement significative. Au BAI : Tendance non significative à augmenter l'anxiété chez les patients CBD (F = 3.00, p =0.09)	Diminution du score VAMS pour le critère anxiété (mais pas pour les autres critères) avec prise de CBD a l'insertion de la canule (t = 2.74, p = 0.02), avant la spectrométrie (t = 3.61, p = 0.006) et après (t = 3.94, p = 0.003)	Au premier suivi, le taux d'amélioration pour l'anxiété et le sommeil sont de 79.2% (57/72) et 66.7% (48/72)	Le CBD améliore régulièrement les issus cliniques du trouble anxieux généralisé, de la phobie sociale et de l'anxiété liée au SSPT	Pour le FNE, la valeur moyenne du Groupe CBD était inférieure en post-intervention (p = 0.02) comparativement au groupe placebo ne démontrant pas de changement significatif (p = 0.29) Pour le LSAS, les analyses démontrent que le résultat est statistiquement plus bas en post traitement chez le groupe CBD (p = 0.03), mais que cette différence n'était pas présente dans le groupe placebo (p = 0.42)
Sources de financement	Plusieurs sources de financements par des bourses	British Medical Association, (Margaret Temple award 2011)	Plusieurs sources de financements par des bourses Financement du CBD par THC-Pharm (Francfort, Allemagne) et STI-Pharm (Brentwood, Royaume-Uni)	Financement du CBD CV Sciences Inc. Las Vegas, Nevada Pas d'autre source de financement	Aucun conflit d'intérêt rapporté par les auteurs	Grants for Excellent Graduate Schools program from the Ministry of Education, Science, Sports, and Culture, Japanese Government

Tableau 2 : Sommaire des articles (suite)

Article 1

Neuropsychopharmacology (2011) 36, 1219–1226

www.neuropsychopharmacology.org

Cannabidiol Reduces the Anxiety Induced by Simulated Public Speaking in Treatment-Naïve Social Phobia Patients

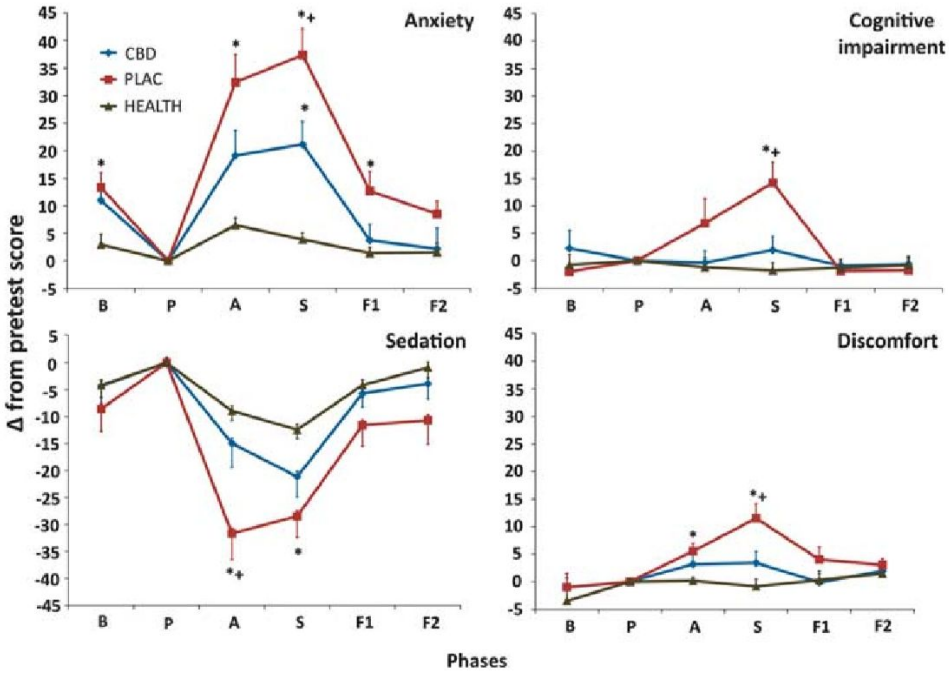
Mateus M Bergamaschi[1,2,3], Regina Helena Costa Queiroz[2,3], Marcos Hortes Nisihara Chagas[1,3], Danielle Chaves Gomes de Oliveira[1,3], Bruno Spinosa De Martinis[3,4], Flávio Kapczinski[3,5], João Quevedo[3,6], Rafael Roesler[3,7], Nadja Schröder[3,8], Antonio E Nardi[3,9], Rocio Martín-Santos[3,10], Jaime Eduardo Cecílio Hallak[1,3], Antonio Waldo Zuardi[1,3] and José Alexandre S Crippa*[,1,3]

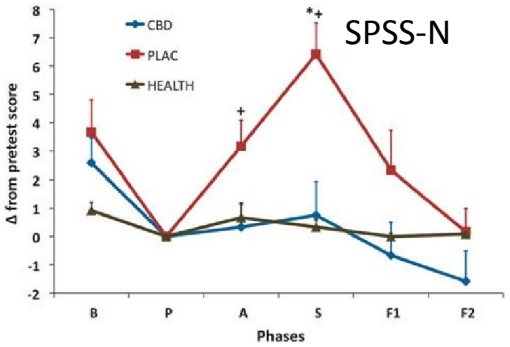
[1]Department of Neuroscience and Behavior, School of Medicine of Ribeirão Preto, University of São Paulo, SP, Brazil; [2]Department of Clinical, Toxicological and Food Sciences Analysis, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, SP, Brazil; [3]National Institute for Translational Medicine (INCT-TM), CNPq, Brazil; [4]Department of Chemistry, School of Philosophy, Science and Literature of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil; [5]Bipolar Disorder Program, Hospital de Clínicas de Porto Alegre, RS, Brazil; [6]Laboratory of Neurosciences, Health Sciences Unit, University of Southern Santa Catarina, Criciúma, SC, Brazil; [7]Laboratory of Molecular Neuropharmacology, Department of Pharmacology, Institute for Basic Health Sciences, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil; [8]Neurobiology and Developmental Biology Laboratory, School of Biosciences, Pontifical Catholic University, Porto Alegre, RS, Brazil; [9]Institute of Psychiatry, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [10]Department of Psychiatry, Institute of Neurosciences, Hospital Clínic, IDIBAPS, CIBERSAM, Barcelona, Spain

Generalized Social Anxiety Disorder (SAD) is one of the most common anxiety conditions with impairment in social life. Cannabidiol (CBD), one major non-psychotomimetic compound of the *cannabis sativa* plant, has shown anxiolytic effects both in humans and in animals. This preliminary study aimed to compare the effects of a simulation public speaking test (SPST) on healthy control (HC) patients and treatment-naïve SAD patients who received a single dose of CBD or placebo. A total of 24 never-treated patients with SAD were allocated to receive either CBD (600 mg; $n = 12$) or placebo (placebo; $n = 12$) in a double-blind randomized design 1 h and a half before the test. The same number of HC ($n = 12$) performed the SPST without receiving any medication. Each volunteer participated in only one experimental session in a double-blind procedure. Subjective ratings on the Visual Analogue Mood Scale (VAMS) and Negative Self-Statement scale (SSPS-N) and physiological measures (blood pressure, heart rate, and skin conductance) were measured at six different time points during the SPST. The results were submitted to a repeated-measures analysis of variance. Pretreatment with CBD significantly reduced anxiety, cognitive impairment and discomfort in their speech performance, and significantly decreased alert in their anticipatory speech. The placebo group presented higher anxiety, cognitive impairment, discomfort, and alert levels when compared with the control group as assessed with the VAMS. The SSPS-N scores evidenced significant increases during the testing of placebo group that was almost abolished in the CBD group. No significant differences were observed between CBD and HC in SSPS-N scores or in the cognitive impairment, discomfort, and alert factors of VAMS. The increase in anxiety induced by the SPST on subjects with SAD was reduced with the use of CBD, resulting in a similar response as the HC.
Neuropsychopharmacology (2011) **36,** 1219–1226; doi:10.1038/npp.2011.6; published online 9 February 2011

Keywords: cannabidiol; CBD; anxiety; simulation of public speaking test; SPST; social anxiety disorder

Devis de l'étude	Essai clinique randomisé double aveugle et avec groupe contrôle
Lieu de l'étude	Sao Paulo, Brésil
Date de l'étude	2011
Population à l' étude	36 patients: 12 contrôles sains, 24 avec phobie sociale: 12 placebos, 12 CBD
Niveau des évidences	faible-modéré
intervention	● 600mg cbd ou placebo ● Anxiété induite par simulation prise de parole publique ● VAMS, SSPS-N, BSS, physiologique
Conclusion	● 1 dose CBD inhibe peur de parler publique chez phobie sociale ● Auto-évaluation négative lors de prise de parole presque abolie





Résultats significatifs pour CBD vs placebo

Test	Moment	p-value
VAMS anxiété	Prise parole	0.012
VAMS cognitif	Prise parole	0.009
VAMS inconfort	Prise parole	0.029
SSPS-N	Phase anticipatoire Prise parole	0.043 0.001
BSS	s/p	s/p

Forces	Faiblesses
Outils validés	Petite population
*Forces des tests - VAMS 0.996 - SSPS-N 0.881	Niveaux plasmatiques inconnus Une dose
Paramètres démographiques comparables	*Manque info sur mise aveugle - randomisation
*Double aveugle - Sélection aléatoire : bien fait, jumelé = tx alternatif au premier	*Pas tx \ placebo chez contrôles sains
*Adhérence 100%	*Manque de rigueur dans la présentation des résultats - graphiques
*Aucune sélection de résultats	Étude = aiguë, condition = chronique
*Groupe contrôle sain	
*2 évaluateurs, Kappa = 0.84	

The effects of cannabidiol on persecutory ideation and anxiety in a high trait paranoid group

Psychopharm

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journals.sagepub.com/home/jop
SAGE

Harneet Hundal[1], Rachel Lister[2], Nicole Evans[2], Angus Antley[3], Amir Englund[1], Robin M Murray[1], Daniel Freeman[2] and Paul D Morrison[1]

Abstract

Background: Previous studies have suggested that cannabidiol has anxiolytic and antipsychotic properties, raising hopes that cannabidiol will translate to the psychiatric clinic. Cannabidiol may be particularly useful for anxiety and paranoia in those at-risk of major mental illness.

Methods: Immersion in a controlled 3D virtual-reality scenario was used to assay persecutory ideation and anxiety in a sample of non-clinical volunteers (n=32) pre-selected for high paranoid traits. Participants were randomised to receive oral cannabidiol (600 mg) or placebo 130 min prior to entering virtual-reality. Well-validated rating scales were used to assay persecutory thinking and anxiety. Salivary cortisol concentration, heart rate and blood pressure were measured over the course of the experimental session.

Results: Immersion in the virtual-reality session elicited anxiety as indexed by the Beck's anxiety inventory (p<0.005), and increased cortisol concentration (p=0.05), heart rate (p<0.05) and systolic blood pressure (p<0.05). However, cannabidiol had no impact upon any of these effects, except for a strong trend to increase anxiety (p=0.09). Cannabidiol had no effect on persecutory ideation as assayed by the Community Assessment of Psychic Experiences questionnaire or the State Social Paranoia Scale.

Conclusions: In contrast to previous studies, there was no evidence of any benefits of cannabidiol on anxiety or persecutory ideation in healthy volunteers with high trait paranoia. However, a larger sample will be required for a definitive study.

Keywords
Cannabidiol, psychosis, paranoia, anxiety, at risk mental state

Introduction

The molecule cannabidiol (CBD) is thought to have anxiolytic and anti-psychotic properties (Blessing et al., 2015; Campos et al., 2012; Iseger and Bossong, 2015; Zuardi et al., 2006). A series of studies have reported that a single oral dose of CBD, in the range 300–600 mg has anxiolytic benefits as measured by rating scales, physiological indices or neuroimaging correlates (Bergamaschi et al., 2011; Crippa et al., 2004, 2011; Fusar-Poli et al., 2009; Zuardi et al., 1993). Studies investigating an anti-psychotic effect of CBD are fewer in number but the results to date have been encouraging, with an excellent side-effect profile (Leweke et al., 2012; Zuardi et al., 2006). Ultimately it is hoped that CBD will translate to the clinic, either as an anxiolytic, an antipsychotic or both.

Cannabidiol treatment could be particularly suited for people deemed to be at high risk for developing a psychotic illness, those said to exhibit an at-risk-mental-state. The at-risk-mental-state controversial (Liu and Demjaha, 2013; McGlashan, 2001). Paranoid thinking and anxious thoughts share similar themes, in that both concern the anticipation of threat and the fear of harm (Freeman, 2007; Freeman and Garety, 2014). Numerous studies have found that anxiety is associated with paranoia and persecutory delusions (Fowler et al., 2006; Freeman et al., 2005a; Hartley et al., 2013; Johns et al., 2004; Martin and Penn, 2001). Anxiety predicts the emergence, persistence and distress of paranoia and persecutory delusions (Freeman and Garety, 2014; Hartley et al., 2014; Huppert and Smith, 2005; Naeem et al., 2006; Startup et al., 2007). If the therapeutic properties attributed to CBD turn out to be confirmed, then CBD could be a viable option for relief of paranoia and anxiety in those suffering from the at-risk-mental-state and possibly also impact on illness progression.

Article 2

Paranoid thinking and anxious thoughts share similar themes, in that both concern the anticipation of threat and the fear of harm (Freeman, 2007; Freeman and Garety, 2014). Numerous studies have found that anxiety is associated with paranoia and persecutory delusions (Fowler et al., 2006; Freeman et al., 2005a; Hartley et al., 2013; Johns et al., 2004; Martin and Penn, 2001). Anxiety predicts the emergence, persistence and distress of paranoia and persecutory delusions (Freeman and Garety, 2014; Hartley et al., 2014; Huppert and Smith, 2005; Naeem et al., 2006; Startup et al., 2007). If the therapeutic properties attributed to CBD turn out to be confirmed, then CBD could be a viable option for relief of paranoia and anxiety in those suffering from the at-risk-mental-state and possibly also impact on illness progression.

Devis de l'étude	Essai clinique randomisé double aveugle et avec groupe contrôle
Lieu de l'étude	Warneford Hospital, Oxford, UK
Date de l'étude	2018
Population à l' étude	• 32 pts: 16 Tx, 16 placebo • pamphlets envoyés à codes postaux Oxford • Puissance 80% pour détecter un large effet
Niveau des évidences	faible-modéré
intervention	• 600mg cbd ou placebo • Immersion en réalité virtuelle • SSPS-N, CAPE, UMACL, BAI, physiologique
Conclusion	• CBD = tendance non significative d'augmenter anxiété • CBD = aucun effet sur paranoia

Test	Résultats
Cape	Session x Tx (F = 0.13, p=0.7) Sous classe Sx positif : (F= 0.13, p=0.7) Négatif pour Sx psychotique
Affect : Éveil énergétique: éveillé - fatigué	Tendance RV < pré-test (F=3.0, p=0.09) *** on s'attendait au contraire Aucune interaction session x tx (F=0.75, p=0.39)
Affect : tonus hédonique: plaisir - mécontentement	Tendance RV < pré test, (F=4.1, p<0.05). *** on s'attendait au contraire Aucune interaction session x tx (F=1.3, p=0.3)
Affect : Éveil tendu: tension - relaxation	Non affecté par session CBD > placebo pré test (F=4.6, p<0.05) *** on s'attendait au contraire Aucune interaction session x tx (F=0.00, p=0.9)
BAI (Beck's anxiety inventory)	RV > pré-test (F=13.5, p=0.001). CBD > placebo pré test (F=5.1, p<0.05). *** on s'attendrait au contraire Tendance session x tx avec BAI > chez groupe CBD vs placebo. (F=3.00, p=0.09)

	Treatment×Session interaction, *F*	*p*
CAPE total	0.13	0.7
CAPE positive	0.13	0.7
Energetic arousal	0.75	0.4
Hedonic tone	1.28	0.3
Tense arousal	0.00	0.9
Beck's Anxiety Inv.	3.00	0.09
Digit-symbol recoding	0.08	0.8
Digit-span forward	0.65	0.4
Digit-span reverse	2.4	0.1
Immediate recall	0.25	0.6
Delayed recall	1.6	0.2

CAPE: Community Assessment of Psychic Experiences; SD: standard deviation.

Table 2. Psychopathology and cognitive scores at baseline and under virtual-reality sessions in the placebo versus the cannabidiol (CBD) treated group.

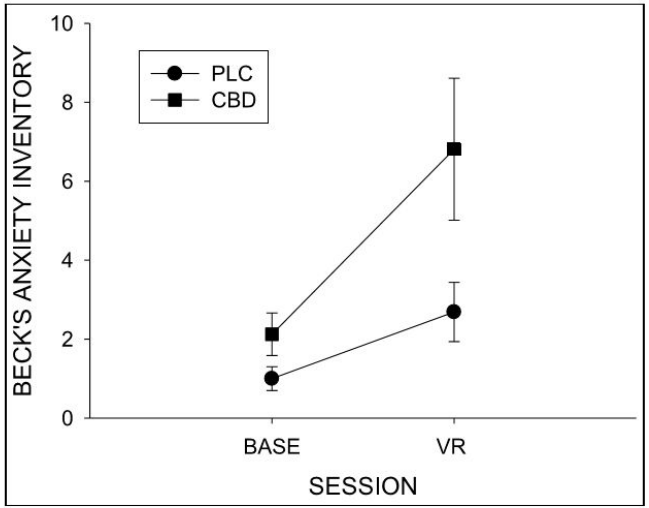

Figure 1. Effect of cannabidiol (CBD) on anxiety under virtual-reality conditions. PLC: placebo.

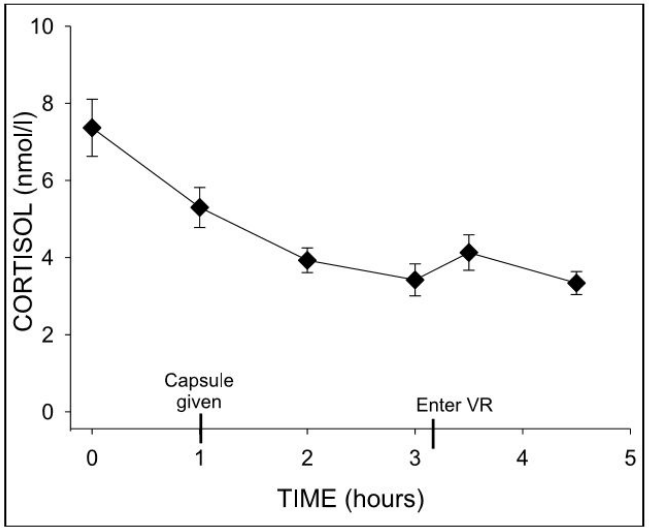

Figure 2. Cortisol levels are increased by the virtual-reality (VR) paradigm.

SSPS

Session RV: CBD > placebo

Différence entre les groupes ≠ significatif, (p=0.15)

Donc CBD pas effet

Forces	Faiblesses
Utilisation d'outils validés Psychiatre pour r/o maladie mentale	Niveaux plasmatiques inconnus Une seule dose
Paramètres démographique comparables	Petite population
Randomisé double aveugle	*Manque info sur mise en aveugle - randomisation
*Adhérence 100%	Étude = aiguë Condition = chronique
*Aucune sélection résultats	Manque de rigueur dans la présentation des résultats
*Puissance 80% pour détecter effet large	*Valeur pré-test suggestive de non validité
	Pas d'analyse statistique démographiques
	*Auteur $ du fabricant: conflit d'intérêt potentiel

Original Paper

Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report

José Alexandre S Crippa[1,2], Guilherme Nogueira Derenusson[1,2], Thiago Borduqui Ferrari[1,2], Lauro Wichert-Ana[3], Fábio LS Duran[4], Rocio Martin-Santos[2,5], Marcus Vinícius Simões[3,6], Sagnik Bhattacharyya[5], Paolo Fusar-Poli[5], Zerrin Atakan[5], Alaor Santos Filho[1,2], Maria Cecília Freitas-Ferrari[1,2], Philip K McGuire[2,5], Antonio Waldo Zuardi[1,2], Geraldo F Busatto[4] and Jaime Eduardo Cecílio Hallak[1,2]

Psychopharm

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We have thus hypothesized that CBD may be effective in SAD. However, no study to date has investigated the effects of CBD on human pathological anxiety and its underlying brain mechanisms. Therefore, in the present study, we applied functional neuroimaging to investigate the neurophysiological basis of the effects of CBD in patients with SAD. Based on previous Single Photon Emission Computed Tomography (SPECT) (Crippa et al., 2004) and functional Magnetic Resonance Imaging (fMRI) (Fusar-Poli et al., 2009) studies of CBD effects, we predicted that, relative to placebo, CBD would reduce anxiety in subjects with SAD and that this effect would be associated with the modulation of the functional activity of temporo-limbic structures (amygdala-hippocampus complex and parahippocampal gyrus) and paralimbic regions, including the cingulate cortex. To the best of our knowledge, this is the first study to directly investigate the neural and/or behavioral effects of CBD in patients with an anxiety disorder.

Devis de l'étude	Essai clinique randomisé transversal double aveugle avec placebo
Lieu de l'étude	Sao Paulo Brésil
Date de l'étude	2011
Population à l'étude	• 10 hommes, droitiers, phobie sociale • Recrutement : échantillon 2320 étudiants universitaires
Niveau des évidences	faible
intervention	• Première visite: CBD 400mg ou placebo, inverse 2e visite • Intra-sujet, CBD vs placebo, 1 semaine d'interval • VAMS différents moments • Circulation cérébrale régionale (rCBF):
Conclusion	• CBD = Diminution de l'anxiété (au VAMS) • CBD = augmentation du flot sanguin dans le gyrus cingulaire postérieur • CBD = diminution du flot sanguin au niveau du gyrus parahippocampal

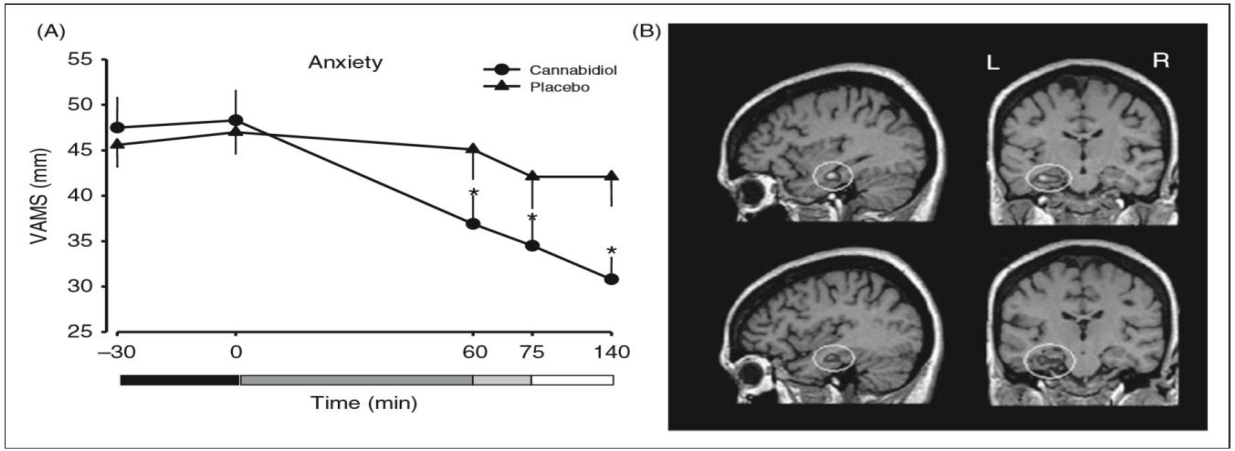

Figure 1. (A) Effect of CBD and placebo (PLCB) on the Anxiety factor of the VAMS. Points are means (±SEM) of the ratings of 10 social Anxiety disorder subjects in the phases of the experiment: pre-drug (■), pre-stess (▩), adaptation (▩) and post-stress(□). Asterisks (*) indicates significant difference from placebo in each phase. (B) The brain focus (circled) of significantly decreased rCBF in Social Anxiety Disorder subjects ($n = 10$) during CBD *vs* placebo on sagittal sections (left side of the figure) and coronal sections (right side of the figure) located in the left hippocampal area.

VAMS	Moment (facteur anxiogène)	Rx	Moment x Rx
Anxiété	F (4,36) = 21,4; p<0.001)	F (1,9) = 6.6; p<0.03)	F (4,36) =10.3, p<0.001 CBD diminue anxiété : - À l'insertion : t=2.74, p=0.02 - Pré Spectro : t=3.61, p=0.006 - Post Spectro : t=3.94, p=0.003
Sédation physique	F (4,36) p=0.99	drug F (1,9); p=3	F (4,36) p=2.34
Sédation mentale	F (4,36) p=1.68	F (1,9) p=1.90	F (4,36) p=1.4
Autres	F (4,36) p=2.66	F (1,9) p=1.46	F (4,36) p=0.05

Table 2. Effect of cannabidiol and placebo on the four factors of the Visual Analogue Mood Scale (means (SD)) for Social Anxiety Disorder subjects ($n = 10$) over the five phases of the experiment

VAMS FACTORS	Drug	Pre-drug (−30′)	Drug intake (0)	Pre-stress (60′)	Adaptation (75′)	Post-stress (140′)
Anxiety	CBD	48.3 (10.4)	47.5 (10.6)	36.9 (9.9)*	34.5 (9.2)*	30.8 (7.7)*
	Placebo	46.9 (7.6)	45.6 (7.6)	45.2 (10.2)	42.1 (11.2)	42.1 (10.3)
Physical sedation	CBD	47.8 (13.3)	47.8 (9.9)	46.7 (9.5)	46.9 (10.7)	43.9 (11.0)
	Placebo	42.6 (6.8)	43.3 (6.9)	43.2 (10.7)	45.2 (10.1)	43.7 (9.8)
Mental sedation	CBD	50.1 (12.2)	44.9 (6.4)	52.2 (7.8)	52.3 (6.2)	58.4 (5.6)
	Placebo	47.8 (7.4)	49.1 (7.7)	46.2 (10.9)	47.5 (6.8)	45.5 (12.0)
Other feelings	CBD	41.2 (11.2)	44.2 (9.4)	41.7 (13.9)	40.8 (13.2)	39.9 (12.7)
	Placebo	38.2 (15.3)	41.7 (13.4)	40.5 (15.2)	39.7 (12.4)	38.4 (14.4)

*Significant difference from placebo in the same phase of the experiment as assessed by paired sample *t*-tests, when the repeated-measures ANOVA showed a significant main effect of drug and a significant interaction between time and drug (see details in the text of the Results section).

Table 3. Areas of significant regional cerebral blood flow change in the cannabidiol condition compared with the placebo condition in subjects with social anxiety disorder ($n = 10$)

Finding	Brain Region	K[a]	*Z*-score[b]	Talairach Coordinates (x, y, z)[c]
CBD > Placebo	Posterior Cingulate Gyrus[R]	28	3.62	8, −26, 31
Placebo > CBD	Parahippocampal Gyrus[L]	31	3.47	−34, −13, −18

[a]Total number of voxels in the cluster.
[b]Z-score for the voxel of maximal statistical significance in the cluster.
[c]Coordinates of the voxel of maximal statistical significance according to the atlas of Talairach and Tournoux (1988).
[R]Right hemisphere.
[L]Left hemisphere.

Aucunes corrélations VAMS et la capture ECD

Forces	Faiblesses	
Utilisation d'outils validés	*Petite population	Niveaux plasmatiques inconnus Une seule dose (biais dose?)
Démographie comparables	Pas d'analyse démographique	*Étude transversale, aucun contrôle: Biais par effet reporté possible
Randomisé double aveugle + placebo	SPECT faible sensibilité	*Puissance non mentionnée
*Adhérence 100%	SPECT = aucune valeur absolue -relatif: capture normalisée -Influence du flot global	*Manque info sur mise aveugle - randomisation
*Aucune sélection résultats	Analyse SPECT = petit foci -Région analyse = large	Manque de rigueur dans présentation résultats
	Étude = aiguë condition = chronique	

Article 4

ORIGINAL RESEARCH & CONTRIBUTIONS

Cannabidiol in Anxiety and Sleep: A Large Case Series

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ABSTRACT

Context: Cannabidiol (CBD) is one of many cannabinoid compounds found in cannabis. It does not appear to alter consciousness or trigger a "high." A recent surge in scientific publications has found preclinical and clinical evidence documenting value for CBD in some neuropsychiatric disorders, including epilepsy, anxiety, and schizophrenia. Evidence points toward a calming effect for CBD in the central nervous system. Interest in CBD as a treatment of a wide range of disorders has exploded, yet few clinical studies of CBD exist in the psychiatric literature.

Objective: To determine whether CBD helps improve sleep and/or anxiety in a clinical population.

Design: A large retrospective case series at a psychiatric clinic involving clinical application of CBD for anxiety and sleep complaints as an adjunct to usual treatment. The retrospective chart review included monthly documentation of anxiety and sleep quality in 103 adult patients.

Main Outcome Measures: Sleep and anxiety scores, using validated instruments, at baseline and after CBD treatment.

Results: The final sample consisted of 72 adults presenting with primary concerns of anxiety (n = 47) or poor sleep (n = 25). Anxiety scores decreased within the first month in 57 patients (79.2%) and remained decreased during the study duration. Sleep scores improved within the first month in 48 patients (66.7%) but fluctuated over time. In this chart review, CBD was well tolerated in all but 3 patients.

Conclusion: Cannabidiol may hold benefit for anxiety-related disorders. Controlled clinical studies are needed.

and vomiting, and in Western medicine it was commonly used as an analgesic.[4,5] In the US, physicians prescribed *Cannabis sativa* for a multitude of illnesses until restrictions were put in place in the 1930s and then finally stopped using it in 1970 when the federal government listed marijuana as a Schedule I substance, claiming it an illegal substance with no medical value. California was the first state to go against the federal ban and legalize medical marijuana in 1996.[6] As of June 2018, 9 states and Washington, DC, have legalized recreational marijuana, and 30 states and Washington, DC, allow for use of medical marijuana.[7] The purpose of the present study is to describe the effects of CBD on anxiety and sleep among patients in a clinic presenting with anxiety or sleep as a primary concern.

CBD has demonstrated preliminary efficacy for a range of physical and mental health care problems. In the decade before 2012, there were only 9 published studies on the use of cannabinoids for medicinal treatment of pain; since then, 30 articles have been published on this topic, according to a PubMed search conducted in December 2017. Most notable was a study conducted at the University of California, San Diego's Center for Medicinal Cannabis Research that showed cannabis cigarettes reduced pain by 34% to 40% compared with placebo (17% to 20% decrease in pain).[8] In particular, CBD appears to hold benefits for a wide range of neurologic disorders, including decreasing major seizures. A recent large, well-controlled study of pediatric epilepsy documented a beneficial effect of CBD in reducing seizure frequency by more than 50%.[9] In addition to endorphin release, the "runner's high" experience after exercise has been shown to be induced in part by anandamide acting on

Devis de l'étude	Cases series de type rétrospectif (étude non expérimentale)
Lieu de l'étude	État-Unis, Colorado. Wholeness Center
Date de l'étude	Juillet 2019
Population à l'étude	72 patients qui ont au moins 1 visite de suivi dont 47 (65.3%) avec plainte primaire anxiété et 25 (34.7%) pour des troubles du sommeil
Niveau des évidences	faible
intervention	● Capsule de CBD de 25 mg/Jour le matin si trouble anxieux et le soir si trouble du sommeil ● Certains ont eu de 50mg/jour à 75 mg/jour. 1 patient avec une histoire de trauma et trouble schizoaffectif a reçue un dose de CBD graduellement augmenté AD 175 mg/jour ● Visite mensuelle: évaluation clinique et documentation par outils de mesures valides :Pittsburg Sleep Quality Index & Hamilton Anxiety Rating Scale
Conclusion	● Les résultats démontrent une tendance à diminuer l'anxiété surtout chez les patients atteints de troubles anxieux, mais avec plusieurs limites statistiques ● Les effets sur les troubles du sommeil sont incertains ● Des études randomisées contrôlées à ce sujet seront nécessaires pour démontrer des évidences cliniques ● Traitement plutôt bien toléré

Table 1. Descriptive statistics for anxiety and sleep scores among adults using cannabidiol treatment

Parameter	HAM-A, mean (SD)	PSQI, mean (SD)
Anxiety (n = 47)		
Baseline	23.87 (9.87)	10.98 (3.43)
1-month follow-up	18.02 (7.56)	8.88 (3.68)
2-month follow-up	16.35 (8.80)	8.59 (2.91)
3-month follow-up	16.36 (9.80)	9.25 (2.46)
Sleep disorder (n = 25)		
Baseline	22.18 (7.55)	13.08 (3.03)
1-month follow-up	17.82 (9.72)	10.64 (3.89)
2-month follow-up	17.36 (10.91)	9.39 (3.81)
3-month follow-up	13.78 (7.86)	9.33 (4.63)

HAM-A = Hamilton Anxiety Rating Scale; PSQI = Pittsburg Sleep Quality Index; SD = standard deviation.

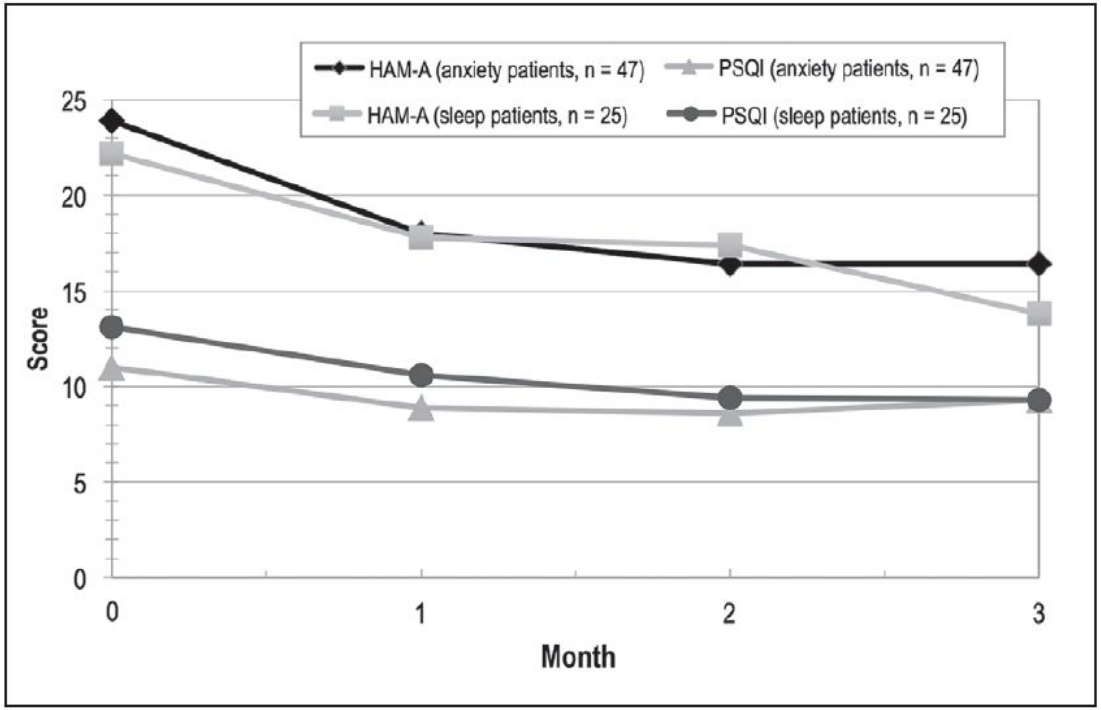

Figure 1. Mean anxiety and sleep scores for adults using cannabidiol treatment.

HAM-A = Hamilton Anxiety Rating Scale; PSQI = Pittsburg Sleep Quality Index.

Forces	Faiblesses
Utilisation d'outils validés tel que le *Pittsburg Sleep Quality Index & Hamilton Anxiety Rating Scale*	Étude de séries de cas rétrospective (étude **non expérimentale**)
Compilation des effets secondaires auto-rapporté	Description peu exhaustive de la population à l' étude
Groupes d'âges comparables entre le groupe trouble anxieux et trouble du sommeil	**Petit échantillon** à l'étude avec différences entres les groupes
	Beaucoup de pertes de vue durant l'étude
	Doses de CBD variables et sous-optimales selon les études de références
	Les patients ont **poursuivi leur traitement psychiatrique** lors de l'étude et des changements de doses ont pu survenir au même moment

Article 5

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REVIEW

Use of cannabidiol in anxiety and anxiety-related disorders

Jessica W. Skelley*, Crystal M. Deas, Zachary Curren, Jonathan Ennis

ARTICLE INFO

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ABSTRACT

Objective: Cannabidiol (CBD) has a proposed novel role in the management of anxiety owing to its actions on the endocannabinoid system. The purpose of this systematic review was to evaluate the current evidence on the safety and efficacy of CBD in anxiety and anxiety-related disorders.
Data sources: A literature search was conducted on PubMed, Google Scholar, and International Pharmaceutical Abstracts from database inception through June 2019. A bibliographic search of relevant articles was also conducted.
Study selection: Articles published from case reports, case series, or randomized controlled trials on human subjects were included in the review if they examined the safety and efficacy of CBD therapy in anxiety and anxiety-related disorders.
Data extraction: Two reviewers independently extracted the following data from the articles: year of publication; study design; patient characteristics (sex; type of anxiety disorder; use of concomitant anxiolytic therapy); dosing strategy and route of CBD administration; and safety and efficacy outcomes.
Results: Eight articles were included in the review: 6 small, randomized controlled trials; 1 case series; and 1 case report. These studies examined the role of CBD in the anxiety response of healthy volunteers; in generalized anxiety disorder; in social anxiety disorder; and in the anxiety component of posttraumatic stress syndrome. No articles that evaluated CBD in panic disorder, specific phobia, separation anxiety, and obsessive-compulsive disorder were identified. In the studies, CBD was administered orally as a capsule or as a sublingual spray and as either monotherapy or adjunctive therapy. Doses varied widely, with studies employing fixed CBD doses ranging from 6 mg to 400 mg per dose. Various anxiety assessment scales were used in the studies to assess efficacy, with CBD demonstrating improved clinical outcomes among the instruments. In general, CBD was well-tolerated and associated with minimal adverse effects, with the most commonly noted adverse effects being fatigue and sedation.
Conclusion: CBD has a promising role as alternative therapy in the management of anxiety disorders. However, more studies with standardized approaches to dosing and clinical outcome measurements are needed to determine the appropriate dosing strategy for CBD and its place in therapy.

Devis de l'étude	Revue systématique
Lieu de l'étude	Samford University, Birmingham
Date de publication	Décembre 2019
Niveau évidence	modéré
intervention	Évaluer les évidences sur la sécurité et l'efficacité de l'utilisation du CBD dans le traitement de l'anxiété et des troubles anxieux
méthodologie	2 réviseurs indépendant pour la recherche et la synthèse des donnée Recherche dans 3 bases de données avec des mots clés établis 3 critères inclusions et 6 critères exclusions
Résultats	8 articles sélectionnés chaque étude a démontré une diminution de l'anxiété ou trouble anxieux avec (P< 0.001 à 0.05)
Conclusion	l'administration de CBD à démontré une amélioration des résultats cliniques lors de trouble anxieux généralisé, trouble anxiété sociale et l'anxiété lié au PTSD peu d'effets secondaire ont été associés à la prise de CBD

Table 1
Study summaries: Efficacy and safety of CBD in anxiety disorders

Citation	N	Classification	Study design	Subject(s)	CBD dose and route of administration	Acute versus chronic CBD dosing	Comparison anxiolytic with or without placebo	Measures of anxiety symptoms
Crippa et al., 2004[17]	10	Anxiety response in healthy volunteers	RCT; crossover	Healthy males without anxiety diagnosis	CBD 400 mg orally x 1 dose, gelatin capsules (n = 10)	Acute	Placebo comparison with crossover (n = 10)	VAMS
Shannon et al., 2019[19]	72	Anxiety response in patients with either GAD or insomnia diagnosis	Open-label, case series	GAD diagnosis (n = 47; 28 males; 19 females) Insomnia diagnosis (n = 25)	CBD 25–175 mg, dosed daily, oral capsules (n = 72)	Chronic	None	HAM-A
Shannon et al., 2016[20]	1	GAD	Case report	10-year-old female with anxiety diagnosis	Months 1–4: CBD 25 mg dosed daily, capsule Months 4–6: CBD 25 mg dosed daily, capsule; and CBD 6–12 mg as needed for anxiety, sublingual spray	Chronic and acute	None	SCARED
Zuardi et al., 2017[21]	59	Healthy volunteer model of SAD	RCT	Healthy males (n = 29) and females (n = 30)	CBD oral capsule x 1 dose: 100 mg (n = 11; 5 males, 6 females) 300 mg (n = 12; 6 males, 6 females) 900 mg (n = 12; 6 males, 6 females)	Acute	Placebo (n = 12; 6 males, 6 females) Clonazepam 1 mg (n = 12; 6 males, 6 females)	VAMS
Zuardi et al, 1993[23]	40	Healthy volunteer model of SAD	RCT	Healthy males (n = 18) and females (n = 22)	CBD 300 mg, oral gelatin capsule x 1 dose (n = 10)	Acute	Placebo (n = 10) Ipsapirone 5 mg (n = 10) Diazepam 10 mg (n = 10)	VAMS
Linares et al, 2019[24]	57	Healthy volunteer model of SAD	RCT	Healthy males	CBD oral capsule x 1 dose: 150 mg (n = 15) 300 mg (n = 15) 600 mg (n = 12)	Acute	Placebo (n = 15)	VAMS
Bergamaschi et al, 2011[25]	36	SAD diagnosis	RCT	SAD diagnosis (n = 24; 12 males, 12 females) Healthy control patients (n = 12; 6 males, 6 females)	CBD 600 mg x 1 dose, oral gelatin capsules (n = 12)	Acute	Placebo (n = 12; 6 males, 6 females)	VAMS
Crippa et al., 2011[26]	10	SAD diagnosis	RCT; crossover	Males with SAD diagnosis	CBD 400 mg oral x 1 dose, gelatin capsules (n = 10)	Acute	Placebo comparison with crossover (n = 10)	VAMS

Abbreviations used: CBD, cannabidiol; RCT, randomized controlled trial; VAMS, Visual Analogue Mood Scale; GAD, generalized anxiety disorder; HAM-A, Hamilton Anxiety Rating Scale; SCARED, Screen for Anxiety-Related Disorders; SAD, social anxiety disorder.

Forces	Faiblesses
Bonne méthodologie	**Risque de biais inhérent** à chaque étude non disponible
beaucoup études de cohorte à double insu	pas d'analyse de **sous-groupe**
Traite la plupart des troubles anxieux	**validité externe faible**
Bon résumé de chaques articles utilisés	**faible échantillon**

Article 6

frontiers in Psychology

ORIGINAL RESEARCH
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Check for updates

Anxiolytic Effects of Repeated Cannabidiol Treatment in Teenagers With Social Anxiety Disorders

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Accumulated evidence indicates that cannabidiol (CBD), a nonpsychotomimetic and nonaddictive main component of the *Cannabis sativa* plant, reverses anxiety-like behavior. The purpose of the present study was to assess the efficacy of CBD treatment for Japanese late teenagers with social anxiety disorder (SAD). Thirty-seven 18–19-year-old Japanese teenagers with SAD and avoidant personality disorder received, in a double-blind study, cannabis oil (n = 17) containing 300 mg CBD or placebo (n = 20) daily for 4 weeks. SAD symptoms were measured at the beginning and end of the treatment period using the Fear of Negative Evaluation Questionnaire and the Liebowitz Social Anxiety Scale. CBD significantly decreased anxiety measured by both scales. The results indicate that CBD could be a useful option to treat social anxiety.

Keywords: cannabidiol, social anxiety disorder, cannabis, cannabinoid, social phobia, avoidant personality disorder, social withdrawal

OPEN ACCESS

Edited by:
Changiz Mohiyeddini, Northeastern University, United States

Devis de l'étude	Essai clinique randomisé à double insu
Lieu de l'étude	Japon
Date de l'étude	Novembre 2019
Population à l'étude	● 37 participants ● 4 critères d'inclusions et 6 critères exclusions
Niveau des évidences	modéré
intervention	● 2 groupes en parallèles CBD VS placebo, randomisation aléatoire à l'aveugle ● reçoit CBD oralement 300 mg en huile en après midi à chaque jour ou placebo d'huile d'olive pour 4 semaines ● Fear of Negative Evaluation Questionnaire (FNE) et Liebowitz Social Anxiety Scale (LSAS) pré-intervention et 4 semaines post-intervention ● Puis rencontre 1x/semaine pour 6 mois (visite clinique psychologue)
Conclusion	● Il semblerait avoir une effet anxiolytique du l'utilisation récurrente du CBD chez des personnes de 18-19 ans atteint de SAD

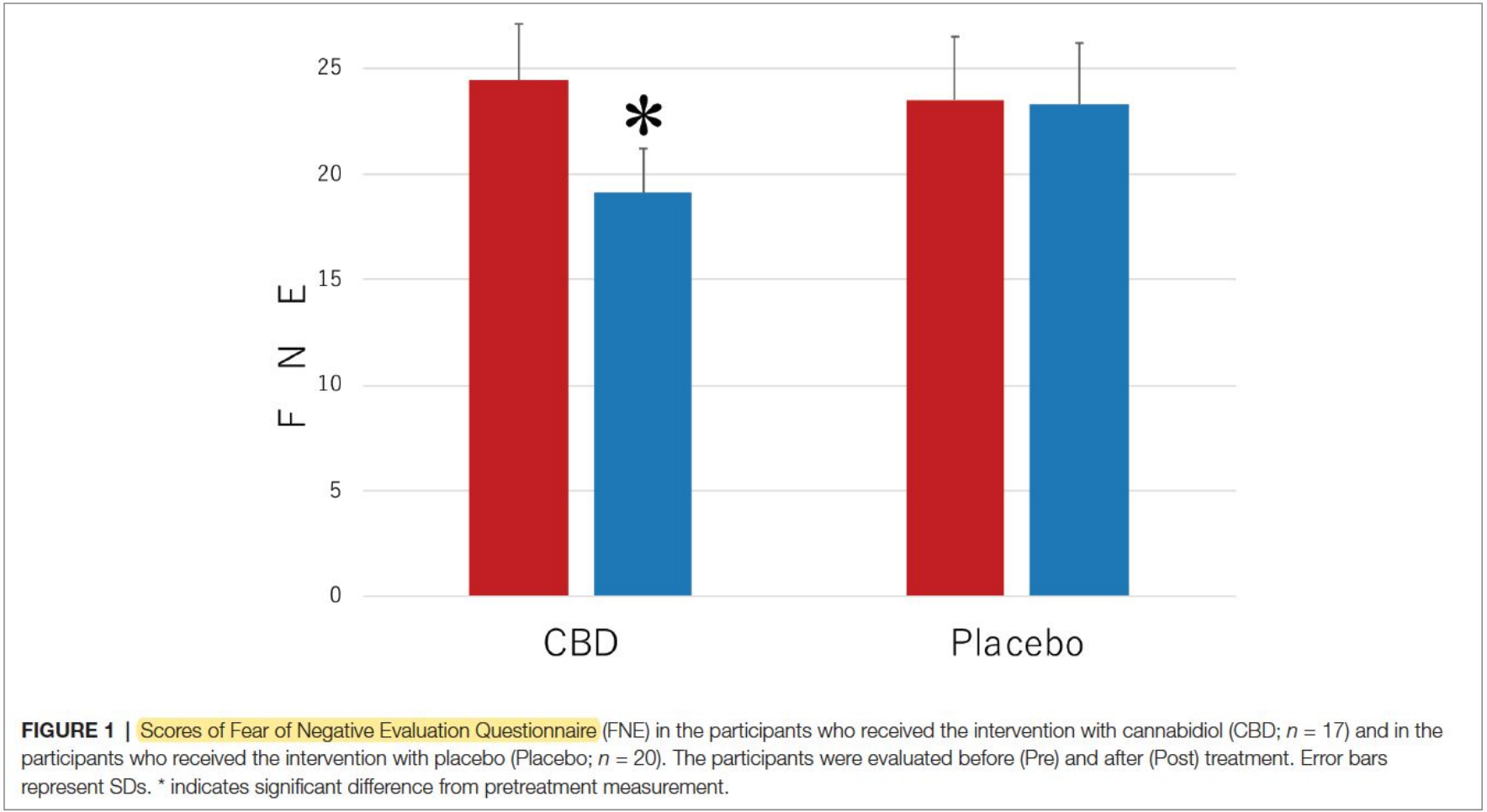


FIGURE 1 | Scores of Fear of Negative Evaluation Questionnaire (FNE) in the participants who received the intervention with cannabidiol (CBD; $n = 17$) and in the participants who received the intervention with placebo (Placebo; $n = 20$). The participants were evaluated before (Pre) and after (Post) treatment. Error bars represent SDs. * indicates significant difference from pretreatment measurement.

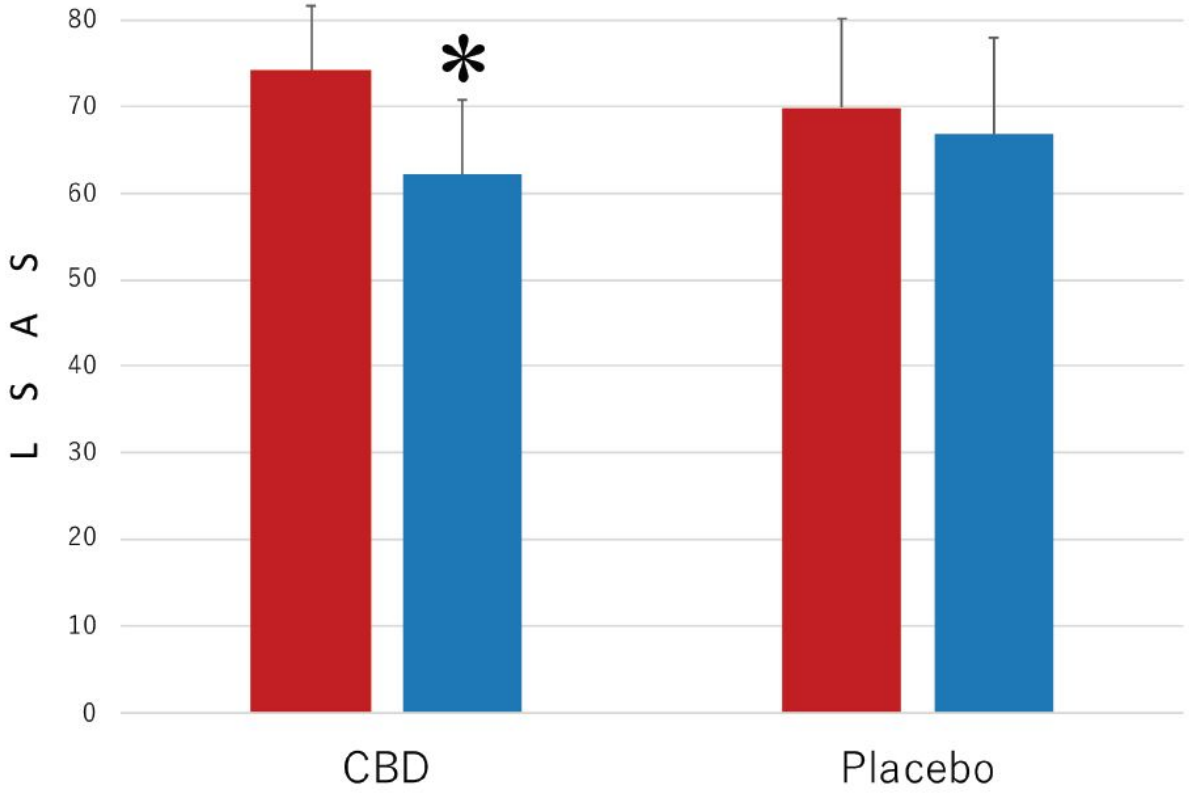


FIGURE 2 | Scores of Liebowitz Social Anxiety Scale (LSAS) in the participants who received the intervention with cannabidiol (CBD; $n = 17$) and in the participants who received the intervention with placebo (Placebo; $n = 20$). The participants were evaluated before (Pre) and after (Post) treatment. Error bars represent SDs.
* indicates significant difference from pretreatment measurement.

Forces	Faiblesses
Étude randomisée à double aveugle	L’**échantillon** spécifique, sans donnés démographiques
Statisticien indépendant	**Formulation du CBD**
2 échelles de mesures utilisés	Pas de mesure prise à 2 semaines
Bonne méthodologie	**Validité externe faible**

Discussion

- Peu d’étude sur patients Tr anxieux
  - Sujets sains, animaux, anatomie, biochimie, physiologie

- Article 5
  - Phobies sociales, TAG, anxiété PTSD
  - Revue systématique: faible validité externe

- Article 2 : conservé, Tendance à exacerber l’anxiété

- Article 4 : Aucune analyse statistique, Risque sévère de biais

Discussion

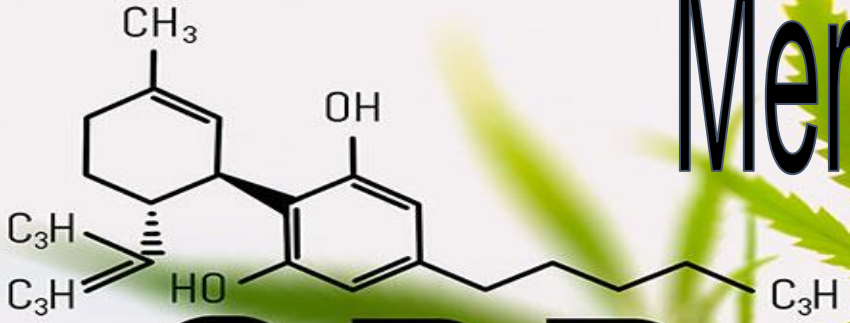
- Phobie sociale (Articles 1-3-6) : impact positif
  - Essaies cliniques randomisés, Mesures validées
  - Qualité faible – modéré : nombreux biais, petite taille, 83 participants

- Article 1 : Groupe sain, Intéressant comme protocole
- Article 3
  - Haut risque de biais par effet reporté
  - Résultats anatomo-physiologiques : interprétation difficile
- Article 6 : Chevauchement, LSAS CBD post tx sans comparatif

Conclusion

- Popularité et accessibilité grandissante
- Études cliniques de meilleure qualité nécessaires
- Résultats encourageants, mais peu fiables
- Deux études cliniques à double insu McMaster:
  - 50 patients: multiples troubles anxieux
  - 160 patients phobie sociale

Merci de votre attention



CBD

Cannabidiol

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