Post-Traumatic Stress Disorder
And The Oregon Medical Marijuana Program

An overview of research and testimony regarding Post-Traumatic Stress Disorder and the use of medical marijuana to treat symptoms.

Contents

Senate Bill 281

Sponsored by Senator BOQUIST (at the request of Todd Dalotto) (Presession filed.)

SUMMARY

The following summary is not prepared by the sponsors of the measure and is not a part of the body thereof subject to consideration by the Legislative Assembly. It is an editor's brief statement of the essential features of the measure **as introduced.**

Adds post-traumatic stress disorder to definition of "debilitating medical condition" for purposes of statutes authorizing medical use of marijuana.

A BILL FOR AN ACT

Relating to medical marijuana; amending ORS 475.302.

Be It Enacted by the People of the State of Oregon:

SECTION 1. ORS 475.302 is amended to read:

475.302. As used in ORS 475.300 to 475.346:

(1) "Attending physician" means a physician licensed under ORS chapter 677 who has primary responsibility for the care and treatment of a person diagnosed with a debilitating medical condition.

(2) "Authority" means the Oregon Health Authority.

(3) "Debilitating medical condition" means:

(a) Cancer, glaucoma, agitation [*due*] **incident** to Alzheimer's disease, positive status for human immunodeficiency virus or acquired immune deficiency syndrome, or **a side effect related to the** treatment [*for*] **of** these **medical** conditions;

(b) A medical condition or treatment for a medical condition that produces, for a specific patient, one or more of the following:

(A) Cachexia;

(B) Severe pain;

(C) Severe nausea;

(D) Seizures, including [*but not limited to*] seizures caused by epilepsy; or

(E) Persistent muscle spasms, including [*but not limited to*] spasms caused by multiple sclerosis; [*or*]

(c) Post-traumatic stress disorder; or

[*(c)*] **(d)** Any other medical condition or **side effect related to the** treatment [*for*] **of** a medical condition adopted by the authority by rule or approved by the authority pursuant to a petition submitted [*pursuant to*] **under** ORS 475.334.

(4) "Delivery" has the meaning given that term in ORS 475.005. "Delivery" does not include transfer of marijuana by a registry identification cardholder to another registry identification cardholder if no consideration is paid for the transfer.

(5) "Designated primary caregiver" means an individual 18 years of age or older who has significant responsibility for managing the well-being of a person who has been diagnosed with a debilitating medical condition and who is designated as such on that person's application for a registry identification card or in other written notification to the authority. "Designated primary

NOTE: Matter in **boldfaced** type in an amended section is new; matter [*italic and bracketed*] is existing law to be omitted. New sections are in **boldfaced** type.

Statement on the Status of Adding Debilitating Conditions to the Oregon Medical Marijuana Act.

Since the enactment of the Oregon Medical Marijuana Act, there have been two attempts to add qualifying conditions through the process prescribed in the Act under section 475.334. These requests were denied.

Oregon Administrative Rule 333-008-0900 defines the process for adding qualifying conditions. This process is outlined below.

Subsequently The Oregon Health Authority has requested this past summer that this rule be amended. The OHA held public hearings regarding this change and have submitted the subsequent change but has not yet adopted the new rule.

Prior to change:

The process under 475.334, calls for a person to petition the Oregon Health Authority who shall, "adopt rules establishing the manner in which the authority will evaluate petitions submitted under this section." Oregon Administrative Rule 333-008-0900, gives the Authority up to 180 days from receipt of petition to reach a final determination and is "subject to judicial review."

The review process allows for an explanation for why the condition should be included, "any literature in support," "letters of support from physicians ..... knowledgeable about the condition" and "suggestions for potential expert panel members." The State Public Health Officer (SPHO) may deny without review any "petition that is frivolous."

The Authority "...shall appoint an expert panel of five to seven individuals to review a petition. The panel shall include the State Public Health Officer or designee, other physicians licensed under ORS 677, at least one patient, at least one patient advocate, and other professionals knowledgeable about the condition being considered." The panel shall "...make recommendations to the Authority regarding approval or denial."

The panel"...*may* examine medical research...." and, "...*may* gather information ... from other parties knowledgeable about the condition being considered," and, ..."will submit individual recommendations to the SPHO and the meetings *will not be considered to be public hearings*." (Italics added)

The subsequent rule change would allow that these hearings now be public but has removed the panel from the process and reaffirmed the final decision be vested with the SPHO where it has always been.

In the last year four different administrators have been appointed to oversee the Oregon Medical Marijuana Program, two interim and two permanent with David Leland now interim director.

This revolving door of administrators along with the pending change for adding qualifying conditions is the reason we are once again before the legislature seeking this addition.

Since the beginning of the Oregon Medical Marijuana Program, although the program allows for additions of qualifying conditions, the only time a condition *has* been added, is by legislative action. This speaks not only to the inadequate means to add conditions provided by statute, but the deeper issue of structural changes needed to OMMA for the increased health and well-being of its patients.

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Key Aspects of State and D.C. Medical Marijuana Laws

State	Year Initially Enacted	Home Cultivation	Caregivers	Possession Limits	Dispensaries	Qualifying Conditions	ID Cards?	Recognizes Out-of-State ID Cards?
Alaska	1998, initiative, revised later by the legislature.	Allowed.	Yes. Caregivers can assist only one patient, unless the caregiver is a relative of more than one patient.	One ounce of marijuana, six plants.	Not allowed.	Cancer, HIV/AIDS, glaucoma, cachexia, severe pain, severe nausea, seizures, and persistent muscle spasms.* The health department can approve additional conditions.	Yes, through the Department of Health and Social Services.	No.
Ariz.	2010, initiative.	Allowed in enclosed, locked facility if the patient does not live within 25 miles of a dispensary.	Yes. Caregivers can assist up to five patients. Caregivers cannot be paid for their services, but they may be reimbursed for actual expenses.	Two and one-half ounces of marijuana, 12 plants for those allowed to cultivate.	Yes. More than 90 Department of Health Services-regulated non-profit dispensaries received preliminary certificates. One has passed inspection and is allowed to open. Subject to 6.6% sales tax.	Cancer, HIV/AIDS, Hepatitis C, ALS, Crohn's disease, glaucoma, Alzheimer's, severe and chronic pain, cachexia, severe nausea, seizures, or persistent muscle spasms. The Department of Heath Services can approve additional conditions.	Yes, through the Department of Health Services.	Yes, for patients with conditions that qualify under Arizona law. Does not allow out-of-state patients to obtain marijuana from dispensaries.

* = Some or all of this state's listed illnesses must be resistant to other treatments.

Last updated: Dec. 3, 2012.

Disclaimer: This grid is not intended for or offered for legal advice. It is for informational and educational purposes only. It also does not capture nuances of the laws, many of which are a dozen or more pages. Please consult with an attorney licensed to practice in the state in question for legal advice.

State	Year Initially Enacted	Home Cultivation	Caregivers	Possession Limits	Dispensaries	Qualifying Conditions	ID Cards?	Recognizes Out-of-State ID Cards?
Del.	2011, legislation.	Not allowed.	Yes. Caregivers can assist up to five patients.	Up to six ounces at one time.	Yes, three compassion centers were scheduled to be registered by Jan. 1, 2013, but Gov. Markell placed that part of Delaware's law on hold. Only revenues above $1.2 million per year are subject to gross receipts taxes.	Cancer, HIV/AIDS, ALS, decompensated cirrhosis, Alzheimer's, PTSD, debilitating pain that has not responded to other treatments or if they produced serious side effects, intractable nausea, seizures, and persistent muscle spasms. The health department can add conditions.	Yes. Issued by the Department of Health and Social Services. Cards should be issued beginning in fall 2012. A defense is available to patients who possess no more than six ounces of marijuana until then.	Yes, for patients with conditions that qualify under Delaware law. Dispensaries can only provide marijuana to patients with a Delaware ID card.
D.C.	1998, initiative, later revised by D.C. Council. Because of intervention by Congress, the law did not go into effect until July 2010.	Not presently allowed, but a committee was supposed to recommend whether to allow it by January 1, 2012.	Yes. Caregivers can assist only one patient.	Up to two ounces in a 30-day period, obtained from a registered dispensary. The mayor can increase this to four ounces.	Yes, the health department selected six growers in March 2012 and four dispensaries in September. Patients will pay 6% sales tax. Dispensaries must have a sliding scale of prices for low-income patients.	Cancer, HIV/AIDS, glaucoma, severe and persistent muscle spasms, and conditions treated with chemotherapy, AZT, protease inhibitors, or radiotherapy. The mayor can approve additional conditions.	Yes, issued by the Department of Health. Not yet accepting applications.	No.
Hawaii	2000, legislation.	Allowed.	Yes. Caregivers can assist only one patient.	A patient and caregiver can collectively possess three ounces and cultivate three mature plants and four immature plants.	Not allowed.	Severe pain, cachexia, severe nausea, seizures, or severe and persistent muscle spasms. The health department can approve additional conditions.	Yes, through the state Department of Public Safety.	No.

State	Year Initially Enacted	Home Cultivation	Caregivers	Possession Limits	Dispensaries	Qualifying Conditions	ID Cards?	Recognizes Out-of-State ID Cards?
Mich.	2008, initiative.	Allowed in enclosed, locked location.	Yes. Caregivers can assist up to five patients at a time.	2.5 ounces. The patient or caregiver can grow up to 12 plants for a patient.	Not provided for in the state law, though some cities have local ordinances.	Cancer, HIV/AIDS, Hepatitis C, ALS, Crohn's disease, nail patella, glaucoma, Alzheimer's, severe and chronic pain, cachexia, severe nausea, seizures, or severe and persistent muscle spasms. The department can add conditions.	Yes, through the Department of Licensing and Regulatory Affairs.	Yes.
Mont.	2004, initiative, restricted by legislature in 2011. Parts of the law have been blocked in court.	Allowed.	Yes. Under the revised law, caregivers can assist only three and cannot be compensated.	Four mature plants, 12 seedlings, and one ounce.	Not explicitly allowed, but caregivers could assist an unlimited number of patients until July 1, 2011, resulting in storefront operations. However, the three patient cap part of the new law is currently enjoined.	Cancer, HIV/AIDS, glaucoma, cachexia, intractable nausea or vomiting, seizure disorder, MS, Crohn's, painful peripheral neuropathy, admittance to hospice care, or in some cases, severe pain or spasms.	Yes, through the Department of Health and Human Services.	No. The state had reciprocity prior to the 2011 amendment to the law.
Nev.	1998 and 2000, amendment to state constitution approved by voters, legislation followed.	Allowed.	Yes. Caregivers must have significant responsibility for managing a patient's well-being. Marijuana cannot be delivered for compensation.	One ounce, three mature plants, four immature plants.	Not allowed, though the state constitution requires the legislature to craft legislation that includes the "authorization of appropriate methods for supply of the plant to patients authorized to use it."	Cancer, HIV/AIDS, glaucoma, severe pain, cachexia, severe nausea, seizures, or persistent muscle spasms. The health department can approve additional conditions.	Yes, through the Department of Health and Human Services.	No.

* = Some or all of this state's listed illnesses must be resistant to other treatments.

State	Year Initially Enacted	Home Cultivation	Caregivers	Possession Limits	Dispensaries	Qualifying Conditions	ID Cards?	Recognizes Out-of-State ID Cards?
R.I.	2006, legislation, revised later by legislature.	Allowed in enclosed, locked facility.	Yes. Patients are allowed up to two caregivers (dispensaries are considered caregivers). Caregivers can assist up to five patients.	2.5 ounces, 12 plants, and 12 seedlings. Caregivers can possess that much per patient, with a total cap of 24 plants and five ounces.. The dispensary cap is 150 plants (99 mature) and 1,500 ounces.	Yes. The health department approved three compassion centers. Gov. Chafee put them on hold, but the law was changed, and they will be granted certificates. Sales tax will be applied, along with a 4% surcharge.	Cancer, HIV/AIDS, Hepatitis C, glaucoma, Alzheimer's, severe, debilitating pain, cachexia, severe nausea, seizures, and persistent muscle spasms. The health department can add conditions.	Yes, through the state Department of Health.	Yes.
Vt.	2004, legislation, revised later by legislature.	Allowed in enclosed, locked facility.	Yes. Caregivers can assist only one patient.	Two ounces of marijuana, two mature plants, and seven immature plants.	Yes. Two non-profit dispensaries received state approval and should open soon. Two more can be approved. It is expected that medical marijuana will not be subject to sales tax.	Cancer, multiple sclerosis, HIV/AIDS, severe pain, cachexia, severe nausea, or seizures.*	Yes, through the Department of Public Safety.	No.
Wash.	1998, initiative, revised later by legislature.	Allowed.	Yes. Caregivers can only assist one patient at a time. Caregivers must wait 15 days between serving two different patients.	24 ounces of marijuana and 15 plants, with a defense for more. Patients can collectively grow, with no more than 10 patients, 72 ounces, and 45 plants.	In Nov. 2012, voters approved allowing stores to sell adults 21 and older marijuana for any purpose.	Cancer, HIV/AIDS, multiple sclerosis, seizure and spasm disorders, intractable pain, glaucoma, Crohn's disease, Hepatitis C, and diseases causing nausea, vomiting, or appetite loss.	No. Note: This law does not include protection from arrest or prosecution. It has an affirmative defense that prevents conviction. However, under Washington law, all adults 21 and older can possess up to one ounce of marijuana for any purpose.	No.

* = Some or all of this state's listed illnesses must be resistant to other treatments.

DEPARTMENT OF VETERANS AFFAIRS
UNDER SECRETARY FOR HEALTH
WASHINGTON DC 20420

JUL 06 2010

Mr. Michael Krawitz
3551 Flatwoods Road
Elliston, VA 24087

Dear Mr. Krawitz:

This is a follow-up response to your letter requesting clarification of the Veterans Health Administration's (VHA) policy regarding the practice of prescribing opioid therapy for pain management for Veterans who provide documentation of the use of medical marijuana in accordance with state law.

If a Veteran obtains and uses medical marijuana in a manner consistent with state law, testing positive for marijuana would not preclude the Veteran from receiving opioids for pain management in a Department of Veterans Affairs (VA) facility. The Veteran would need to inform his provider of the use of medical marijuana, and of any other non-VA prescribed medications he or she is taking to ensure that all medications, including opioids, are prescribed in a safe manner. Standard pain management agreements should draw a clear distinction between the use of illegal drugs, and legal medical marijuana. However, the discretion to prescribe, or not prescribe, opioids in conjunction with medical marijuana, should be determined on clinical grounds, and thus will remain the decision of the individual health care provider. The provider will take the use of medical marijuana into account in all prescribing decisions, just as the provider would for any other medication. This is a case-by-case decision, based upon the provider's judgment, and the needs of the patient.

Should you have further questions, please contact Robert Kerns, PhD, National Program Director, New England Healthcare System at (203) 932-5711, extension 3841.

Sincerely,

Robert A. Petzel, M.D.

Report & Recommendations to the New Mexico Secretary of Health

From the Medical Advisory Board to the Medical Cannabis Program

From a Public Hearing on Wednesday 7 November 2012 at the Harold Runnels Building Auditorium, 1190 St. Francis Drive, Santa Fe NM

Report prepared by Steven Jenison, M.D., Chair, for the Medical Advisory Board. This report was reviewed and approved by all Members of the Medical Advisory Board who participated in the Public Hearing.

A public hearing of the Medical Advisory Board to the New Mexico Medical Cannabis Program was held in the Harold Runnels Building Auditorium at 1190 St. Francis Drive in Santa Fe NM from 1:00 PM to 5:00 PM on Wednesday 7 November 2012.

A. Introductory Comments and Introduction of Board Members

Dr. Jenison called the meeting to order at 1:05 PM.

Board members present:

1. Eve Espey, MD, Obstetrics / Gynecology
2. Steven Jenison, MD, Infectious Diseases (Chair)
3. William Johnson, M.D., Psychiatry
4. Timothy Lopez, MD, Oncology
5. R. Elden Pennington, MD, Ph.D., Rehabilitation Medicine
6. Mitchell Simson, MD, Internal Medicine

Members excused:

1. Eve Elting, Internal Medicine

The position that became vacant upon the resignation of Dr. Erin Bouquin, MD, from the Medical Advisory Board on 1 February 2012 remains unfilled.

Present representing the Department of Health:

1. Chris Woodward, JD, Office of General Counsel
2. Kenneth Groggel, Director, Medical Cannabis Program
3. Andrea Sundberg, Program Coordinator, Medical Cannabis Program

B. Actions of the Secretary of Health on the Recommendations of the Medical Advisory Board from the Public Hearing on April 18, 2012

The Medical Advisory Board submitted its report from the public hearing of April 18, 2012, to Dr. Catherine Torres, M.D., Secretary of Health, on May 2, 2012. In the interim, Dr. Torres resigned from her position with the Department of Health. Interim Secretary of Health, Mr. Brad McGrath, reported actions on the Board's recommendations on Tuesday, November 6, 2012. The document "Final Decision Regarding Petitions for the Approval of Conditions for Participation in

to the attention of the Department was in regard to pesticide / herbicide contamination of medical cannabis and a cannabis "gummy bear" from a licensed medical cannabis producer. The New Mexico State Laboratory Division tested samples provided to the Department. Three cannabis samples obtained in April 2012 were tested for 104 pesticides, herbicides and other organic compounds and were found to be negative for all of these compounds. The cannabis "gummy bear" was tested for 26 pesticides and was negative for all of these compounds.

Mr. Groggel had no information on specific policies and procedures that the Department of Health medical personnel followed in evaluating and approving PTSD applications, or whether or how frequently the DOH clinician evaluating the application spoke directly with the certifying clinician and/or psychiatrist. He stated that all Medical Cannabis Program patient applications are reviewed by DOH medical personnel, and that these clinicians spend about 6 to 8 hours each week reviewing applications.

Mr. Woodward, Office of General Counsel, had been asked prior to the meeting to provide the Medical Advisory Board with an explanation of the Department of Health's authority to remove qualifying conditions from eligibility for participation in the Medical Cannabis Program. Mr. Woodward reviewed the Department's opinion in that regard at the public hearing. The following is the written opinion provided to the Medical Advisory Board by Mr. Woodward in an email on October 24, 2012:

"In a nutshell, the Department's legal authority to remove or modify a DOH-approved condition is the same as its authority to approve a condition – albeit with certain limitations imposed via DOH regulation.

The Compassionate Use Act at NMSA 26-2B-3(B) defines "debilitating medical condition" as including seven specified conditions (cancer, glaucoma, M.S., etc.). The definition also specifies "any other medical condition, medical treatment or disease as approved by the department." By this text, the statute vests with the Department of Health the ability to identify conditions (in addition to those specified in statute) that may qualify someone for participation in the medical cannabis program. The Department's authority to adopt and amend regulations is based in the Department of Health Act at NMSA 9-7-6(E), which provides that "[t]he secretary may make and adopt such reasonable and procedural rules as may be necessary to carry out the duties of the department and its divisions". The requirements for adoption and amendment of rules are as specified in the Department of Health Act, the State Rules Act, and associated rules on rulemaking adopted by the NM State Records & Archives Center.

At the end of 2010, when the medical cannabis program regulations were last amended, the Department added a provision at 7.34.3.8(C) NMAC, which states:

Modification or removal of department-approved conditions: The secretary may remove or modify a department-approved condition only if the secretary determines, on the basis of substantial credible medical and scientific evidence, and after an opportunity for review of the proposed removal or modification by the medical advisory board, that the use of cannabis by patients who have the approved condition would more likely than not result in substantial harm to the patients' health.

The Department's ability to modify or remove a DOH-approved condition is limited as stated in this regulation. However, there is no other limitation identified in statute or regulation concerning the Department's ability to amend its regulations to approve or not approve a

maintenance of his New Mexico medical license. He does not hold Board Certification in a subspecialty of psychiatry including Addiction Psychiatry, Brain Injury medicine, Child and Adolescent Psychiatry, Hospice and Palliative Medicine or Pain Medicine. He has published no original medical research papers. He has published no review articles on the topics of PTSD, marijuana abuse or psychosis. Dr. Ulwelling published one case report in 1985 (Ulwelling W, 'Pseudo-allergy: treatment with an MAO inhibitor, *Psychosomatics* **26**: 535-6, 1985) and two Correspondences in 1984 (Ulwelling W, Reflections of residents' values or the researchers'? *American Journal of Psychiatry*, **141**: 326-7, 1984) and 1985 (Ulwelling W, Winter births and seasonal affective disorder, *Archives of General Psychiatry* **42**: 105-6, 1985). He has not held a position on the academic faculty of a medical school. He is a Distinguished Life Fellow of the American Psychiatric Association and currently serves as the New Mexico representative to the Assembly of the APA. In his petition, he listed among his credentials "Clinical Assistant Professor, UNM School of Medicine". He states that this is incorrect and that his appointment as Clinical Assistant Professor expired on December 31, 2007 and was not renewed by the University of New Mexico. He states that this was an oversight on his part as he unaware that his clinical faculty position had expired because he did not receive the letter from the UNM Health Sciences Center notifying him of this. He became aware of the error after the submission of his petition and before the time of this public hearing.

Dr. Ulwelling states that his petition represents only his personal position as a psychiatrist. Specifically, he states that it does not represent the position of the Department of Psychiatry at the UNM Health Sciences Center, the UNM Health Sciences Center, the Psychiatric Medical Association of New Mexico, the American Psychiatric Association or the New Mexico Medical Society. No individuals or organizations have submitted materials or letters in support of Dr. Ulwelling's petition.

Included in the petition is an "Action Paper" titled "Disapprove Medical Marijuana as a Treatment for PTSD" that Dr. Ulwelling prepared and presented to the Executive Committee of the Psychiatric Medical Association of New Mexico (PMANM) and to the Assembly of the APA. The Psychiatric Medical Association of New Mexico has between 150 and 170 physician members. [There are currently 401 licensed physicians in New Mexico who list psychiatry as their primary specialty. Of those, 265 list New Mexico addresses. There are 276 New Mexico psychiatrists who are certified by the American Board of Psychiatry and Neurology listed on the Board's website.] Dr. Ulwelling presented the Action Paper to the PMANM Board Meeting on January 10, 2012. By his report, no supporting materials were presented as part of the discussion of the Action Paper. Seven members of the Board were present and one participated by telephone. A motion to endorse the Action Paper passed unanimously. Dr. Ulwelling confirms that the Action Paper received consideration from only 8 members of PMANM (including himself) out of 150 to 170 PMANM members and approximately 270 psychiatrists practicing in New Mexico. Dr. Ulwelling presented the Action Paper to the Assembly of the American Psychiatric Association at its May 2012 meeting in Philadelphia PA. A representative of the APA, in an email in response to a request for information on the consideration of the Action Paper, states:

"However, unlike the policies and procedures of the American Medical Association, the APA Assembly's approval is only the first step in the APA's process for implementing association policy. The final decisions are reviewed and voted on by the APA Board of Trustees, the fiduciary body of the organization. This document is currently under review

The following individuals presented evidence through oral testimony:

a. Dr. Florian Birkmayer, Psychiatrist, Albuquerque
b. Dr. Lisa Walker, Psychiatrist, Santa Fe
c. Dr. Carola Kieve, Psychiatrist, Las Vegas
d. Keith Marker, Patient
e. Vicky Eckerdt, Mother of patient
f. Nat Dean, Patient
g. Cisco McSorley, New Mexico State Senator
h. Antonio Maestas, New Mexico State Representative
i. Gerald Ortiz y Pino, New Mexico State Senator

Three New Mexico physicians (Drs. Birkmayer, Walker and Kieve) presented their experience as currently practicing psychiatrists who care for PTSD patients enrolled in the Medical Cannabis Program. Letters from each of these psychiatrists is included in the technical information submitted by the Drug Policy Alliance. They stated that some patients benefit in terms of their PTSD symptoms when other treatment options have failed to bring relief or have caused unacceptable side effects. They were unaware of patients who had developed signs or symptoms of acute psychosis as a result of the use of medical cannabis. They recommended retaining PTSD on the list of eligible conditions for participation in the Medical Cannabis Program so that it would be available as an option for those patients for whom other treatment options had failed.

Two PTSD patients currently enrolled in the Medical Cannabis Program (Keith Marker & Nat Dean) and the mother of a PTSD patient (Vicky Eckerdt) testified that medical cannabis had provided symptomatic relief for their PTSD symptoms when prescription medications had failed to do so. They stated that previous prescription medications had caused severe and debilitating side effects.

Three current members of the New Mexico Legislature (Sen. Cisco McSorley, Sen. Jerry Ortiz y Pino, and Rep. Antonio "Moe" Maestas) stated their support for retaining PTSD as a qualifying condition under the New Mexico Medical Cannabis Program. They pointed out that some of the arguments presented in the petition were arguments against medical cannabis program in general, and that the appropriate place for those arguments was before the New Mexico Legislature. They warned that the suggestion that current patients enrolled under PTSD should be "grandfathered-in" while discontinuing new enrollments was a double standard that would not withstand legal challenges.

3) Mr. Bryan Krumm, Clinical Nurse Practitioner and representing the Zen Zion Coptic Orthodox Church – presentation of technical evidence

The written technical evidence submitted by Mr. Krumm is included as an attachment.

Mr. Krumm is a psychiatric Clinical Nurse Practitioner. He presented his experience in providing care to PTSD patients including many enrolled in the Medical Cannabis Program. He provided extensive information on the biological and clinical rationale for the use of medical cannabis in the management of PTSD.

Mr. Krumm's petition includes a draft of a journal manuscript that he wrote titled

ended with 'suggestive' conclusions (rather than the 'inadequate' conclusions the committee finally reached), the core message that better-quality research is needed would not have been rendered less urgent in consequence."

At that time, the IOM study concluded that there was inadequate evidence to support any psychopharmacologic treatments for PTSD, and sufficient evidence only for "exposure therapies" as a behavioral treatment. Other key findings of the IOM study included:

"The majority of drug studies were funded by pharmaceutical manufacturers and many of the psychotherapy studies were conducted by individuals who developed the techniques or their close collaborators."

"Available research leaves significant gaps in assessing the efficacy of interventions in important subpopulations of veterans with PTSD, especially those with traumatic brain injury, major depression, other anxiety disorders, or substance abuse, as well as ethnic and cultural minorities, women and older individuals."

"The research on treatment of PTSD in U.S. veterans is inadequate to answer questions about interventions, setting, and lengths of treatment that are applicable in this specific population."

"Studies of PTSD interventions have not systematically and comprehensively addressed the needs of veterans with respect to efficacy of treatment and the comparative effectiveness of treatments in clinical use."

In the interim, one large meta-analysis of pharmacotherapy for PTSD has been published through the Cochrane Collaboration (Stein DJ, 2009). Quoting three key statements from the study:

"This is a systematic review of 35 short-term randomized controlled trials of pharmacotherapy for PTSD (4597 participants). A significantly larger proportion of patients responded to medication (59.1%) than to placebo (38.5%) (13 trials, 1272 participants). Symptom severity was significantly reduced in 17 trials (2507 participants). The largest trials showing efficacy were of the selective serotonin reuptake inhibitors (SSRIs), with long-term efficacy also observed for these medications."

"Neither the potential clinical (presence of combat trauma, comorbid expression) or methodological (single versus multi-centre trials, industry versus non-industry funding) predictors of medication response tested in this review can account for the substantial proportion (41%) of patients who do not appear to respond to medication."

"This review found some evidence that war veterans are more resistant to pharmacotherapy than other patient groups, at least with regards to the reduction of symptom severity."

A recent meta-analysis of treatment of PTSD in U.S. combat veterans within the VA system by Goodson et al. found a "medium" effectiveness of PTSD treatments such that the average treated patient fared better than 66 percent of untreated patients (Goodson J et al., 2011).

"The VA has initiated a "national rollout" providing training in CPT (Cognitive Processing Therapy) and PE (Prolonged Exposure) to providers across the country to increase patient access to these two therapies. However, the actual implementation of such interventions across large institutions like VA and the DoD can be a substantial challenge. Another related challenge to accessing these treatments is the significant time commitment that is required, which can be difficult for active duty personnel, working veterans, and individuals living in rural locations who may have to travel long distances to meet with a therapist. Telehealth and intern-based interventions have been proposed to increase access to care in remote locations, and such treatments are currently under investigation. Pharmacological treatments are thought to be easier to disseminate, but not all veterans are willing to take psychotropic medications, and pharmacological treatments for PTSD are only modestly effective. Additionally, many pharmacological interventions have undesirable side effects, such as impaired sexual functioning, making compliance difficult." (Wisco TE et al., 2012).

The intent of the New Mexico Legislature and the New Mexico Governor in enacting the Lynn & Erin Compassionate Use Act was not to promote cannabis for the treatment of any condition. Rather, it recognized that many individuals have found relief through the use of medical cannabis for certain serious conditions where they found no relief through standard medical treatments, and that those individuals should not be liable for criminal prosecution and imprisonment for the use of medical cannabis. In cases in which the condition causes considerable distress or is life-threatening, in which there is biological plausibility for efficacy, and especially in cases in which standard therapies are either lacking entirely or are ineffective in a large proportion of patients, inclusion for eligibility in the New Mexico Medical Cannabis Program is warranted. These considerations were carefully weighed at the time that the original PTSD petition was heard. It was the conclusion of the Secretary of Health that PTSD met the intent of the Lynn & Erin Compassionate Use Act, and Dr. Vigil adopted the recommendation of the Medical Advisory Board in that regard. Since the addition of PTSD to the conditions eligible for enrollment in the New Mexico Medical Cannabis Program, there have been no adverse events reported to the Department of Health related to PTSD patients in the Program. In the opinion of the Medical Advisory Board, there is no new compelling medical or scientific evidence that should cause a serious reconsideration of that decision.

There is an association between PTSD and cannabis use. Cannabis use is strongly associated with severity of PTSD symptoms and is inversely related to Distress Tolerance (Bonn-Miller MO et al., 2011; Bremner JD et al., 1996; Cougle JR et al., 2011; Hogan J et al., 2010; Potter et al., 2011; Tepe E et al., 2012; Villagonzalo, K-A et al, 2011; Zvolensky MJ et al., 2009). There are considerable data that support the hypothesis that cannabis is used by patients as a coping mechanism to decrease symptoms associated with PTSD, notably anxiety symptoms, hyperarousal and sleep disturbances. One study of cannabis use among patients with concurrent Social Anxiety Disorder (SAD) and Cannabis Use Disorder (CUD) found:

"although not statistically significant, there was a trend toward patients with the SAD-CUD comorbidity being more likely to be rated as having better adolescent and current psychosocial functioning compared to SAD patients without CUD. This could perhaps support findings from previous studies that suggest that marijuana may be used as a social lubricant to facilitate social interactions, similar to alcohol, amongst individuals

be able to monitor their clinical outcomes and make recommendations for other treatment options. There are also some data that suggest that the cannabinoid compound cannabidiol has anti-anxiety and anti-psychotic effects whereas the cannabinoid delta-9-tetrahydrocannabinol (THC) may have the opposite effects. It may be an advantage to those individuals who are using medical cannabis to treat their symptoms to have access to well-characterized cannabis with known cannabidiol and THC content available through licensed medical cannabis producers.

Dr. Ulwelling's petition raised the issue of the addiction potential of cannabis use. It is generally held that cannabis has both psychological and physical dependency potential, more so in some people than in others. A survey was conducted among psychiatrists and addiction specialists in Britain in order to attempt to rank illicit drugs and legal drugs of abuse with regard to dependency and harm (Nutt D et al., 2007). In the ranking of drugs by dependency potential, cannabis ranked below heroin, cocaine, barbiturates, street methadone, alcohol, ketamine, amphetamines, tobacco and buprenorphine; it ranked above LSD, anabolic steroids and Ecstasy. In the ranking of physical harm, it ranked below all of these other drugs. The abuse potential of the major cannabinoids present in marijuana, Δ-9-tetrahydrocannabinol and cannabidiol, was recently assessed by reviewing all published papers on the use of the prescription medication Sativex®. (Robson P,., 2011). Sativex® is an inhaled oromucosal spray that contains these cannabinoids extracted from *Cannabis sativa* leaves and flowers. It is currently licensed in the United Kingdom, Spain, Germany, Denmark, the Czech Republic, Sweden, New Zealand and Canada for the treatment of moderate to severe spasticity associated with multiple sclerosis (MS); it is not currently licensed in the United States. Based upon a review of all of the clinical trials and the integrated safety analysis data for Sativex®, the study concluded:

"In clinical trials, intoxication scores have been low and euphoria reported by only 2.2% of patients. Tolerance has not occurred, abrupt withdrawal has not resulted in a formal withdrawal syndrome, and no cases of abuse or diversion have been reported to date. A formal abuse liability study of Sativex in experienced cannabis smokers showed some abuse potential in comparison with placebo at higher doses, but scores were consistently lower than equivalent doses of THC. Evidence to date suggests that abuse or dependence on Sativex is likely to occur in only a very small proportion of recipients.

There are as yet no clinical trials data on the safety and efficacy of medical cannabis in the treatment of PTSD. It is widely perceived by those who seek to investigate medical cannabis that the National Institute on Drug Abuse (NIDA) has created and maintained barriers to medical cannabis research, both by limiting funding and by denying access to medical cannabis grown for NIDA by the University of Mississippi (the sole source of medical cannabis that is legal according to Federal law). Federal barriers to medical cannabis research led the State of California to establish the Center for Medicinal Cannabis Research at the University of California at San Diego (www.cmcr.ucsd.edu) funded through the state. Dr. Sue Sisley, a psychiatrist and professor at the University of Arizona downtown Phoenix campus, began application to NIDA in 2010 for a study of medical cannabis in veterans with chronic, treatment-resistant PTSD. That study has received Institutional Review Board approval from the University of Arizona, and the protocol has been approved by the Food & Drug Administration. Dr. Sisley is awaiting a response from NIDA on whether they will allow her the necessary access to federal cannabis for the purposes of her study. Dr. Sisley's experience prompted the Arizona Medical Association House of Delegates on June 2, 2012, to unanimously adopt a

recommends retaining PTSD in the Medical Cannabis Program so that PTSD patients who have derived relief through the use of cannabis can continue to be protected from criminal liability under state law. In every regard, the inclusion of PTSD in the New Mexico Medical Cannabis Program meets the intent of the Lynn & Erin Compassionate Use Act. In our opinion, the petition to remove PTSD does not meet the standards set forth in the New Mexico Medical Cannabis Program Regulations at 7.34.3.8(C) NMAC, and the Secretary of Health should reject the petition.

Citations:

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G. PUBLIC COMMENT

Comments were taken from members of the public in attendance.

Review

Drug Testing and Analysis

Received: 3 February 2012 Revised: 3 May 2012 Accepted: 4 May 2012 Published online in Wiley Online Library: 26 June 2012

(www.drugtestinganalysis.com) DOI 10.1002/dta.1377

Mitigation of post-traumatic stress symptoms by *Cannabis* resin: A review of the clinical and neurobiological evidence

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It is known from clinical studies that some patients attempt to cope with the symptoms of post-traumatic stress disorder (PTSD) by using recreational drugs. This review presents a case report of a 19-year-old male patient with a spectrum of severe PTSD symptoms, such as intense flashbacks, panic attacks, and self-mutilation, who discovered that some of his major symptoms were dramatically reduced by smoking cannabis resin. The major part of this review is concerned with the clinical and preclinical neurobiological evidence in order to offer a potential explanation of these effects on symptom reduction in PTSD. This review shows that recent studies provided supporting evidence that PTSD patients may be able to cope with their symptoms by using cannabis products. Cannabis may dampen the strength or emotional impact of traumatic memories through synergistic mechanisms that might make it easier for people with PTSD to rest or sleep and to feel less anxious and less involved with flashback memories. The presence of endocannabinoid signalling systems within stress-sensitive nuclei of the hypothalamus, as well as upstream limbic structures (amygdala), point to the significance of this system for the regulation of neuroendocrine and behavioural responses to stress. Evidence is increasingly accumulating that cannabinoids might play a role in fear extinction and antidepressive effects. It is concluded that further studies are warranted in order to evaluate the therapeutic potential of cannabinoids in PTSD.

Keywords: cannabis resin; THC; cannabinoids; posttraumatic stress disorder (PTSD); psychopharmacology; endocannabinoid system

Introduction: PTSD and cannabinoids

Clinical evidence obtained from clinical studies shows that people suffering from post-traumatic stress disorder (PTSD) may use recreational drugs to cope with their symptoms.[1] Some specific psychopharmacological effects of cannabis, such as sedation, relaxation, reduction of anxiety and sleep-induction, may explain its use as an attempt to cope with some PTSD symptoms.[1–4] Cannabis products have been used medicinally in Asia and Europe as sedatives or calmatives, including the Western medical tradition up to the early twentieth century.[5] Cannabis was also listed in the United States Pharmacopeia and Formulary until its removal in 1941.[6] Many patients with PTSD may actually cope with their symptoms in this way, as stated by the discoverer of Δ^9-tetrahydrocannabinol (THC)[7] who reported that use of cannabis led to improved sleep, significant reduction of nightmares and sleep interruption.[8] Marijuana use has emerged as one of the most commonly used illicit substance in treatment-seeking adolescents[9] and it has been suggested that cannabis use is significantly more common among adolescents with PTSD than in those without this condition.[10] More recently, some studies and surveys found even stronger evidence that cannabinoids are used in a larger population of patients with PTSD for coping with their symptoms.[11–15] Bonn-Miller *et al.*[11] examined cannabis use in PTSD patients and the interaction of PTSD-related sleep disorders, symptom severity, and motivations for use. These authors found a strong correlation between the severity of PTSD-related sleep disturbances and the amount of cannabis use. These results have to be taken with caution, because the evidence for sleep-enhancing effects of cannabis resin and marijuana is equivocal (see subsection on sleep-enhancing effects). An effect on sleep may also result from the decrease of symptoms of over-arousal, which would be consistent with findings involving self-medicating populations of PTSD patients.[1,2,13] Bujarski *et al.*[13] also studied alternative motives for use and demonstrated that in adolescents with PTSD the coping motive was the primary cause for use and all other motives examined, i.e. 'social', 'enhancement' or 'conformity', were close to zero. These results were limited to a population of PTSD patients seeking treatment for substance abuse, and therefore, generalizability seems limited. Another study reported a strong correlation between PTSD symptom severity and the amount of cannabis use[14,15] and discussed the self-medication hypothesis as a possible

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or psyche that renders the person unable to handle the impact at the moment of occurrence. A typical example is rape and a significant number of people who have experienced one or more such traumatogenic situations will develop symptoms of PTSD. These usually consist of a heightened level of general central nervous system (CNS) arousal, sleep disturbances, nightmares, psychological instability, depression, anxiety, avoidance behaviour, emotional numbing, and repeated intrusions of parts of the experience into consciousness ('flashbacks').[23]

On the neurophysiological level, patients with PTSD develop a hyperactivity of the amygdala[24] which is a central part of the fear network which is involved in the assessment of threat-related stimuli.[25,26] In these patients, the amygdala is especially hyper-responsive to the presentation of trauma-relevant stimuli.[27] Morphological studies were inconclusive in regards to structural changes in the amygdala,[28] but the amygdala appears to be implicated in extinction learning. The hippocampus is involved in learning and explicit (declarative) memory, working memory,[29] episodic memory,[30] and has also a role in the regulation of stress.[31] A decreased hippocampal volume of gray matter is a regular finding in chronic PTSD patients and there is evidence that elevated blood flow in the hippocampus is related to episodic, spatial and contextual memory and emotional responses. Activity in parahippocampal structures can be triggered by symptom provocation tests like trauma-relevant imagery.[32]

In contrast to over-activation of the amygdala, hippocampus and parahippocampal structures, and the anterior cingulate cortex (ACC), show decreased activity in acute[32] and chronic PTSD.[28,33] On the other hand, a sub-region of the ACC, the dorsal ACC (dACC), which is involved in emotional regulation, recall of emotional experiences and processing of emotional responses,[34] is over-activated in PTSD during symptom provocation tests (e.g. playing combat sounds to war-related traumatized PTSD patients).[35] In a study using [^{15}O]H_2O-PET, the exposure to traumatic imagery, which induces flashback-like memory, activated the medial posterior orbitofrontal cortex, the insular cortex, the anterior temporal pole, and the medial temporal cortex.[27,36] A deactivation of the rostral ACC was also observed.[37] The ACC is part of the medial prefrontal cortex and is also involved in the process of fear extinction conditioning.[38,39] The insular region mediates somatosensory processes, feelings and recall of emotional events such as emotional memory. A comparison between acute and chronic PTSD showed that acute PTSD displayed a more extended and unstable pattern of activation while chronic conditions included more circumscribed and stable neurofunctional abnormalities.[36] Flashback memories are typically induced by inner or outer stimuli which activate the amygdala and induce the retrieval of 'unmetabolized', but instead hypermnestically stored, memories from the hippocampus. Another important structure for the maintenance of PTSD is the ventromedial prefrontal cortex, which plays a major role in extinction learning ('forgetting') by interacting with the amygdala in a reciprocal fashion, i.e. leading to inverse correlation during emotional activity. This happens via inputs to inhibitory GABAergic cells that block information flow from the amygdala's lateral to central nucleus[40] and also regulates the hippocampus in regard to extinction recall.[41,42] The medial prefrontal cortex appears to be hypoactive in PTSD.[33,43]

From the evidence cited, the hypothesis was formed that a major cause for the persistent inappropriate fear responses and the diminished extinction of conditioned fear in PTSD patients may include under-activation of the ACC and the medial prefrontal cortex which may help to explain the emotional dysregulation observed in these patients. Learned fear associated with PTSD can persist for tens of years. Therapeutic interventions for PTSD include extinction learning and psychotherapeutic approaches for PTSD aim to strengthen the function of the medial prefrontal cortex to enhance the capability of extinction learning and to break the cycle of an over-activated fear system (amygdala, hippocampus, parahippocampal structures) while under-activating ACC and medial prefrontal cortex. Animal experiments have shown that extinction learning and recall involve different cellular mechanisms and possibly different brain regions.[44]

Possible mechanisms involved in the effects of cannabinoids in PTSD

The endocannabinoid system

The plant *Cannabis sativa* has been used by humans for thousands of years because of its psychoactive properties. The major psychoactive ingredient of cannabis is THC, which exerts effects in the brain by binding to a G-protein-coupled receptor known as the cannabinoid CB_1 receptor.[45] Two putative endocannabinoid ligands, arachidonylethanolamide (anandamide, AEA) and 2-arachidonylglycerol (2-AG), have been identified as major endogenous transmitters of the endocannabinoid system (eCB). The eCB system is distributed throughout the brain and regulates synaptic release of excitatory and inhibitory neurotransmitters. A key role of the eCB system is the activation of the CB_1 receptor which is widely represented in the brain showing a 10-fold higher distribution level in comparison with opioid receptor levels. Endocannabinoids such as AEA and 2-AG that interact with these receptors are post-synaptically synthesized signalling molecules and are not stored in vesicles. Instead, they appear to be generated on demand and liberated to act in a retrograde fashion on presynaptically localized CB_1 receptors.[46] Recent research revealed that the eCB system is homoeostatic in that it prevents extreme cortical excitation and inhibition and that it may be dysfunctional in some mental disorders. eCB signalling is widely distributed throughout corticolimbic circuits that are linked to the stress response. The general level of cortical excitability is determined by the neurotransmitter systems using GABA and glutamate. Stress, especially linked to some severe psychiatric disorders like PTSD, may produce an imbalance in the eCB system. This system serves as a modulator, comparable to a 'dimmer switch' that helps to prevent excessive excitatory or inhibitory activity.[18] Since the discovery of the endocannabinoid system a growing body of psychiatric research has emerged focusing on the role of this system involved in major psychiatric disorders like schizophrenia, bipolar disorder, major depression and anxiety disorders.[47] For example, the CB_1 receptor antagonist rimonabant was reported to cause depression and anxiety in a significant proportion of psychiatrically normal subjects.[48]

Cannabis and exocannabinoids

Three major exocannabinoids are THC, CBD and cannabinol (CBN) and represent the main constituents found in cannabis resin.[49] THC is the major psychoactive constituent and is responsible for the mood and consciousness-changing effects.[50] Reports concerning anxiolytic properties are inconsistent, and in some subjects, anxiogenic effects can be generated instead.[51,52]

Besides THC, CBD is the main non-psychoactive phytocannabinoid found in *C. sativa* which can constitute up to 40% of its

(sedation and changes in memory) have been correlated with the presence of CB_1 receptors in the limbic system and striatum.

Endocannabinoids also play a role in inhibiting neurotransmitter release. The research carried out by Marciano *et al.*[76] demonstrated the impact of endocannabinoids on learning and plasticity. It was shown that CB_1 receptor knock-out mice could learn and later recall association of a tone with a foot shock but were unable to extinguish the memory, i.e. their emotional response to the tone. These authors found that during the extinction period, the levels of endogenous AEA and 2-AG were raised in the basolateral amygdala in mutant and normal mice which implied a role for endocannabinoids in the extinction of conditioned fear. CBD also facilitated extinction in a contextual aversive conditioning model after intracerebral ventricular administration.[54]

Effects of endo- and exocannabinoids via stress-related hormonal systems

Stress can be defined as confrontation with stimuli that presents a challenge to homoeostasis, typically a perceived stress to the well-being of the organism. In humans, acute and chronic stressful situations correspond with the secretion of glucocorticoid hormones. The paraventricular nucleus (PVN) of the hypothalamus releases corticotropin-releasing hormone (CRH) and the anterior pituary gland releases the adrenocorticotropic hormone (ACTH) into general circulation. Subsequently, glucocorticoid hormones, such as cortisol (from the adrenal cortex), are released to mobilize energy stores and to induce a range of effects on cardiovascular, immune, metabolic, and neural systems that facilitate optimal responses to aversive stimuli.[90] Although this may have adaptive functions in the short term, in cases of repeated stress exposure, prolonged glucocorticoid secretion can produce deleterious effects on metabolic, immune, cardiovascular and neurobiological functions.

Both hippocampus and PFC exert inhibiting effects on the hypothalamic-pituitary-adrenal (HPA) axis whereas antidepressive agents can normalize its hyperactivity. Furthermore, it has been shown that eCB signalling responds to and regulates the activity of the HPA axis which governs their secretion of stress hormones.[91] The eCB system, maintaining homoeostais of the stress system, can activate as well as terminate the HPA axis response to acute and repeated stress. Accumulating evidence indicates that the eCB tone provides a steady-state inhibition of the HPA axis activity.[92] Prominent in these behavioural stress responses is the interaction between eCBs and the HPA-axis. Data indicate that glucocorticoids induce eCB signalling through a rapid non-genomic process in CRH neurons of the PVN.[93] This induction of eCB signalling inhibits glutamatergic inputs to CRH neurons and thus decreases the excitatory drive to the HPA axis.[92] Glucocorticoids are self-regulated through negative feedback and eCB mediates glucocorticoid fast feedback mechanisms. Fast feedback inhibition of HPA axis stress responses by direct glucocorticoid action at the PVN of the hypothalamic rapidly inhibits restraint-induced ACTH and corticosterone release consistent with feedback actions at the cell membrane.[94] It was demonstrated that following repeated exposure to stress AEA is persistently decreased throughout the corticolimbic stress circuit whereas 2-AG is elevated (exclusively in the amygdala) in a stress-dependent manner.[95] This divergent regulation of AEA and 2-AG contributes to distinct forms of HPA axis habituation. Inhibition of AEA hydrolysis or intra-amygdala administration of a CB_1 receptor antagonist before the final stress exposure prevented the repeated stress-induced development of basal hypersecretion of corticosterone.[91] Thus, there is evidence for both GABAergic and CRH-mediated mechanisms involved in the anxiolytic effects of THC.

Reduction of anxiety and amygdala reactivity and the eCB system

The amygdala has been identified as one of the primary limbic structures involved in activating the HPA axis in response to stressful stimuli. There is also accumulating evidence that glucocorticoid-mediated induction of eCB signalling is also a relevant feature, because glucocorticoids enhance the long-term consolidation of emotionally arousing experiences.[92] Presence of eCB signalling within stress-sensitive nuclei of the hypothalamus as well as upstream limbic structures, such as the amygdala, suggests a role in regulating the stress response. Administration of CB_1 antagonists into the basolateral nucleus of the amygdala (BLA) blocks the ability of corticosterone to facilitate aversive memory consolidation[96] which highlights an important role of the eCB system in this complex adaptive process. During extinction training, but not initial fear conditioning, eCB levels in the amygdala, but not in the prefrontal cortex, were elevated. Mice lacking the CB_1 receptor exhibit prolonged expressions of fear behaviours during extinction training.[76] In mice exposed to brief inescapable electric foot shock subsequently presented a neutral tone, the CB1 receptor-deficient mice failed to suppress the conditioned fear response when the shock was stopped and showed persistent fear on on repeated tone exposures.[97] From these studies it was concluded, that 'the feardampening effects of eCBs become evident only in highly aversive situations and are independent of CRH and corticosterone action'.[97] The dampening of anxiety and over-arousal, especially in regard to inducing flashback memory appears significantly reduced in the case described in the beginning of this review.

During the adaption to stress and aversive stimuli the amygdala shows no change in 2-AG in response to acute stress.[98–100] However, following repeated stress/aversive stimuli a 2-AG increase was progressively observed[99] followed by decrease after 1 h and complete reversal within 24 h of exposure.[101] As far as habituation to homotypical stress is concerned, this reaction pattern is critically involved in the habituation of the HPA axis. Accordingly, the increase of 2-AG correlates directly with HPA axis suppression and the local administration of a CB_1 receptor antagonist into the BLA reversed the expression of stress habituation.[101] Transient augmentation of 2-AG signalling upon repeated stressor exposure dampens excitatory inputs to the BLA by decreasing outflow of the amygdala, which would include stimulation of the HPA axis.[101] This would be consistent with corticosterone inhibition of glutamatergic inputs to the BLA through an eCB-mediated mechanism but only in animals with history of previous stress exposure.[102] BLA administration of CB_1 antagonists blocks the ability of systemically administered corticosterone to facilitate aversive memory consolidation.[96] Glucocorticoids recruit eCB signalling in the BLA to modulate aversive memory consolidation. The amygdala's GABAergic system is known to modulate memory storage[103] and activation of CB_1 receptors decreases GABA release via rapid inhibition of Ca^{2+} entry into the terminals.[104] A recent fMRI neuro-imaging study in humans demonstrated that THC discretely attenuated localized limbic (amygdala) reactivity to threatening stimuli without affecting performance on other complex tasks.[105] Interestingly, these results resemble those shown with lorazepam.[106]

especially nightmares. The main conclusion from experiments carried out in humans with cannabis resin/marijuana, which includes a mix of cannabinoids (usually mainly THC and CBD), is that increases in sleep appear to be consistent features.[119,129–131]

An unexplained fact is the significant increase of 'strange dreams' for more than two weeks during withdrawal from heavy cannabis smoking,[132] which does not appear to depend on REM rebound. In a study examining regular cannabis users during a few days abstinence period, participants had a mild to moderate degree of decreased sleep efficiency, total sleep time, percent time spent in Stage 1 and Stage 2 sleep, REM latency and subjective sleep quality, as well as increased sleep latency and time spent in REM sleep when compared to these patterns when using cannabis.[133] In rats, which were sleep deprived for 24 h, it was demonstrated that the usually seen REM rebound was very much reduced when the CB_1 receptor antagonist SR 141716A was given before sleep.[134] However, a reduction in REM sleep observed with cannabis does not seem to be a consistent finding,[135,136] which may point towards different possible implications. It may lead to decreased periods of wakefulness and nightmares, although less REM sleep is also discussed to alter affect regulation and memory-related processes[137–139] and that it may also play a role in depression.[140]

Discussion

It seems obvious from more recent studies of clinical and non-clinical populations that cannabis is used by a significant number of PTSD patients in the attempt to cope with their symptoms.[10–15] It appears that through different levels of actions (physiological, transmitter and molecular) eCBs are involved in the etiological mechanisms of certain mental disorders. The field of research investigating the eCB system is growing rapidly. The effects of cannabinoids, even if in some important aspects not well researched in humans, are complex and include effects on mood, stress and distress mechanisms, mainly involving the HPA axis and its regulation via fast feedback/presynaptic mechanisms. Endocannabinoid systems also show direct effects on major limbic and paralimbic structures, especially in fear conditioning, habituation and extinction. Therefore, it appears that modulation of the eCB system might be a rewarding target for psychopharmacological drug development. It might even be possible that some cannabinoids may offer potential to compete with commonly employed antidepressive agents, at least in some respects (Table 1).

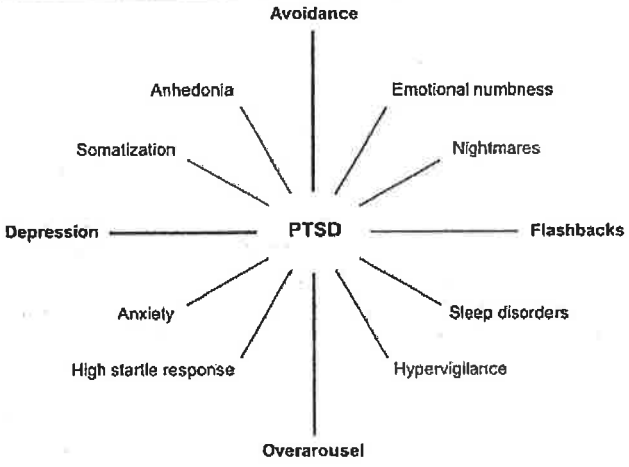

Figure 1. Symptom clusters typically involved in PTSD.

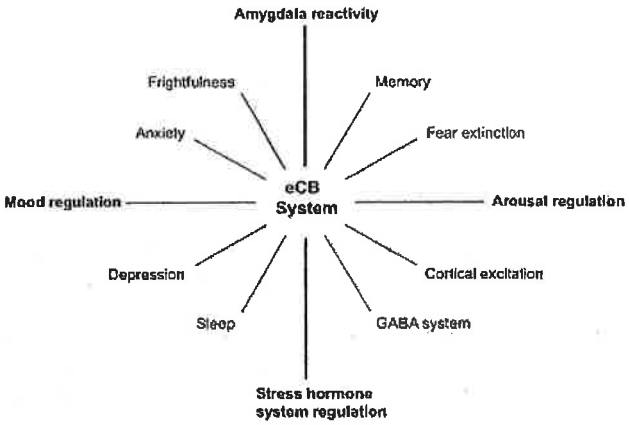

Figure 2. Involvement of the endocannabinoid system in neurobiological systems.

If one looks at the symptoms specific for PTSD (Figure 1) it also appears that effects at multiple levels that involve eCB signalling may be helpful when coping with symptoms of PTSD (Figure 2). Reduction of over-arousal, nightmares, sleep disorder, flashbacks as well as antidepressant and anxiolytic effects, may be achieved.

Table 1. Effects of Cannabis (THC, CBD) and antidepressants on symptoms of PTSD based on data given in cited references and clinical experience. + = effective; ++ = very effective

Symptom	Cannabis resin (THC + CBD)	Antidepressants (SSRI-type)	Antidepressants (Trimipramine/Amitriptyline-type)
Overarousal	+		+
Flashbacks	++ (frequency and intensity)	+	
Nightmares	++ (less REM)		+ (mirtazapine)
Anxiety	+	+	
Depression	+	++	++
Sleep disorders			
Sleep onset	++		++ (mirtazapine, amitriptyline)
Awakenings during night	++		+

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Cannabis in Post-Traumatic Stress Disorder (PTSD): A Neurobiological Approach to Treatment

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Acknowledgements:

The author currently has a rescheduling petition for cannabis pending with the DEA. The author has no financial interests in the New Mexico Medical Cannabis Program.

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Abstract

The endocannabinoid system is intricately involved in regulation of the neurobiological processes which underlie the symptomatology of Post Traumatic Stress Disorder (PTSD). This paper discusses the neurobiological underpinnings of PTSD, and the use of cannabis for treating PTSD in the New Mexico Medical Cannabis Program.

occurring suicidality, report significant reductions in frequency and severity of suicidal thoughts. In many cases, patients report complete cessation of suicidality.

We are currently facing an epidemic of suicide in the military. According to the Department of Defense, as of June 1 there were 140 suicides of active duty troops in 2012, combined with 18 suicides a day among Veterans. More service members have died by suicide than by enemy action, among those deployed to Iraq and Afghanistan.[14] The Veterans Administration has called on all mental health and substance abuse health care providers to share responsibility for zero tolerance for suicide.[15] Developing new treatment modalities for PTSD is critical given the number of retuning Veterans who require psychiatric help and are at high risk for suicide.

Raphael Mechoulam, perhaps the world's leading authority on cannabinoids and the endocannabinoid system, points out:

> "It has been suggested that pharmacological treatments in psychiatry have been overly reliant on neurotransmitter systems and their agonists. In the last several decades, advances in psychopharmacology have reduced side effects but have failed to lead to major disease improvement. The endocannabinoid system may shed new light on the physiological basis of psychiatric diseases leading to new and more effective treatments."[7]

There are three predominant symptom clusters in PTSD:[16]

- Re-experiencing symptoms are characterized by intrusive/distressing thoughts, recurrent nightmares, flashbacks, intense emotional upset at reminder, intense physical reactions at reminder.

- Avoidance and numbing symptoms are characterized by avoiding thoughts/feelings, avoiding activities/situations/places, inability to recall important aspects of event(s), loss of interest in activities, detached/cut-off from others, impaired range of emotions, and changed future plans/hopes.

- Hyperarousal symptoms are characterized by difficulty sleeping, irritability/anger, difficulty concentrating, overly alert, and becoming jumpier/easily startled.

The broad range of symptoms seen in PTSD have made treatment challenging. PTSD involves central neurotransmitter imbalances and neuroanatomical disruptions, with potential dysregulation of immune, autonomic, endocrine, and cardiovascular function.[17] Recent neuroimaging studies have helped to elucidate the underlying neurobiological processes involved in the symptomatology of PTSD, and the role of the endocannabinoid system in managing these neurobiological pathways.

PTSD is associated with dysfunction in the amygdala, the anterior cingulate cortex (ACC), the medial prefrontal cortex (mPFC), and the hippocampus. Structural impairments include decreased hippocampal volume and decreased ACC volume. Dysregulation in threat-related processing in response to trauma exposure leads to a cascade of neural changes causing a state of amygdala hyperresponsivity, triggering hyperarousal and vigilance. Inadequate top-down control by the mPFC and ACC perpetuates the state of amygdala hyperresponsivity, increasing attention to trauma-related stimuli.[18]

The hypothalamic-pituitary-adrenal (HPA) axis coordinates neuroendocrine stress response systems, and has been a major focus of scrutiny in patients with PTSD. Exposure to stress triggers neurons in the hypothalamic paraventricular nucleus (PVN) to secrete corticotropin-releasing hormone (CRH) which stimulates the

system drug-drug interactions and the acute medical risks of THC as used in clinical trials are low. [36] Inhaled cannabis is generally well tolerated and has been shown to reduce the intensity of pain, decrease anxiety and improve sleep.[37]

Cannabinoids may reduce, or entirely eliminate nightmares and patients using cannabinoids report improvement in sleep time, quality of sleep, and reduction of daytime flashbacks and night sweats.[38] Many of my medical cannabis patients report improvements in sleep onset and duration, as well as quality of sleep. They also report decreased frequency and severity, or total cessation of nightmares.

Alcohol abuse has been significantly linked to PTSD[39] and *cannabis has been shown to act as a substitute for alcohol.*[40] Many of my PTSD patients struggle with alcohol abuse, often in an attempt to self medicate. The majority of patients I have referred to the medical cannabis program, who have co-occurring alcohol abuse issues, have reported significantly decreased use and in many cases complete cessation of alcohol.

Cannabinoids have been shown to reduce aggressive behavior,[41,42,43] which has important implications in PTSD. My patients commonly report significant reductions in irritability and anger. Oftentimes patients are accompanied by family members, friends, and/or treatment team members who confirm reductions in aggressive behavior.

Many of my PTSD patients have co-occurring psychotic disorders. Although use of cannabis in patients with schizophrenia has typically been reported to worsen psychosis,[44] increases in population cannabis use have not been followed by increases in psychotic incidence.[45] THC has been shown to improve symptoms in treatment-refractory schizophrenic patients, including reduction in core psychotic symptoms, with no clinically significant adverse effects.[44] When compared to non-using patients, schizophrenic patients who use cannabis, and patients with a history of cannabis at first episode of psychosis, have superior neuropsychological functioning.[46] My medical cannabis patients often report reductions in both positive and negative symptoms of schizophrenia which have failed to resolve with traditional antipsychotic medications.

Strains of cannabis containing CBD in addition to THC may prevent the psychotic-like symptoms sometimes caused by strains with high levels of THC but a lack of CBD.[47] Cannabis of the Sativa and Ruderalis biotypes typically contain higher levels of CBD and lower levels of THC while Indica biotypes tend to have higher levels of THC and more variable levels of CBD. [48] Unfortunately, finding consistent access to CBD rich strains proves difficult for many patients and finding the best strain for any individual is largely a matter of trial and error. A comprehensive study of 4 legal medical cannabis patients in the federal Investigational New Drug Program, found only mild changes in pulmonary function associated with long term heavy use. No functionally significant adverse effects were noted in any other physiological system examined in the study.[49]

Although changes in pulmonary function can be seen with chronic high use of cannabis, occasional and low cumulative marijuana use of up to 1 joint a day for 7 years, is not associated with adverse effects on pulmonary function.[50] Many of my patients are able to maintain low overall use while still gaining significant therapeutic benefits.

In my practice, cannabis has proven to be generally well tolerated and efficacious for treating PTSD. Many of my medical cannabis patients have been able to decrease the use of other medications, including opioid pain medications, after beginning medical cannabis. In some cases they have eliminated other medications entirely. Very few have reported stopping cannabis due to adverse effects.

The most commonly reported adverse effects are mild anxiety or mild paranoia which is largely dose related and/or strain related. The vast majority of my patients who do experience occasional adverse effects, report that the benefits outweigh the risk, and choose to continue treatment with cannabis while avoiding strains which are more likely to cause these problems.

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October 23, 2012

Medical Cannabis Program
New Mexico Department of Health
1190 St. Francis Drive, S-3400
Santa Fe, New Mexico 87502 505-827-2321

Dear Secretary of Health and the NM Medical Cannabis Medical Advisory Board,

It is with great importance that Drug Policy Alliance submits the enclosed evidentiary packet in response to Dr. William Ulwelling's July 29th petition requesting PTSD be rescinded as a qualifying condition.

Per the public notice published on October 6, 2012, I, Emily Kaltenbach, State Director, Drug Policy Alliance and the following individuals formally request to present technical evidence in opposition to Ulwelling's petition at the November 7th Medical Cannabis Advisory Board meeting:

- Dr. Lisa Walker, M.D., Board Certified Psychiatrist, Licensed in NM (3 minutes)
- Dr. Florian Birkmayer, M.D., Board Certified Psychiatrist, Licensed in NM (3 minutes)
- Dr. Carola Kieve, M.D., Board Certified Psychiatrist, Licensed in NM (3 minutes)
- Keith Marker, Patient, Military Veteran, Albuquerque (3 minutes)
- Derrick Duran, Patient, Military Veteran, Albuquerque (3 minutes)
- Vicky Eckerdt, Mother, Ruidoso (3 minutes)
- Cynthia M, Patient, Las Vegas (3 minutes)
- Representative Antonio Maestas, House District 16 (2 minutes)
- Emily Kaltenbach, State Director, Drug Policy Alliance (2 minutes)

Enclosed please find exhibits to be offered into evidence for the hearing:

- Exhibit 1: Written testimony from Dr. Lisa Walker, Dr. Florian Birkmayer, and Dr. Carola Kieve;
- Exhibit 2: Patient Stories/Written Testimony;
- Exhibit 3: Drug Policy Alliance Statement: Medical Marijuana – Effective Harm Reduction Strategy
- Exhibit 4: List of public endorsements of the *Don't Take Away Our Medicine* campaign;
- Exhibit 5: Citizen petition asking Governor Martinez and Secretary of Health to deny Ulwelling's request;
- Exhibit 6: Medical Cannabis Licensed Producer Sign-on letter;
- Exhibit 7: Summary of media coverage; and,
- Exhibit 8: Research supporting the medical use of cannabis for PTSD.

We are the Drug Policy Alliance.

October 22, 2012

Department of Health
NM Medical Cannabis Program
Medical Advisory Board
1190 St. Frances Drive
Santa Fe, NM 87502

Dear NM Medical Cannabis Program's Medical Advisory Board Members and DOH Secretary,

As a Board Certified psychiatrist, licensed in New Mexico, who is also a US Navy veteran, I strongly support the Lynn and Erin Compassionate Use Act, which allows the beneficial use of medical cannabis in a regulated system for alleviating symptoms caused by debilitating medical conditions and their medical treatments.

I strongly disagree with Dr. Ulwelling's arguments against the use of medical cannabis based on the following points:

1. Dr. Ulwelling submitted the American Psychiatric Associations (APA), Practice Guidelines for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder which lists two dozen medications that can be used in treating PTSD. I would like to point out that only two of the medications included in that list are FDA approved for treating PTSD –sertraline (Zoloft) and paroxetine (Paxil). Thus, all of the other medications such as benzodiazepines, antipsychotics, and mood stabilizers are being used off-label. All of the medications have numerous unwanted side-effects that can range from nuisance level to life-threatening. Furthermore, they have demonstrated limited efficacy with approximately only 20-30% of combat veterans achieving remission of symptoms. Over 100 veterans with PTSD died between 2008 and 2010 as a result of deadly drug cocktails that included antidepressants and antipsychotics.

   I'm not sure if Dr. Ulwelling is aware, but earlier this year the Army Surgeon General and the Assistant Secretary of Defense issued statements warning against prescribing antipsychotics to Vets with PTSD and specifically contraindicated risperidone. I would also like to point out that the APA's own treatment guidelines for PTSD state that recent studies show less confidence in the use of selective serotonin reuptake inhibitors (SSRI's) in the treatment of combat-related PTSD.

   The National Institute on Drug Abuse has refused to provide cannabis to American researchers who have had FDA approval for a PTSD study for a year. However, there are government-supported human studies going on in other countries that offer data to

appropriate history-taking when the use of medical cannabis is contra-indicated due to an apparent vulnerability to psychosis. Most cannabis users do not develop psychosis. The risk associated with cannabis occurs during vulnerable time of development and is modifiable.

Dr. Ulwelling cited in his petition that the responsibilities of the Medical Cannabis Program Advisory Board include a review of new medical and scientific evidence pertaining to currently approved conditions that would support the board taking action to remove a specific condition. I question whether or not in fact any such new research has come to light.

Since 2009, PTSD has been recognized as a qualifying condition by the Medical Cannabis Advisory Board. The current pharmaceutical cocktails given to sufferers of PTSD have limited efficacy, have significant debilitating side-effects, and have in many cases proven deadly. Given these facts, along with the experience of thousands of patients whose quality of life has been improved by its use, medical cannabis should continue to be an available treatment for the suffers of PTSD in the state of New Mexico.

Sincerely,

Lisa Walker MD

Lisa Walker, M.D.
Board Certified Psychiatrist
Licensed in New Mexico

for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder discusses, even these treatment options do not have a strong evidence base, as studies in PTSD are generally lacking.

We as a profession have tried our best to utilize the best tools possible for patients who suffer from debilitating symptoms of PTSD, but these tools do not work for everyone. PTSD, as many psychological conditions are, is complicated, and there is no one-size-fits-all approach to treatment. What we can do, is make referrals to what we know are safe and effective options.

As an experienced provider, I have seen patients fail other therapies for their condition and have also seen the benefits of medical cannabis, which is not listed in the guidelines but it is also not advised against. (There are several effective treatments for PTSD that are not mentioned in Exhibit 1 so medical cannabis not being included cannot be used to suggest it doesn't work. It is simply not mentioned, like several other treatments.) In submitting these guidelines as an exhibit in this petition, there is no scientific evidence that medical cannabis should not be considered as a clinically safe and reasonable therapy <u>if patients have failed other treatment options</u>.

In the section of the guidelines titled, "Neurobiology for PTSD: Implications for Treatment," the authors discuss developing research in neurotransmitter systems of the body, specifically the receptors involved in extinction learning which is a function altered in PTSD patients.

Dr. Ulwelling does not discuss this science in his petition, and does not acknowledge the growing body of scientific evidence that supports intervention opportunities for these patients, specifically, the use of cannabis for post-traumatic stress symptoms because of how it acts on the bodies' endocannabanoid system.

<u>Exhibit 2</u>: Cannabis, Synthetic Cannabinoids, and Psychosis Risk: What the Evidence Says by JM Pierre.

Interestingly, while this article discusses psychosis as a risk of cannabis use, the author does not provide any evidence that this is a legitimate risk in PTSD or other medical cannabis patients. The author in fact discusses that in a review of the literature related to medical marijuana, there has only been one, single case of psychosis reported. Furthermore, this patient had an underlying, undiagnosed case of schizophrenia which is not the case in most PTSD patients.

PTSD and schizophrenia are not the same psychological condition and thus no scientific conclusion about medical cannabis and PTSD can be drawn from this. In fact the author specifically states that, "causality cannot be established based on this report." One of his "clinical points" is that, "the magnitude of psychosis risk tied to cannabis use is modest and most users do not develop psychosis."

debilitating symptoms of PTSD but are now able to maintain relationships with family and friends and hold down jobs.

Our ethical responsibility is to do no harm. Removing PTSD would cause more harm than good to patients whose lives have been changed for the better as a result of their option to use this medicine.

Our responsibilities also include making decisions grounded in science, none of which Dr. Ulwelling's exhibits adequately provide. Admirably, New Mexicans worked hard in 2009, bringing forward evidence that supported making available a medicine that I have seen work for patients suffering from PTSD. Let us not go backwards, but keep moving forward in improving access to safe medicine that works.

Sincerely,

Florian Birkmayer, M.D.

remained sober from alcohol as well as substances other than cannabis for over 17 months. I saw her two weeks ago. She is happy, health, vivacious and healing her relationships with husband and other family members. She is SO grateful for the ability to use Medical Cannabis for her symptoms when she needs it.

Anthony M. is a similar case, but he is younger and more recently sober. Anthony's case of PTSD is so severe that he is currently receiving disability because he has been unable to work. He has a wife and small children. His self-esteem is extremely poor due to his inability to support his family. He too is a recovering alcoholic. He did not stop drinking until AFTER he began using Medical Cannabis.

Anthony is receiving weekly individual psychotherapy and has been compliant with his appointments, something not common in this patient population, and has been making steady progress. He is less anxious, is sleeping better, is better able to relate to his wife and children and has hope for his and his family's future. He told me recently that the Medical Cannabis has enabled him to avoid drinking alcohol, even when people around him are drinking.

I do not believe that cannabis is a "gateway" drug. I do believe that adolescents should not use it, as it can stunt emotional development in this population, something that is never a good thing. However, I see absolutely no harm with its use in patients with PTSD and believe that it is an invaluable tool in the treatment of PTSD in selected patients.

Carola Kieve, MD

Carola Kieve, M.D.