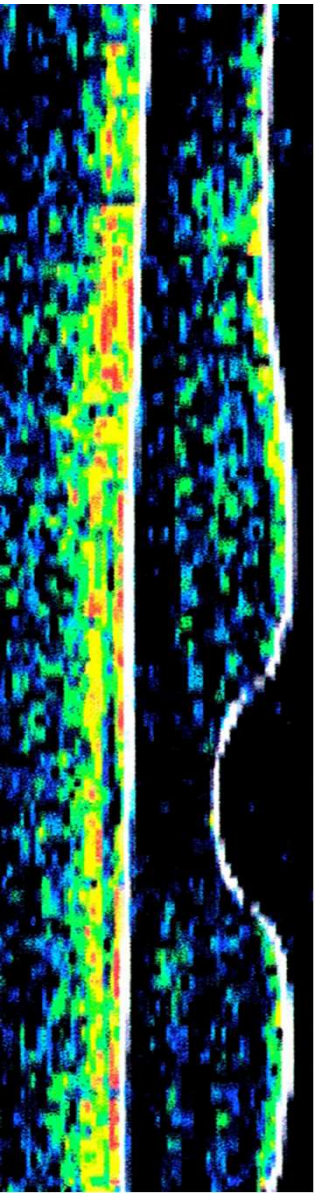


IMMAD

Impairment Measurement Marijuana and Driving

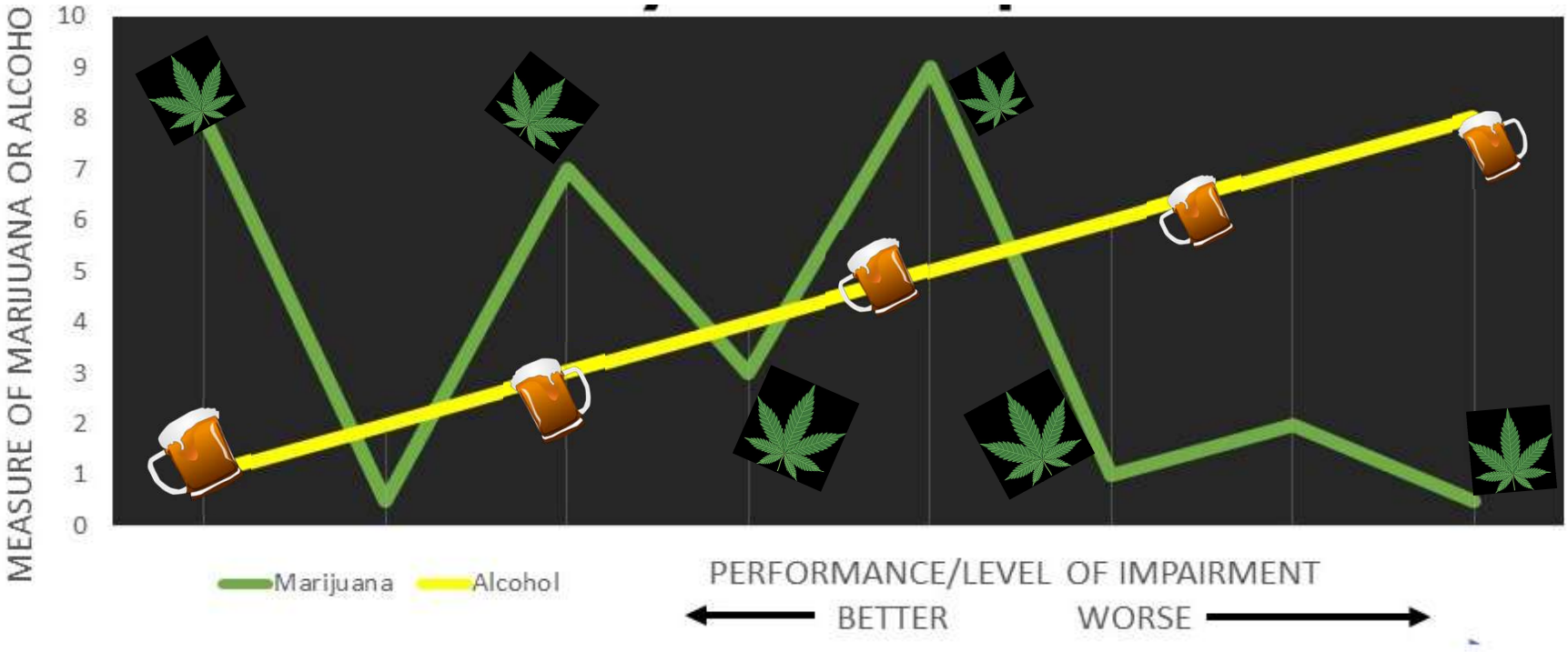
A social equity marijuana business certified in Massachusetts.

deniseavalenti@gmail.com
617 347-8737

IMMAD is developing objective technology that can identify actual impairment from marijuana use.

Unlike alcohol, there is no breathalyzer or standard field sobriety test.

Unlike alcohol the breath or blood is not linearly related to actual impairment. IMMAD would not used instead of blood, breath or saliva, but in addition to them.

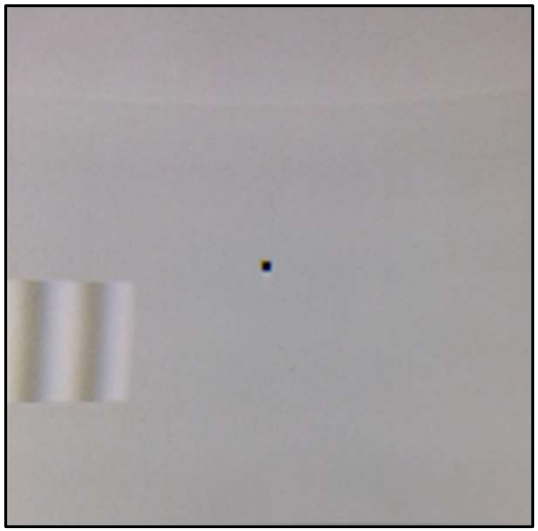


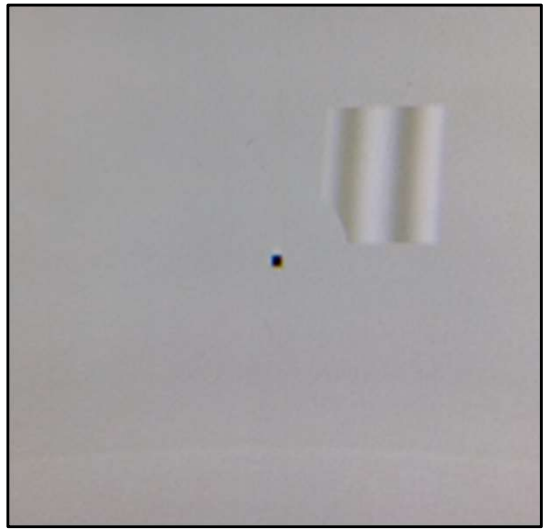
IMMAD: In Memory of Mark Alvin DeSyliva Age 15

Image of Angel Naranjo funeral age 16

https://www.reviewjournal.com/wp-content/uploads/2023/08/MINIBIKE-TEEN-FUNERAL-AUG13-23-008.jpg

IMMAD





Research participants press a button whenever they see striped squares in their vision.

Participants with recent marijuana use, cannot see many of the squares.

Massachusetts CCC Research License

IMMAD does not require any license to undertake our federally funded research.

Began the process formally in 2018.

To date only one research license has been granted in Massachusetts.

Fall 2024 Curaleaf Newton, MA.
Multistate, multicountry operator.
Seeking to relocate.

No permits to undertake human research have been awarded in Massachusetts.

IMMAD Innovation Is Already Recognized Nationally, Internationally

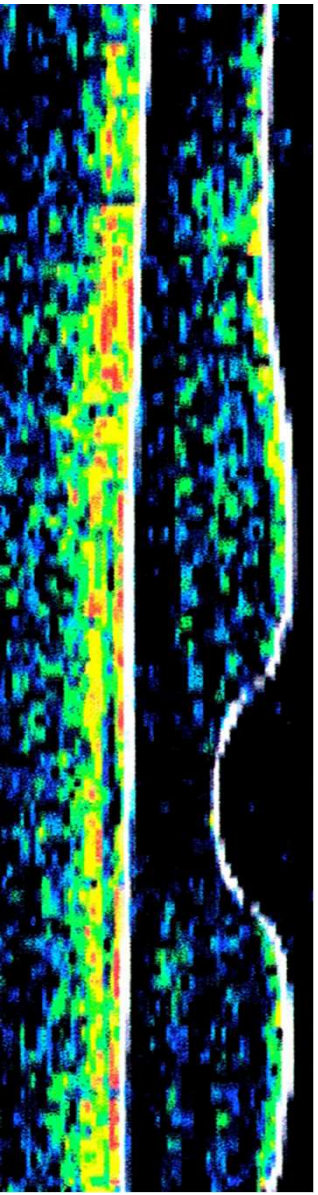
Success At Federal Grants

National Institute of Justice 2022-2024
National Institutes of Health 2018

Dr. Marc Pomplun
Chair Computational Sciences
University of Massachusetts Boston
Died Suddently: January 2025

National Institutes of Health 2025
Pending/ Withdrawn
No funding 2025-2027

IMMAD has several federal grants under review

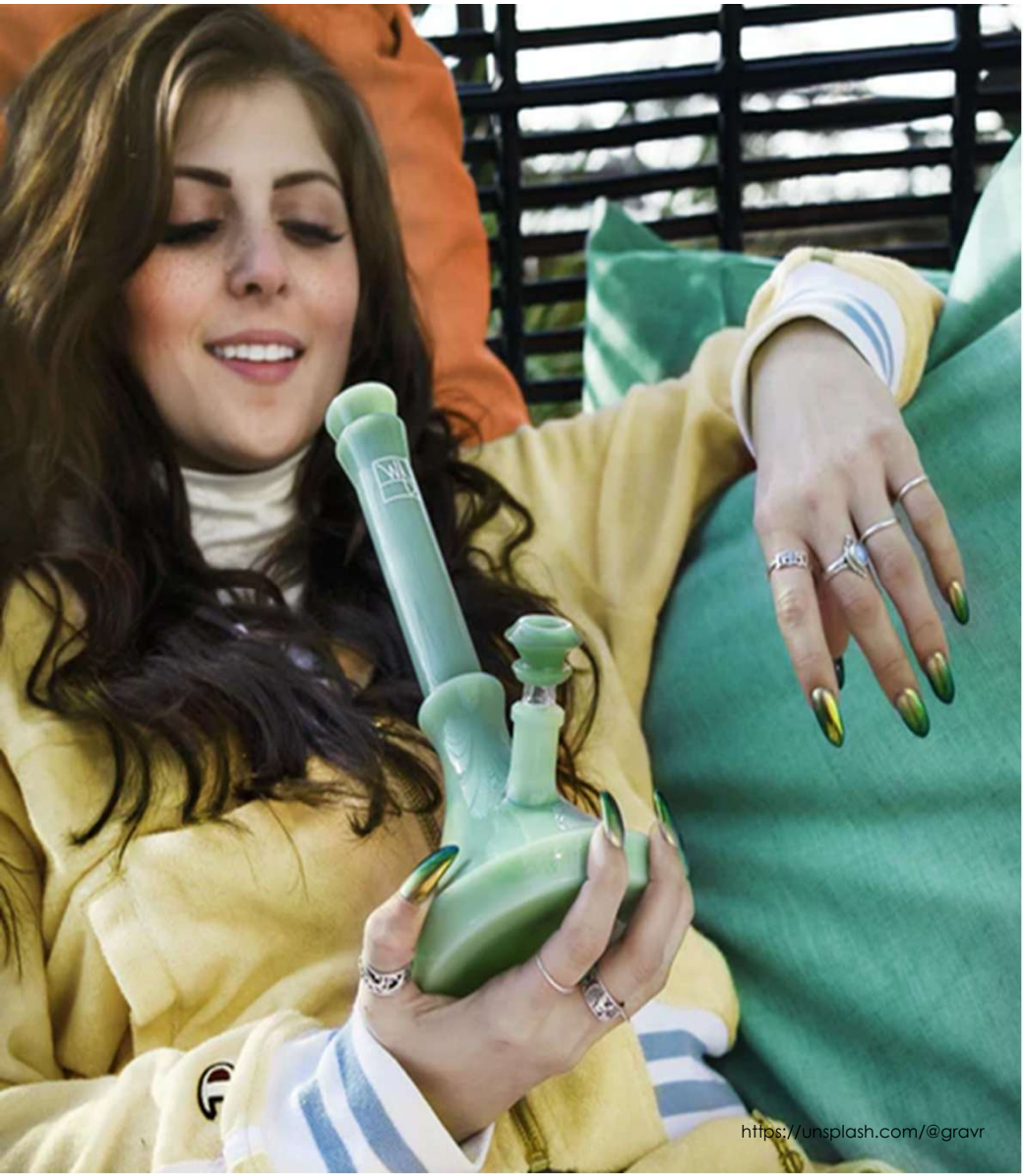


IMMAD Workbar 24 School St

There is never marijuana on site, do not require the license to undertake research.

IMMAD could be first to be issued MCCC research permit.
This is separate from a license.
IMMAD has IRB approval for opportunistic dosing.

Massachusetts marijuana laws require study of driving impairment.



Opportunistic Dosing

Not Ideal Way to do research. It is what the government can fund.

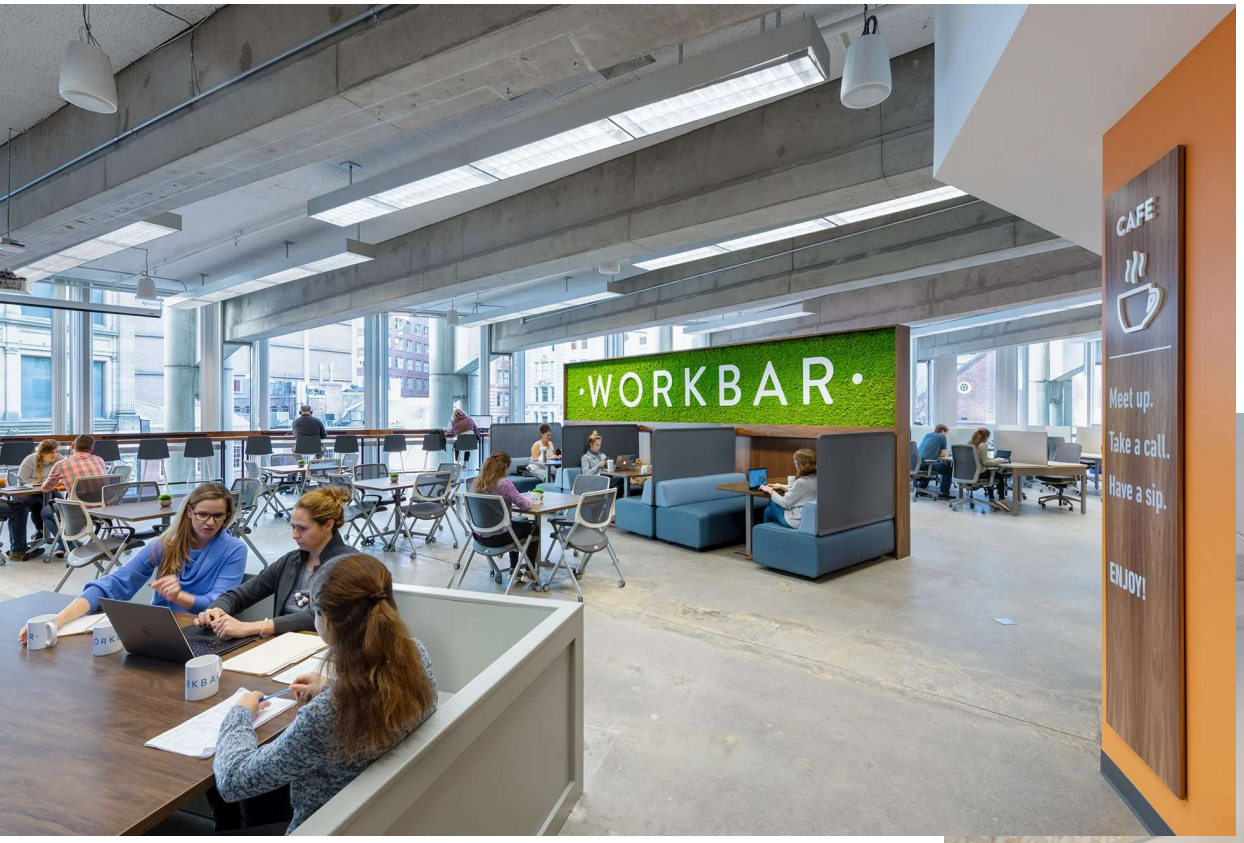
IMMAD consents and evaluates participants when they have reported not to have used any products or alcohol. Discuss when and where the participant will be using their own product.

Arrange transportation to the test site and re evaluate the participant. Arrange return transport.

IMMAD uses extensive questionnaire of use take saliva and blood at both visits.

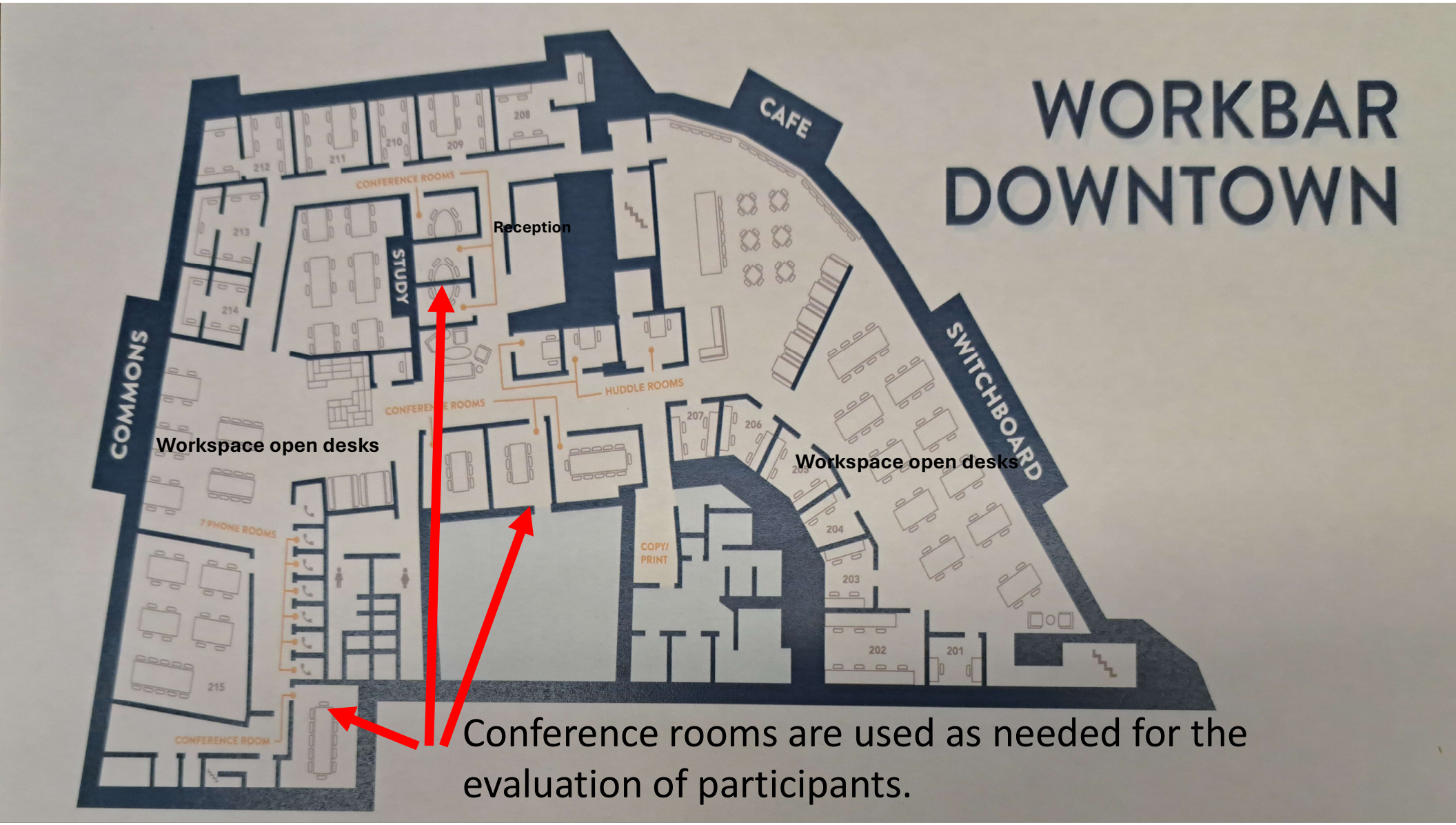

Walgreens


24 SCHOOL STREET
WORKBAR



Shared workspace, desks.

Reserved conference space, as needed.


WORKBAR
DOWNTOWN
CAFE
COMMONS
SWITCHBOARD
CONFERENCE ROOMS
Reception
STUDY
HUDDLE ROOMS
Workspace open desks
Workspace open desks
7 PHONE ROOMS
COPY/
PRINT
CONFERENCE ROOM
208
209
210
211
212
213
214
215
201
202
203
204
206
207
Conference rooms are used as needed for the evaluation of participants.

Densest Population Facility in State:

420 Abutters

Density of residences advantage for research.

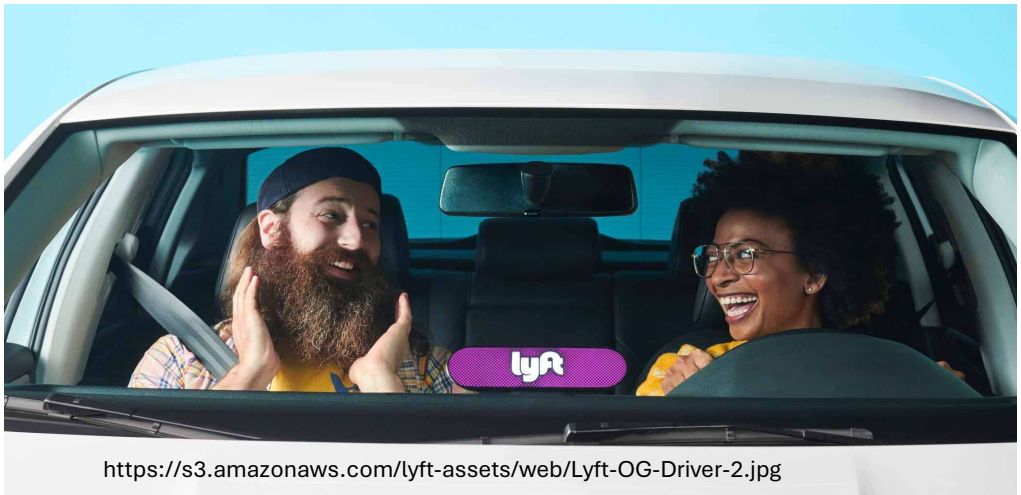
420

Security

Security is provided by Northeast Security, Inc
Managed by Indira Frederico
The space is in a building with 24 hour security. Access is by key pass and identification by the security. To enter the building one must be granted access by security. This enables access to the elevators. The space in on the second floor. There is a receptionist at the entry point during traditional hours; 9 to 5.

When There are Participants "Customers" On Site

During periods of participant evaluation IMMAD has two staff meeting and greeting participants at the entry street level. We run one participant at a time unless they have scheduled together as "friends". The two staff remain with the individual during their entire visit and escort them back to street. If dosed, the staff remain with the individual until they have entered car.

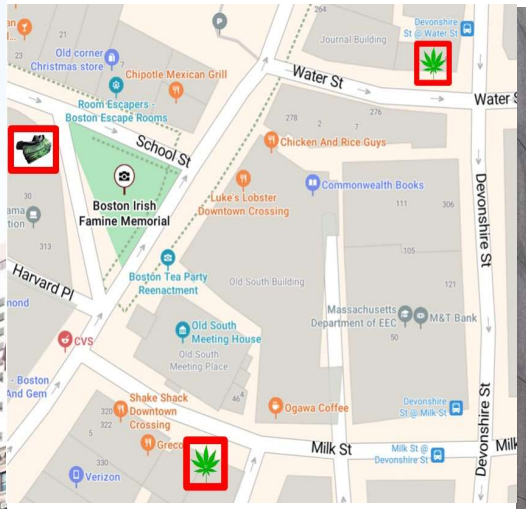


https://s3.amazonaws.com/lyft-assets/web/Lyft-OG-Driver-2.jpg

IMMAD NOT Comparable to Recreational Retail

Curaleaf: 21 Milk 300 ft, 1 block

Proposed



Less than 450 apart

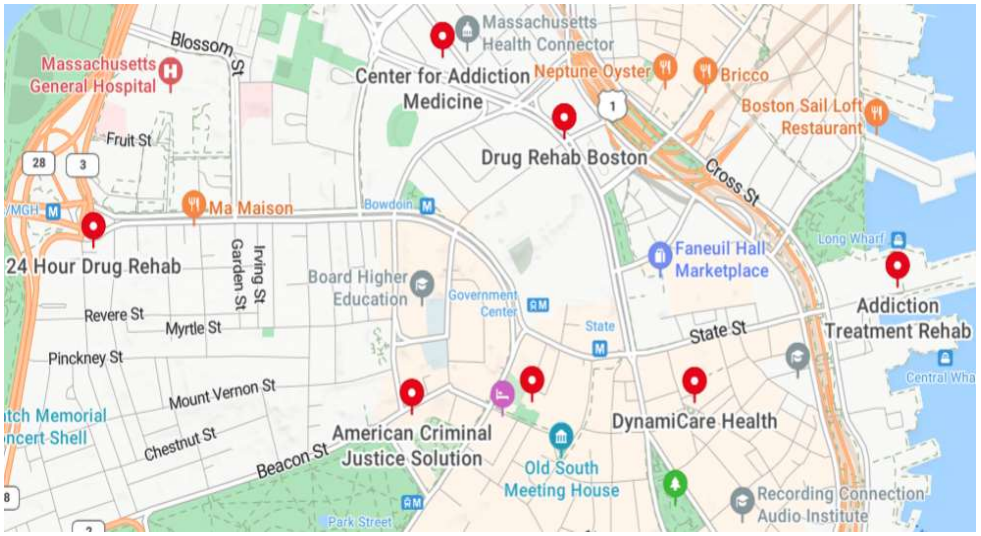
Pure Oasis: 85 Devonshire 365 ft, 2 blocks

Open

Parallel Businesses Within Four Blocks
All Probably More Disruptive Than IMMAD

Mental Health Services
Drug detoxification center 400 feet, State Street
Psychology/Psychiatry three blocks, Devonshire
Internal medicine practice across street on Washington
Psychotherapist four blocks, Broad Street
Therapeutic services two blocks, Tremont Street
Mental Health Clinic four blocks, Court Street

Addiction Services



Criminal or DUI Legal Consult
Two practices less than block, School Street
One practice two blocks, Tremont Street
Four practices three blocks, Devonshire Street
One practice three blocks, Congress Street
One practice four blocks, Post Office Square

We Want Participants High

We Will Not Be in Compliance With Boston Cannabis Regulation: Intoxicated Patrons

"A person who is intoxicated or who appears to be intoxicated shall not be permitted to enter the Licensed Premise. All employees shall be trained to be aware of the signs of intoxication. Employees must notify a manager of an intoxicated patron and,if necessary, assist in escorting the intoxicated patron from the LicensedPremise. Once outside or in the lobby if a responsible person cannot be located to assist this patron then the employee should call 911 to request police assistance. "

But we are compliant with:

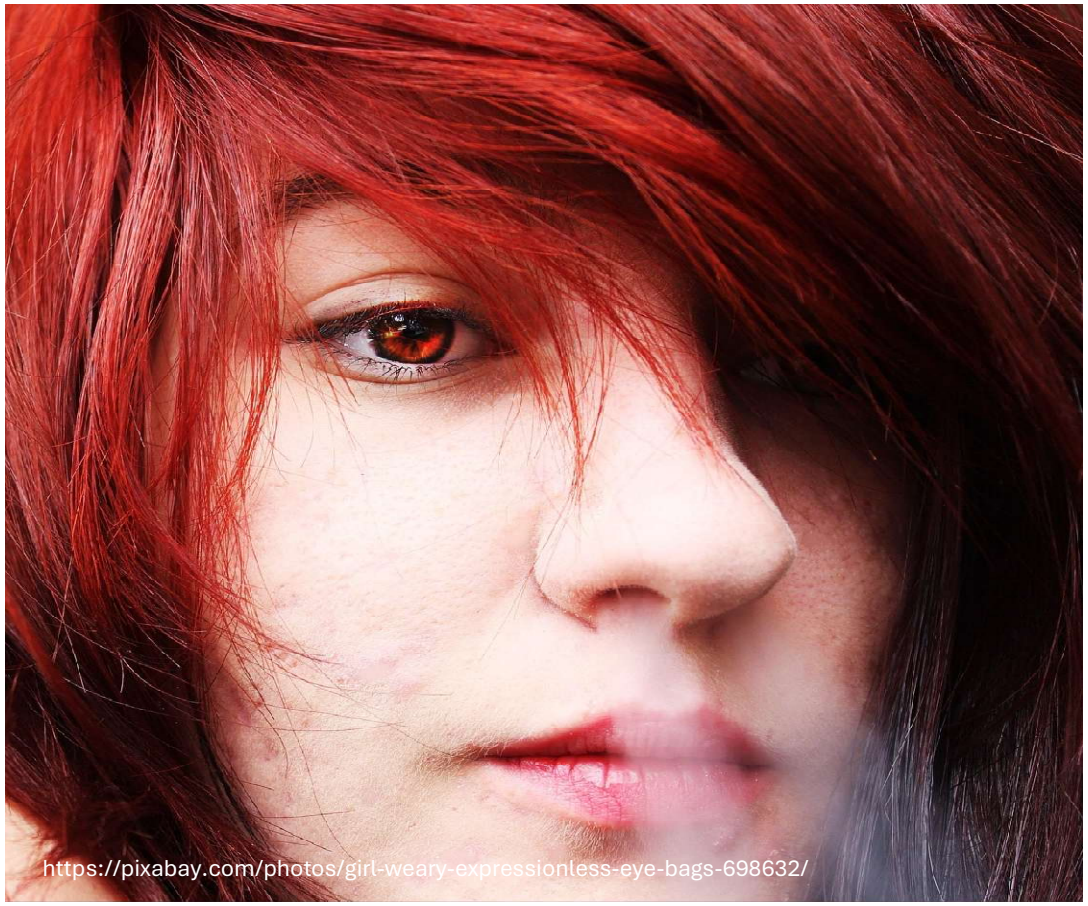
"Reasonable attempts, absent physical restraint, should be made to prevent a severely intoxicated patron from leaving the licensed premise by themselves due to safety concerns."

https://pixabay.com/photos/search/kermit%20pink/

50% of Visits

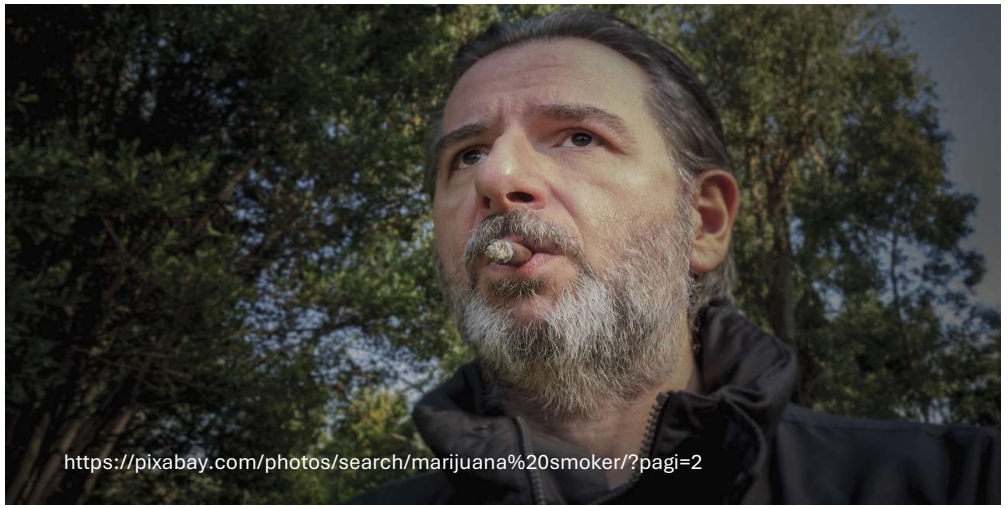
Participants will have self dosed at home and arrived by shared ride; Uber or Lyft.

No One Underage



No One Under 21

We Do Card On The Other Side of Age IRB Approved Under Age 40


https://pixabay.com/photos/search/marijuana%20smoker/?pagi=2


https://pixabay.com/photos/man-portrait-cigar-self-portrait-544287/


https://pixabay.com/photos/man-cigarette-e-cigarette-smoking-2634401/

IMMAD Diversity

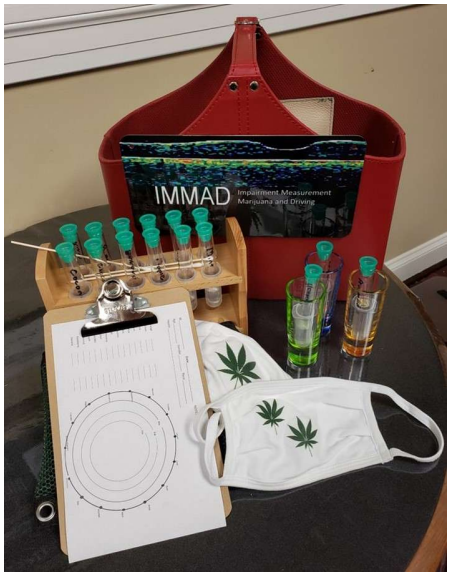
Staff Diversity

All Jobs Posted In VA Office

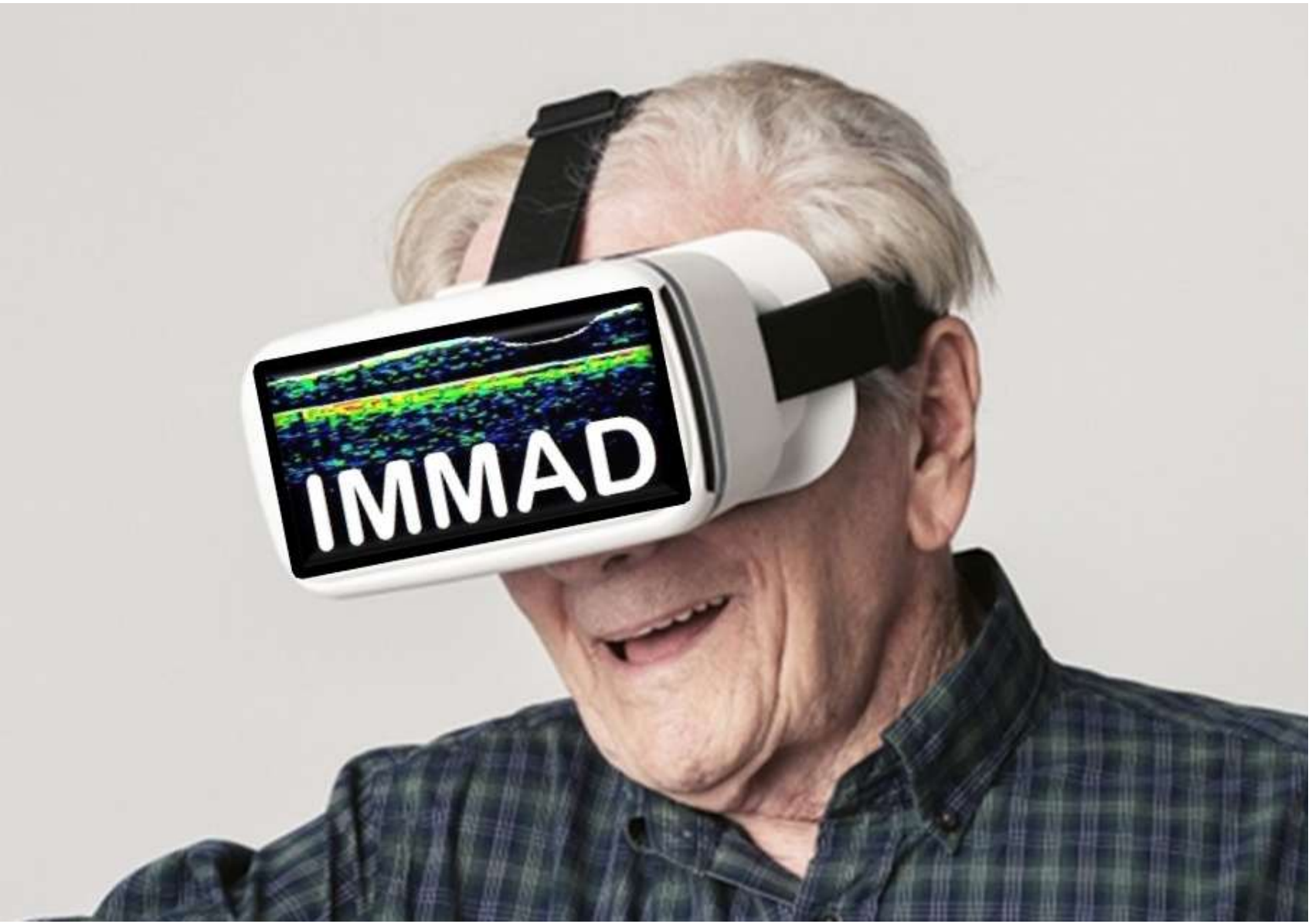
Participant Diversity

MCCC Research License Application

- IMMAD has been doing federally funded research since 2018.
- First site CIC 25 Milk Street. NIH funding. 26 participants.
- Second site 1325 Hancock Street, Quincy, MA. NIJ funding.
  50 participants. 12 real car, closed road Weymouth.
- Current site 24 School Street. Boston, MA.
  Propose up to 90 participants a year.

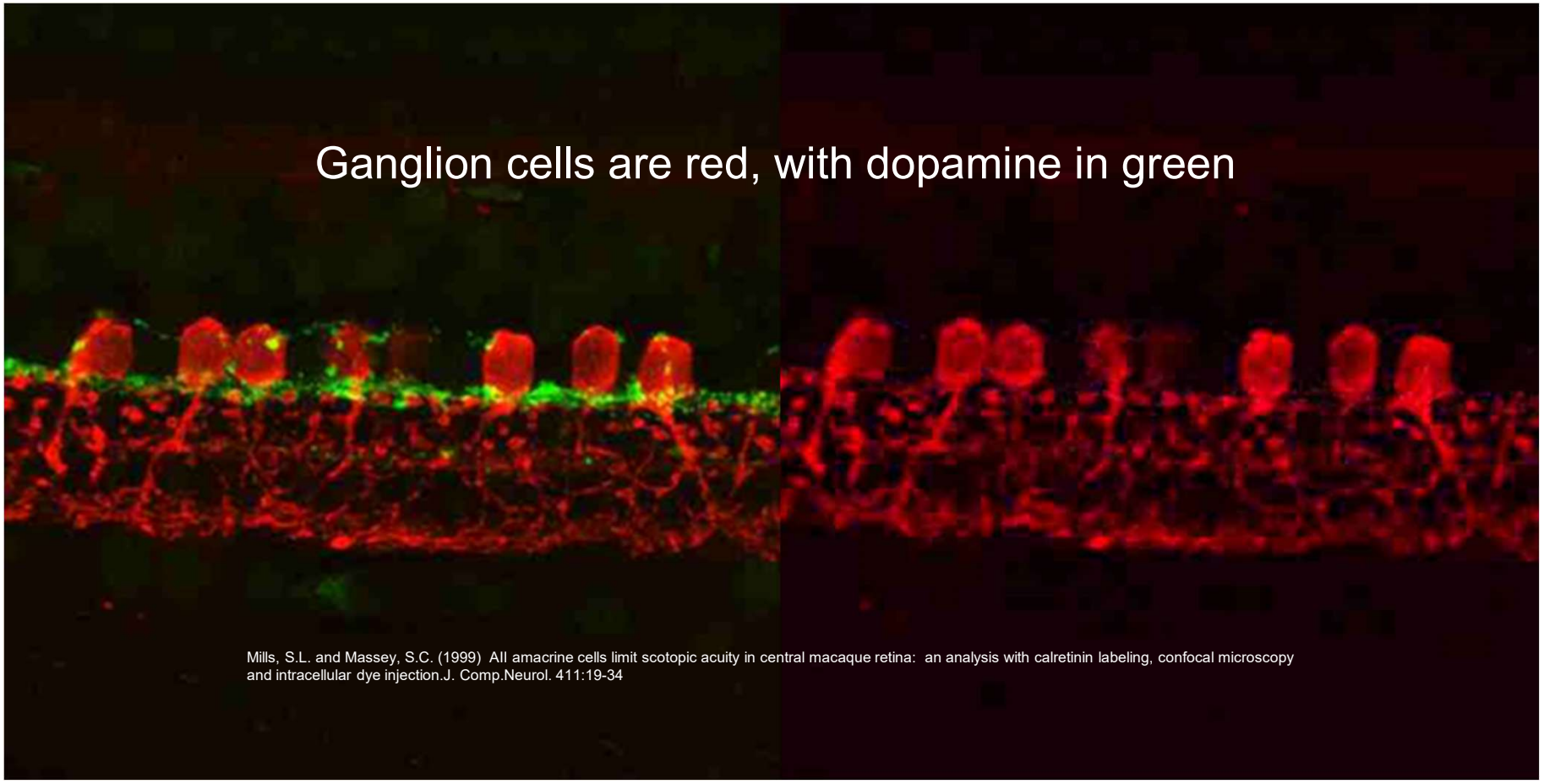



IMMAD



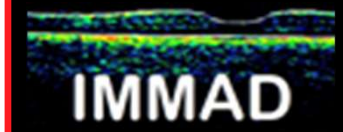
IMMAD
As A Test:
Easy

Science Complex:
Cannabis Inhibits Dopamine Production In Retina

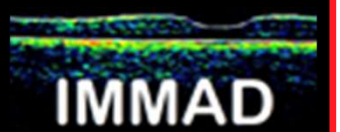


Mills, S.L. and Massey, S.C. (1999) AII amacrine cells limit scotopic acuity in central macaque retina: an analysis with calretinin labeling, confocal microscopy and intracellular dye injection.J. Comp.Neurol. 411:19-34

Acute Marijuana Use: Retinal Function



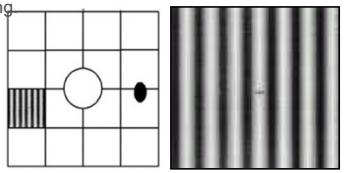
Denise A. Valenti, OD, FAAO
IMMAD-Impairment Measurement Marijuana and Driving
deniseavalenti@gmail.com
Christopher Wu, OD
University of Houston College of Optometry



Background and Methods

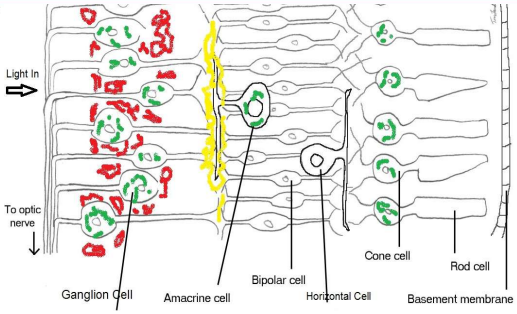
We evaluated, using an IRB approved opportunistic dosing protocol, twenty participants. Participants were seen undosed and baseline was measured. The participants used their own product off site and were picked up and returned to the same location by ride share. Blood was obtained during the dosed sessions. Thirteen had reliable data. Reasons for exclusion were mismatch of blood to use reports or unreliable results based on technology. We used a visual field screening technology assessing visual field function within the central forty degrees of vision. We elected to use the instrument's threshold strategy rather than screen program. Research shows decreases in visual function with acute use. The technology checks false positives and negatives as well as fixation. We did identify chronic heavy users having dysfunction in fixation, with more unreliable results. Understanding deficits associated with cannabis is particularly critical for tasks such as driving.

The stimulus, far right, is a low spatial frequency grating of 10°, presented at 1 of 17 test locations, shown near right. The grating alternates at 25 Hz. The frequency doubling illusion is the subjective perception that the grating has twice the number of dark and light bars (i.e., its spatial frequency appears to be 0.50 cpd), as shown in the diagram.



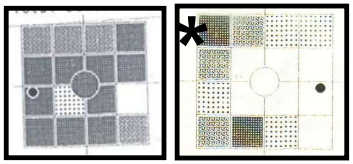
Cannabinoids And The Retina

Cannabinoid receptors are throughout the retina (3). Cannabis depletes retinal dopamine (4). Retinal amacrine cells are involved in processing acetylcholine and cannabinoids disrupt this neuroprocessing in the retina (5). To the right is an image of the retina. Cannabinoid receptors are shown in green, acetylcholine is yellow and dopamine is depicted with red.



Outcome: Retinal Ganglion Cell Dysfunction

Disruptions in neurotransmitter balance due to disease, medications or drugs can result in dysfunction in the retinal ganglion cells (RGCs). Chronic cannabis use as well as acute use causes dysfunction in the RGCs (6). Functional tests can demonstrate such losses. Near right is an example of retinal ganglion cell dysfunction specific to dopamine depletion in Parkinson's (7).



The image to the far right is an example of acetylcholine inhibition secondary to medication, methotrexate (8). The images, OD and OS, below are the results of the cannabis group. Red is significant dysfunction. The P values are displayed. There were trends showing potential gender differences with females (equal numbers have participants) having lesser impairment in all but one quadrant. Acute cannabis impairs functions related to temporal processing and contrast as demonstrated with this research. Further research is warranted.

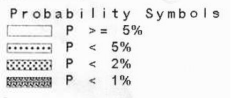
Conclusion

Acute use of marijuana has been reported to cause retinal ganglion cell dysfunction. This research in visual system shows functional impairment that is caused by acute marijuana use.

References and Images

1 Ortiz-Peregrina A: Science Reports. 2021 Jan; 11(1)
2 Adams AJ: Psychopharm. 1978 Jan; 31; 56(1):81-6
3 Straiker A: Proc N Acad Sci. 1999; 96(25):14565-70
4 Mills, SL: Comp Neurol. 1999; 411:19-34
5 Strang CE: Invest Ophthalmol Vis Sci. 2010; 51(5):2778-89
6 Schwitzer T: JAMA Ophthalmol. 2017 Jan 1; 135(1):54-60
7 Valenti DA: Invest Ophthalmol Vis Sci. 2005 May; 46(5):626
8 Valenti DA: Invest Ophthalmol Vis Sci. 2006 May; 47(5):4480

Key To Results



IMMAD, LLC

Impairment Measurement Marijuana and Driving
A company specializing in the responsible use of cannabis.

Visual Function and Acute Marijuana Use: Casual and Chronic Users

Denise A. Valenti, OD, FAAO - IMMAD, LLC
Chris Halsor, Esquire and David Carbonneti - Understanding Legal Marijuana, LLC

Introduction There are cannabinoid receptors throughout the retina (1). Marijuana/cannabis causes dysfunction in human retinal ganglion cells with acute use (2) and chronic use in the abstinent state (3). Central glare dysfunction has been reported with acute marijuana consumption (4). Tunneling of vision is described by users consuming marijuana acutely. However the only report in the literature of peripheral dysfunction were reductions along the only meridian measured, 180 degrees (5). An animal model shows cannabis impairs the lateral geniculate nucleus and superior colliculi (6) raising potential for eye movement changes. Despite being recognized as legal in nine states, marijuana is still classified as a Schedule I drug by the federal government and the opportunity to undertake double blind , placebo controlled studies are limited. We evaluated opportunistically, during vision screenings, seven participants who reported to have acutely self-dosed with marijuana/cannabis. Three participants were casual users by self reports and four were self reported as having chronic long term use. Of the seven, only four had reliable testing, the three casual users and only one eye of a chronic user. Undertaking this type of research is not without problems, but does allow for collecting preliminary information to guide future research.

Methods Two participants were seen at a general health screening and evaluated after acute marijuana use and reported only casual use of marijuana.. The others were seen at an event specific to cannabis; GreenLabs under the direction "Understanding Legal Marijuana, LLC". GreenLabs are offered on a regular basis to train law enforcement specialists. The purpose of the eye screening was to evaluate at baseline and under marijuana use, visual functions that may be contributing to observations made by the officers taking the course. Medical professionals took measures of heart rate, blood oxygenation and blood pressure from all participants as well as other biologic measures. Three of the five participants visually screened had blood drawn as a part of the drug training to determine levels of tetrahydrocannabinol (TCH). The visual screenings included best corrected distance vision OD, OS and OU using an EDTRS chart at ten feet. All participants had best corrected vision 10/20 or better OD, OS and OU. We also utilized a Zeiss 710 Frequency Doubling Technology (FDT) visual field test. FDT is often used for large group visual screenings and has been demonstrated to be reliable in young children (7) as well as cognitively impaired adults (8). FDT uses a variable contrast low spatial frequency grating of 10°, presented at 1 of 16 test locations, a 5° target centrally and tests the central midperipheral forty degrees of vision. The grating alternates at 25 Hz. We used the instrument threshold strategy. FDT has twelve reliability measures; six fixation tests, three false positive and three false negatives.

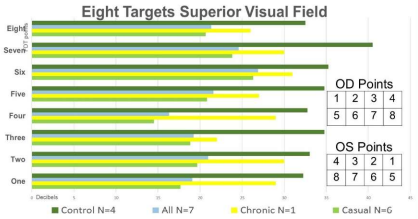
Six participants had a vision screen during the GreenLab drug education course for law enforcement officers. Of these six, only three were included in the data under discussion and shown below. One was a casual user. There were three potential periods of testing; prior to dosing, after an initial dosing and at the end of the entire session. The time span for testing was four and one/half hours. Testing was done as participants were able and interested in the testing. Only one participant had testing during all three times, and this participant turned out to be the only chronic participant with reliable testing. All those used for analysis participated in a session within one hour or less of dosing. If a participant had three or more failures in reliability indices; fixation loss, false positive or false negative, the test was considered unreliable and not included in statistical analysis. Of the six, one was found to have been a "malingerer" identified during blood THC level testing and had not likely consumed marijuana. Another that had been tested during a pre-dosing session was too impaired after dosing, having used a product unfamiliar to them, to participate in any further testing. One participant had unreliable indices in the pre-dosing session with four with the right eye and five with the left and the dosed session six with the right eye and seven with the left. One participant had only been tested at the close of the session, four hours after consumption and the data was not included in discussions or analysis Of the remaining three participants one was a chronic user and had an unreliable test in one eye . This was the only participant having been tested during all three sessions. The other chronic user, while able to fully participate and perform the test, had unreliable tests for both eyes. The casual user had reliable tests for both eyes. Two staff members administering protocols during the GreenLab were used as controls.

Results The casual users are labeled 1, 2, and 3 in the chart below. They all had reduced sensitivity in each eye and had negative mean deviations in both eyes. The chronic users both showed high positive mean deviations in the eyes considered to be unreliable based on errors and the standard deviations were also high. T-tests of probability were done on each of the seventeen test points comparing the three casual user's six eyes to those of the two control's four eyes. Three points were significant to P< 0.01 and the data are shown to the right. The printout showing the decibels for each point and total deviation for one control participant and the three casual users are far right. The printout for the two chronic users also include the mean deviation and standard deviation.

Discussion Using opportunistic participants for marijuana/cannabis studies is problematic. However, given the barriers to the study of marijuana/cannabis the testing of these participants was instructive and valuable. The results show possible differences between long term chronic users and non-long term users. One potential adaptation may be scanning patterns that are enhanced, using microsaccdes much like what occurs with those with long standing stable visual field defects. It is likely the brain has reorganized to adapt to the visual changes. Animal studies support this and additional studies are warranted.

Volunteer Age		No MJ OD Error	No MJ OS Error	No MJ OD Mean Deviation	No MJ OS Mean Deviation	No MJ OD Stand Deviation	No MJ OS Stand Deviation	OD Error	OS Error	OD Mean Deviation	OS Mean Deviation	OD Stand Deviation	OS Stand Deviation
Control	33							1	2	+3.00	+4.03	+3.78	+7.20
Control	60							0	0	+2.68	+2.85	+2.35	+2.56
One	22							1	0	-20.22	-8.34	+11.45	+8.95
Two	24							1	1	-5.56	-3.61	+5.97	+4.48
Three	33							0	0	-1.74	-4.48	+6.74	+3.17
A	36	4	5	+5.85	+2.97	+7.30	+3.68	6	10	+9.28	+7.84	+12.27	+13.32
B	49	2	1	+2.20	-0.74	+4.05	+4.41	5	2	+6.62	+0.33	+10.16	+7.02

FDT Function

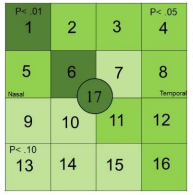


OD Points

1	2	3	4
5	6	7	8

OS Points

4	3	2	1
8	7	6	5

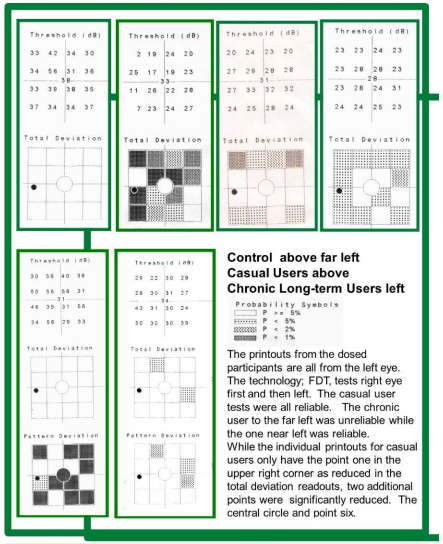


To left is data specific to casual users. The right and left eyes are combined. N is six eyes, compared to normal control N of four eyes.
1: t-value -3.49607 p-value .008126
6: t-value -3.72385 p-value .005839
17: t-value -4.26025 p-value .00276
Aggregate data for nasal and temporal hemispheres were compared, with no significant differences. This indicates that brain laterality effects are unlikely. Superior and inferior visual fields were compared, with no significant differences.

Biologic Measures

	Age	gender	oxygen	Heart rate	Blood pressure	Blood mg/ml	THC/marijuana product
3	33	male	97 96	84 92	150/90 160/100	None	Dab 80% 2 hits
A	36	female	93 96	94 82	138/100 146/98	N/D,1.2,9.9 6.7,3.5,22.30	Flower 9 hits
B	49	female	96 92	95 124	118/82 120/84	1.0,2.3,58.5 11.5,8.8,77.6	
C	30	female	98 74	68 142	124/69 132/77	none	Flower 22.7% 4 pipes
D	29	female	98 97	94 100	124/88 134/84	none	Hybrid 20% Dab
E	25	female	93 96	90 98	129/83 135/80	none	Indica hybrid

FDT Printouts



Control above far left
Casual Users above
Chronic Long-term Users left

The printouts from the dosed participants are all from the left eye. The technology; FDT, tests right eye first and then left. The casual user tests were all reliable. The chronic user to the far left was unreliable while the one near left was reliable. While the individual printouts for casual users only have the point one in the upper right corner as reduced in the total deviation readouts, two additional points were significantly reduced. The central circle and point six.

References

1 Straiker A: Proc N Acad Sci. 1999; 96(25):14565-70
2 Schwitzer T: Eur Addict Res. 2016;22(6):287-291
3 Schwitzer T: JAMA Ophthalmol. 2017 Jan 1; 135(1):54-60
4 Adams AJ: Psychopharm. 1978 Jan; 31; 56(1):81-6
5 Moskowitz H: Percept Mot Skills. 1972 Dec;35(3):875-82
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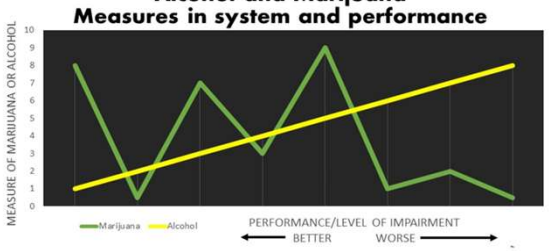
7 Nesser R: J Glaucoma. 2004 Aug;13(4):278-82
8 Valenti DA: ISRN Neurol. 2013 Sep 25;2013:

Ophthalmic Impact of Cannabinoids

Denise A. Valenti, OD, FAAO CEO IMMAD LLC David Calixte Engineering BFCIT
Xueling Zou Clinical NECO Trevor Koppy Chemistry UMBoston
Rhoda Nankabirwa Data UMBoston Allen Mello, MS Forensics Wisconsin State Lab of Hygiene

Cannabinoids: Not like alcohol

There is a linear relationship to the quantity of alcohol and impairment.
There is no such direct relationship with measures of cannabinoids in fluids and impairment. There needs to be both a measure of presence of cannabinoids and a separate measure of impairment that is related to the ability to safely drive a motor vehicle or perform tasks. Measures of impairment need to be objective, free of racial bias and easily performed roadside by law enforcement professionals. To date saliva is an efficient means to detect cannabinoids and we propose a simple retina test of impairment.



Cannabinoids: Biologics Include Tears

Measures of Cannabinoids Urine, blood, saliva, breath, sweat and tears (1) have all been shown to identify cannabinoids in humans. Of these, urine and blood are the most frequently used roadside. Urine is particularly problematic as it is only an indication of use several hours or more prior to the time it is collected. It measures the inactive cannabinoid metabolites, Delta-9 Carboxy THC. Blood can demonstrate more recent use and can quantify the presence of the active Delta-9 THC as well as its active metabolite 11-Hydroxy Delta-9 in addition to inactive THC. THC has an affinity to the lipids of the body making the possibility of testing breath difficult. Saliva is less problematic, but still not as reliable if cannabis is consumed in edible form. Tears contain a lipid layer that would possibly be a means for detection of cannabinoids, but a practical means of retrieval has yet to be identified. We are fortunate that Northeastern Biomedical Engineering Capstone teams are working on this problem.

References and Conclusions

1. Mello A, Valenti DA, Foss J, Botch-Jones S. International Cannabis Research Society, 2021
2. Straiker AJ, Maguire G, Mackie K, Lindsey J. Invest Ophthalmol Vis Sci. 1999 Sep;40(10):2442-8
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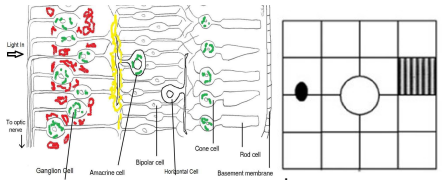
While promising, tears are not yet practical as a measure of cannabinoids when retrieved roadside. Acute use of marijuana has been reported to cause retinal ganglion cell dysfunction. This research in the visual system shows functional impairment that is caused by acute marijuana use and the impairment can be demonstrated using patented IMMAD Virtual Reality forensics technology having variable contrast striped targets. Such technology can be used roadside by law enforcement.

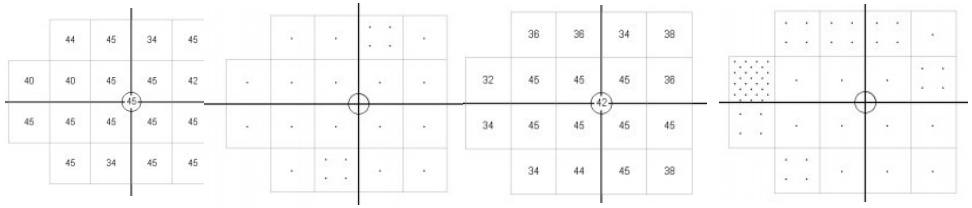
Contact: deniseavalenti@gmail.com

Funding: NIJ 15PNIJ-22-GG-04417-RESS

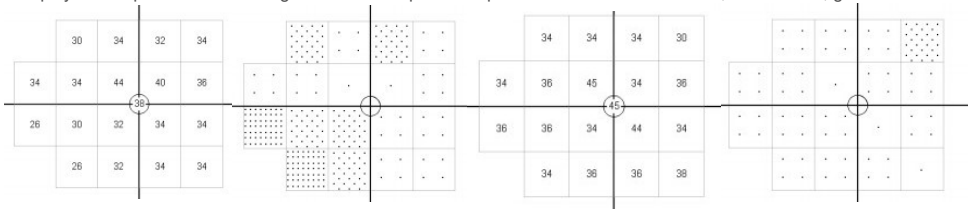
Retinal Functional Impairment



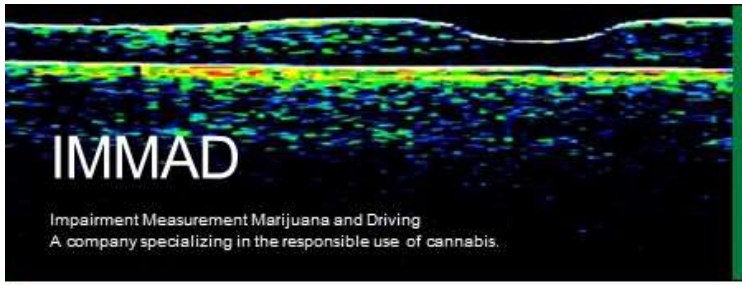
Cannabinoid receptors are throughout the retina (2). Cannabis depletes retinal dopamine. Retinal amacrine cells are involved in processing acetylcholine and cannabinoids disrupt this neuroprocessing in the retina (4). To the left is a drawing of the retina. Cannabinoid receptors are shown in green, acetylcholine is yellow and dopamine is depicted with red. Functional tests can demonstrate such losses. IMMAD is such a test (4). IMMAD displays small striped squares in a simple virtual goggle.
A striped square is shown left. The stripes are of variable contrast.



Casual Cannabis Use – O ng/mL cannabinoids in system at baseline
1.0 11-Hydroxy Delta-9 THC, 16 Delta-9 Carboxy THC, 5.7 Delta-9 THC when dosed.
Acute cannabis impairs functions related to temporal processing and contrast as demonstrated with this research. Above are the results from an undosed and dosed participant who was a casual, non chronic user. Below are the undosed and dosed result from a chronic cannabis user. The numbers displayed are detection of decibels of contrast in the stripes displayed. Stripes cover a ten degree area. Grid pattern is percent deviation from normal, denser dots, greater deviation.



Chronic Cannabis Use – Reductions in IMMAD at baseline and had cannabinoids in system at baseline. 0 11-Hydroxy Delta 9 baseline and 1.2 at dosed session. 36 Delta-9 Carboxy THC baseline and 37 dosed, 2.1 Delta-9 THC baseline and 9.0 dosed session. Unit ng/mL



IMMAD

Impairment Measurement Marijuana and Driving
A company specializing in the responsible use of cannabis.

Medical Marijuana and Glaucoma: The United States Experience

Denise A. Valenti, OD, FAAO

Objective: There are twenty-eight states that allow for the use of medicinal plant cannabis and all but six have glaucoma specified as an approved pathology for which cannabis can be used. This is an analysis of the data related to the certification to use marijuana/cannabis as a means to treat glaucoma. Of note; Israel, considered to be on the forefront in cannabis medicine, recently dropped glaucoma as an approved disease for marijuana/cannabis treatment.

Methods: A review was made of each state's website. Some had statistical reports, those that did not and specified glaucoma, were contacted by email. Not all states collect information specific to a diagnosis. There were diagnosis specific information for eleven states. The number of certifications specific to glaucoma were compared to the prevalence data related to glaucoma for each state as published by Prevent Blindness. The number of glaucoma certifications were compared to the total state certifications for all pathologies in each respective state. The data from the first quarter of 2017 were used for all but Massachusetts and Montana. For those states the data from Fall of 2016 were used.

Results: An estimated 4,416 patients are using cannabis/marijuana related to glaucoma. Twenty-two states have glaucoma as a disease to be treated with marijuana. Of these, there were data from eleven states. Of the twenty-two states, four states had new programs not yet enrolling. Three states stand out when comparing rate of certifications to the rate of prevalence. Montana and Colorado for having high rates and Minnesota for having low rates. Massachusetts did not respond to requests for an update and Montana had listed cancer, HIV and glaucoma in one category for the January 2017 report. Alaska, Florida, Maine and California responded and acknowledged they do not collect diagnosis data that is available to the public. Connecticut, Illinois and Washington did not respond to multiple requests.

Discussion: The higher prevalence in Colorado may be influenced by the recreational products being taxed higher compared to medicinal marijuana. Oregon has a higher rate of glaucoma certification and the reasons may also be related to taxation. The low prevalence rate in Minnesota may have been influenced by greater restrictions on the recreational style of consumption. New Jersey and Florida maintained data bases accessible by patients listing clinicians that can certify for marijuana use. *New Jersey listed specialties and there were eight ophthalmologists listed. New Jersey does not specify glaucoma among allowable diseases but report 220 patients being treated for glaucoma out the total 6120 certifications (3.59%) and glaucoma prevalence of 83,013 (0.26%).* New York maintains a data base of clinicians and specialty but this was only accessible to referring clinicians. Minnesota's program is unique as it restricts the mode that marijuana can be consumed to primarily to medicinal vaping systems and oral tinctures. Smoking plant materials, edibles such as candy and brownies are not allowed. Minnesota has developed systems to track patient self response. The survey of self response included four glaucoma patients, one reported no benefit and the other three reported positive response. Connecticut has a very different system. That state rescheduled cannabis to a Schedule Two drug requiring all dispensing to be supervised by a licensed pharmacist. While they do certify for glaucoma, there was no response to two email inquiries. Montana does not yet have dispensaries and all medical cannabis is grown by patients or caregivers. Montana does have the ruling that should a medicinal patient receive a conviction for marijuana DUI, they must surrender their medicinal certification.

Conclusion: The certification to use cannabis for glaucoma varies across states and there is no consistent reliable data collection among many states. There is little indication of patients being followed in a manner optimum for vision health. Data collection in cases where an eye care provider is involved will help clarify efficacy. The use of cannabis/marijuana to treat glaucoma is a public health concern.

Glaucoma Percentage of State Glaucoma

Arizona	765/50,879	1.50%
Colorado	1,183/35,859	3.30%
Hawaii	302/15,064	2.00%
Massachusetts*	227/58,588	0.39%
Minnesota	43/42,873	0.10%
Montana*	281/ 8,461	3.32%
Nevada	408/20,459	1.99%
New Hampshire	42/10,798	0.34%
New Mexico	225/17,352	1.30%
Oregon	919/ 31,900	2.88%
Rhode Island	21/9,718	0.22%

Prevalence data of glaucoma rate in each state from:
http://www.visionproblemsus.org/glaucoma/glaucoma-map.html

Glaucoma Percentage of All Disease Certifications

Arizona	765/108,883	0.70%
Colorado	1,183/94,577	1.25%
Hawaii	302/15,334	1.97%
Massachusetts*	227/22,700	1.00%
Minnesota	43/4,017	1.07%
Montana*	281/8,461	1.21%
Nevada	408/24.465	1.67%
New Hampshire	42/2,089	2.01%
New Mexico	225/34,909	0.64%
Oregon	919/ 63,120	1.46%
Rhode Island	21/16,418	0.13%
Total Glaucoma	**4,416**	**Total 394,973**

* Previous Year

Glaucoma & IOP A Few Cannabis Studies

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DETECTION OF Δ9-TETRAHYDROCANNABINOL AND METABOLITES IN THE MEIBOMIAN LIPIDS OF TEAR SAMPLES THROUGH LC-MS/MS

Allen Mello [1], Denise Valenti, OD [2], Jamie Foss [3], and Sabra Botch-Jones [1]

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Introduction

With an increased use of recreational marijuana, the risk of Driving Under the Influence of Drugs (DUID) is steadily increasing. There exists limitations with current methods of detection of Δ9-Tetrahydrocannabinol (THC), the primary psychoactive component of marijuana, in DUID cases with the need for invasive sample collection (e.g., blood) and roadside collection. This work explored the use of meibomian tear fluid as a novel matrix to detect THC and its accompanying analytes.

This research focused on the detection and quantitation of THC, 11-Hydroxy- THC (11-OH-THC), and 11-nor-carboxy-THC (THCOOH) as these analytes are produced in the metabolism of Δ9-THC. Meibomian fluid maintains a high lipid concentration and Fatty Acid Binding Protein 5 (FAPB5), a protein known to bind to cannabinoids. Due to the lipophilic nature of THC, tear fluid could be used as a less-invasive biological matrix to test for the presence of THC and its metabolites.

Methods

Collection was completed by BVI Weck-Cel® Sterile Cellulose strips (Beaver-Visitec International, Waltham, Massachusetts, USA), measuring approximately 2 x 20 mm, and placed in Thompson eXtreme PVDF 0.2 µm, pre-slit, red cap, filter vials (Thomson Instrument Company Oceanside, California, USA) containing Quantisal buffer (Immunalysis Corporation Pomona, California, USA) solution. All analysis and calibrations were completed with fortified matrix standards with concentrations ranging from 0.25 - 250 ng/mL. Method validation was consistent with Academy Standards Board (ASB) Standards of Forensic Toxicology Standard 036, First Edition 2018.

Tear samples were collected from participants according to Institutional Review Board (IRB) standards before and after administration of Marijuana. Samples were collected approximately 30 minutes post. Samples and calibration standards were analyzed using Liquid Chromatography Tandem Mass Spectrometry (LC/MS-MS) with the QSight® 220 CR LC-MS/MS (PerkinElmer, Waltham, Massachusetts, USA) and using a Halo® C18 3.0x50 mm (2.7 µm) column.

Table 1: LC Method Conditions

Time (Min)	Rate (mL/Min)	A%	B%
0.00	0.80	70	30
0.50	0.80	70	30
5.00	0.80	10	90
8.51	0.80	70	30
10.50	0.80	70	30

Column Temperature: 40°C
Injection Volume (Full Loop): 20 µl
Mobile Phase A: 0.1% Formic Acid in Millipore Water
Mobile Phase B: 0.1 Formic Acid in Acetonitrile

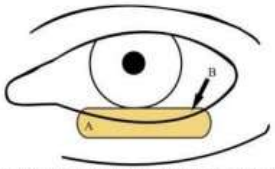
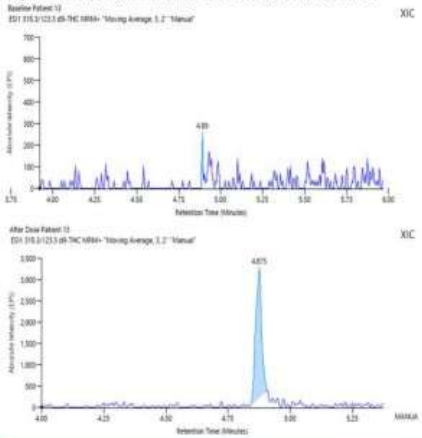


Figure 1. Tear Collection with BVI Weck-Cel® Cellulose strips: A) Cellulose strip covers a majority of the area of the lower eyelid for enhanced saturation B) Location of meibomian glands

Figure 2. Collection and use of filter vials: A) cellulose strip is placed into the bottom portion of the vial B) Top portion, with the filter, is introduced and compressed with the bottom portion C) Analyte collected in the cellulose is forced through the filter in the top portion as the cellulose is left in the bottom portion

Results

Figure 3 & 4: Baseline and After Dose Results from Patient 13



LOD & LOQ

Limit of Detection (LOD) and Limit of Quantitation (LOQ) for THC was calculated at 0.25 ng/mL. Limit of Detection of THCOOH was detected at 0.25 ng/mL and Limit of Quantitation was calculated at 1 ng/mL.

Patient Sample Evaluation

Patient 13 is the best indicator of ability to detect cannabinoid analytes. When evaluating the data of a Patient 13, it was noted that THC could be detected at a peak intensity of approximately 4,000 cps, a peak area of 5,513 counts, and a retention time of 4.875 minutes. These criteria were all indicative of the confirmed presence of THC due to peak intensity corresponding to specific MRM transitions and quantitative and qualitative ion ratios. Similar results occurred for other patient samples at lower concentrations

QSight® 220 CR LC-MS/MS

Conclusions & Future Directions

It was determined that THC and metabolites could be detected and quantitated in tear fluid. However, it is noted that insufficient sample volume in collection of this type of sample is an issue that leads to poor quantitation and should be optimized in future research.

Utilizing the current procedure, it would be of benefit to cultivate and optimize these methods into tools to aid in roadside DUID enforcement. The development of technologies to create roadside detection tools is a current topic in impairment assessment. Because of the issues that arise with current methods of detection, the use of tear fluid may be a simplified and non-invasive collection tool that could be of use in law enforcement agencies.

BOSTON UNIVERSITY

Utilizing Blood Molar Metabolites to Determine Recent Inhaled Cannabis Use

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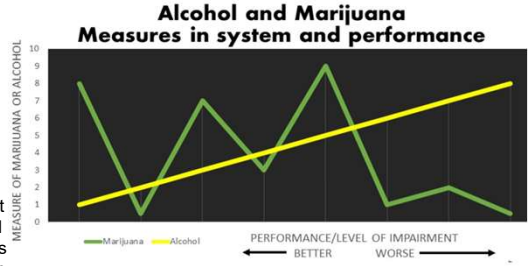
Cannabinoids: Not like alcohol

There is a linear relationship to the quantity of alcohol and impairment.

There is no such direct relationship with measures of cannabinoids in fluids and impairment. Many states use a THC concentration of 2-5 ng/mL to indicate impairment, similar to a BAC of .08. THC is a lipophilic molecule and can stay in blood and tissues for a far longer period than alcohol and thus THC concentration alone should not be used to measure impairment. Because THC's impairing effects can last for hours, determining when someone last consumed may be a better alternative to determine if someone is under the effect of cannabis than how much THC is in their system.



Cannabinoids: Biologics Include Tears

Measures of cannabinoids Urine, blood, saliva, breath, sweat and tears (1) have all been shown to identify cannabinoids in humans. Of these, urine and blood are the most frequently used roadside.

Urine is not useful as it is only an indication of use several hours or more prior to the time it is collected. It measures the inactive cannabinoid metabolites, Delta-9 Carboxy THC. Blood can demonstrate more recent use and can quantify the presence of the active Delta-9 THC as well as its active metabolite 11-Hydroxy Delta-9 in addition to inactive THC. THC has an affinity to the lipids of the body making the possibility of testing breath difficult. Saliva is less problematic, but still not as reliable if cannabis is consumed in edible form. Tears contain a lipid layer that would possibly be a means for detection of cannabinoids, but a practical means of retrieval has yet to be identified. We are fortunate that Northeastern Biomedical Engineering Capstone teams are working on this problem.

References and Conclusions

1. Mello A, Valenti DA, Foss J, Botch-Jones S. International Cannabis Research Society, 2021
2. Kosnett, M.. (2023). Blood cannabinoid molar metabolite ratios are superior to blood THC as an indicator of recent cannabis smoking.

THC is an impairing substance the same way alcohol is; however, THC stays in the body much longer than alcohol does and any measurement of THC concentration does not correlate to impairment. THC's psychoactive impairing effects start within minutes and can last for hours, Understanding when someone has last consumed can help better determine if they are impaired from THC. Blood molar metabolite ratios can be a better alternative to THC alone as a sign of recent cannabis use. While promising, tears are not yet practical as a measure of cannabinoids roadside.

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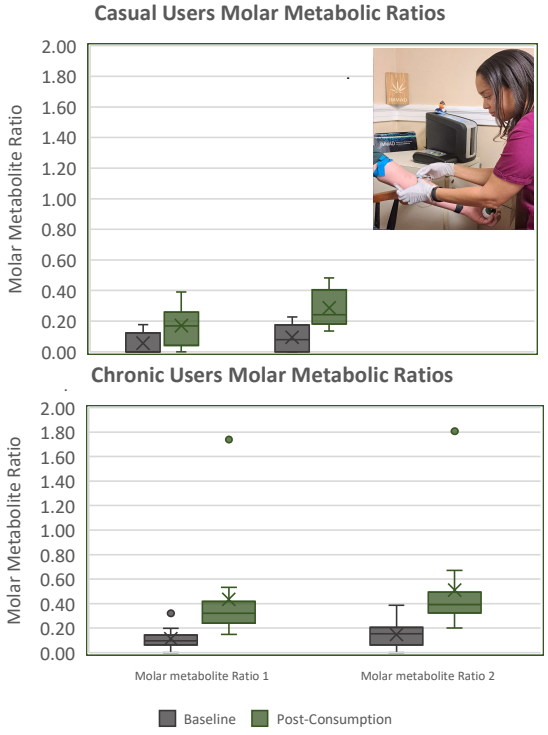
Funding: NIJ 15PNIJ-22-GG-04417-RESS

Blood Metabolites Show recent Cannabis Use

Blood Molar Metabolites are a more accurate form of measurement to determine recent cannabis use

(2). Because THC is a lipophilic molecule and can remain in the blood long after impairing effects have worn off, THC concentration alone cannot be used as an accurate indicator of recent cannabis use. Instead, The ratio of THC to its metabolites 11-Hydroxy-THC and 11-Nor-9-Carboxy-THC can be used to determine recent cannabis use. There are 2 Molar Metabolite Ratios, 1: $[THC]/[11-Carboxy-THC]$ and 2: $([THC]+[11-Hydroxy-THC]/[11-Carboxy-THC]$



Casual Cannabis Users Molar Metabolite Ratios.

Six casual cannabis user's whole blood samples were measured, ages ranging from 24-32 years old, the time since last smoking ranged from 30 min-40. All users started consuming cannabis before the age of 16. Casual cannabis users may show very little to no residual THC in their system and after consumption, blood THC levels rise to similar amounts to chronic users at baseline, while showing signs of impairment. The molar metabolite ratios increase to above the 0.18 and 0.27 cutoffs, showing that while THC concentration is still relatively low, there has been recent cannabis consumption.

Chronic Cannabis Users Molar Metabolite Ratios.

There were twelve chronic users aged 22-38 who have been smoking cannabis before the age of 16, All users were asked to consume cannabis before arrival, the time since inhalation ranged from 5 min-75 min. For chronic cannabis users, their THC blood levels may remain elevated even if not impaired, the blood molar metabolite ratios can help determine if someone's bloodwork shows they have recently smoked cannabis or not. At baseline, chronic cannabis users have a low molar metabolite ratio. After consumption, the molar metabolite ratio increases significantly to above 0.18 for molar metabolite ratio 1 and above 0.27 for molar metabolite ratio 2. These cutoff points are used to distinguish between recent (<75 min) and older use. All cannabis consumption was inhaled product only, no edible use data is used.

Neurobiological Effects of Cannabis on the Visual System and the Relation to Schizophrenia Expression

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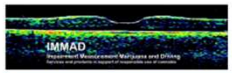

INTRODUCTION

This study seeks to enhance our understanding of the neuroprocessing mechanisms involved in schizophrenia and its development, specifically exploring the relationship with cannabinoids. The investigation involves direct measurements of retinal ganglion cell function in early initiators of cannabis use (before age 16) who are chronic cannabis users (defined as more than three days per week). In this study, a single case is used to examine the neuroprocessing intricacies of schizophrenia in relation to cannabinoids. Several studies report that the brain volume of the orbito- frontal cortex are reduced with early initiation of cannabis. Orbital frontal processes are related to lower spatial frequencies which are involved in the perception of facial expressions. The hypothesis guiding this study posited that retinal ganglion cell function could serve as a direct measure of amacrine ganglion retinal cell response.

MATERIALS and METHODS

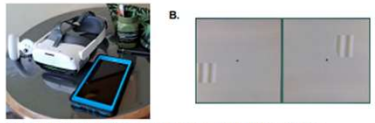

Figure 1. (A) Virtual reality goggle test of visual field functioning, programmed with IMMAD-VR, to determine impairment to drive. (B) IMMAD-VR displays small striped squares of variable contrast stripes. Participants press a button when they see the striped squares.

The study, conducted under an IRB-approved protocol, employs abstinent use confirmation through questionnaires, saliva, and blood measures. (n=1), the subject is a white male, age 37, started cannabis consumption at age 11, currently using 5-6 times a week, and has used every day in the previous month besides the last 24 hours leading up to the test. We used a molar metabolite ratio using the blood measures to additionally confirm there was no recent inhaled cannabis use; ([THC] + [11-Hydroxy-THC]) / [11-Carboxy-THC]. Measurement of retinal ganglion cells was conducted using Frequency Doubling Perimetry within a simplified visual reality Google system with eye-tracking capabilities (Fig. 1A). Frequency Doubling Technology (FDT) perimetry relies on flicker illusion generated through counterphase flickering of a low spatial frequency sinusoidal grating at a high temporal frequency (Fig. 1B). Testing lasts 4 minutes per eye. A literature review aimed to contextualize the study and the neurobiological factors linking cannabis use and the expression of schizophrenia, with a specific focus on visual system effects associated with the disorder.

RESULTS

Cannabinoid		Results (ng/mL)	Reporting limit (ng/mL)
11-Hydroxy Delta-9 THC	Active Metabolite	1.6	1
Delta-9 Carboxy THC	Inactive Metabolite	38	5
Delta-9 THC	Active THC	6.9	0.5

Table1. Blood metabolite levels collected when abstinent from cannabis for 24 hours. The subject uses enough that even if abstinent for 24 hours there are levels of active and inactive metabolite THC circulating.

Saliva test came back negative for THC. Blood measures show 1.6 ng/mL of the active metabolite 11-Hydroxy Delta-9 THC, 38 ng/mL of the inactive metabolite Delta-9 Carboxy THC, and 6.9 ng/mL of active THC Delta-9 THC (Table 1). This subject uses cannabis enough that even if abstinent for 24 hours, there are still active and inactive levels of THC circulating the blood. The molar metabolite ratio resulted in .24, confirming no recent inhaled cannabis use (results <2.7 indicate no recent inhaled cannabis use). The IMMAD-VR results (Fig. 2) show the left and right eye tests, expressing raw numbers which are percent contrast in decibels, and a dot chart expressing abnormalities. Each square is a section of the visual field measuring 5 degrees each square. Regarding the raw numbers, anything <40 is a deficit compared to normal, <35 is significantly abnormal, and <30 is severely abnormal. Regarding the dot chart, 1 dot is considered normal and the more dots, correlate to more abnormality.

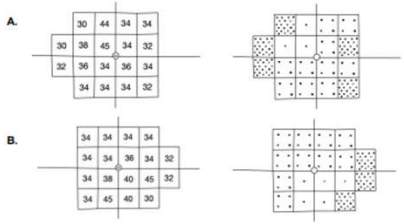

Figure 2. Results from IMMAD-VR, abstinent from cannabis for 24 hours. (A) Right eye, (B) Left eye. The raw numbers are percent contrast in decibels, anything below 40 is considered a deficit compared to normal. Regarding the dot charts, the more dots the more abnormal.

Acknowledgements

Research reported in this poster was supported fully by Research and Development in Forensic Sciences for Criminal Justice Purposes from the National Institute of Justice under grant number 15PNIJ-22-GG-04417-RESS.

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CONCLUSIONS

The findings indicate that a chronic cannabis user who started before the age of 16 even when abstinent has THC circulating the blood. IMMAD-VR results show deficits in retinal ganglion cell function even when abstinent for 24 hours. Early initiation of cannabis causes dysfunction in the perception of low spatial frequency signals and may result in poor perception of facial emotion. Accurate perception of low spatial frequency signals is necessary to interpret/see facial expressions. Schizophrenia also causes dysfunction in the perception of low spatial frequency signals, while also reducing perception of facial emotion. These findings suggest that cannabis impacts the same visual structures as schizophrenia and may contribute, though not necessarily cause, an earlier and more pronounced expression of the disorder. Further research is needed to determine if dysfunctions in the visual system neuroprocessing in cannabis are a biomarker or predictor of an expression of Schizophrenia later in young adulthood.

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IMMAD Studies Eye Movement

Colliculii influence eye movement.

Animal studies show death to colliculi with high potency.
DeSalu 2017 *wjpmr, 2017,3(6), 22-26*

Chronic long term human users have probable changes.

Eye microsaccades, tiny movement are common.

We Research Pupils and Wavelength

Rebound dilation is identified with prominent blue wavelength light in room and dim illumination.

Rebound dilation is identified with prominent red wavelength light in dim illumination.

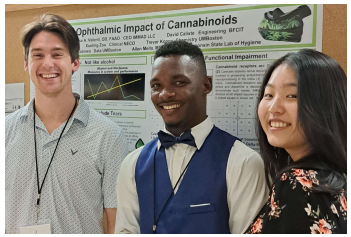
Green has no effect, does not illicit marijuana rebound finding.

White light, standard medical lights do not illicit rebound dilation finding.

We Study Eye Tears

Research Olfactory Changes With Marijuana Use

- Olfactory cells proliferate more and undergo less cell death.
- Olfactory cells can regrow.
- IMMAD data show marijuana increases ability to smell, but decreases ability to differentiate similar smells. Dopamine related.



IMMAD Team

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Founder
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Research expertise in cognitive dysfunction , visual systems and driving impairment.

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In honor: Deceased 1/18/2025

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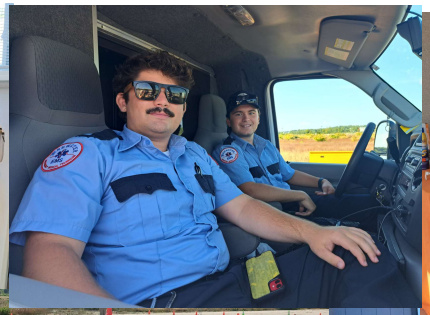
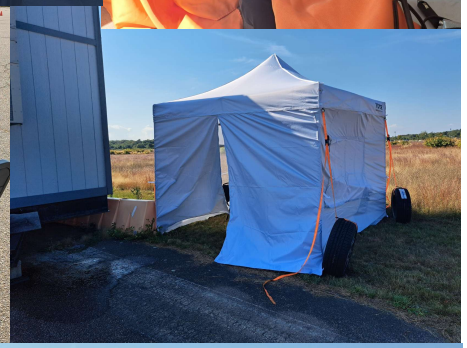
Optical technology patent specialist.

Real Car Closed Road



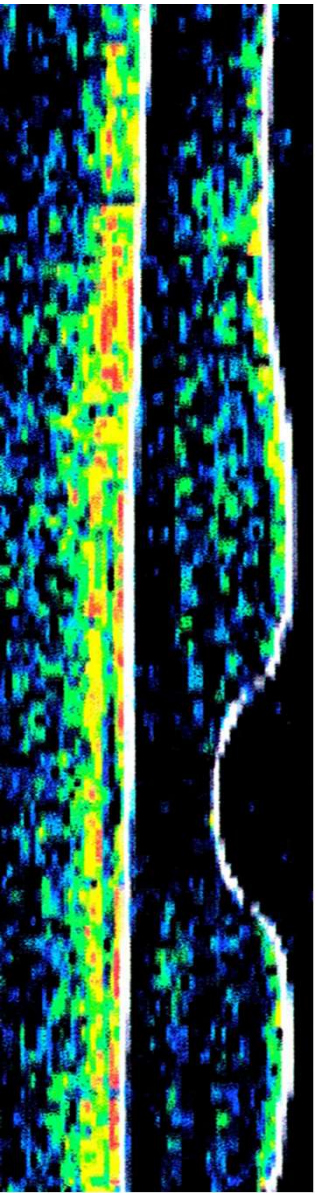










Colorado Uses Opportunistic Dosing Van Outside Homes



IMMAD

Impairment Measurement Marijuana and Driving

A social equity marijuana business certified in Massachusetts.

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