Marijuana: Retina Driving Impairment

Dr. Denise A. Valenti
Disclosures

- Dr. Valenti is owner of IMMAD, LLC - a company specializing in technology, education and services for the responsible use of marijuana.

- Technology, IMMAD-Impairment Measurement Marijuana and Driving is specific to the assessment of fitness to drive with acute use of marijuana.

- Currently receiving

- NIH NIDA SBIR Phase I contract funding
As required by the 2019 NACS Conference

I/we have signed a disclosure statement and note the following conflict/s of interest:

- Dr. Valenti is owner and chief scientist of IMMAD, LLC.
- We are currently receiving NIH NIDA SBIR funding.
Users report tunneling of vision with some products.

NHTSA reports tunneling of vision.

Never has been a study on peripheral vision and cannabis.
Marijuana – Tunnel Vision

- Even education campaigns discuss tunnel vision.
- http://eggsonweed.ca/
  Have a video on “tunnel” vision
Single Study on Humans and Peripheral Vision

- Measured the 180 degree meridian only.
- With peripheral testing only, found no reductions related to alcohol.
- Found significant reductions related to marijuana.
- Used blinking lights at 6 degree intervals.


Figure 1 The design of the study by Moskowitz & Sharma (1976).
Cannabinoid Receptors Numerous In Human Retina

A. Straiker A. Proc Natl Acad Sci. 1999 Dec 7;96(25):14565-70
Studies have shown that cannabis may improve night vision. This was demonstrated with populations of fishermen in Jamaica and Morocco.


Merzouki A; J Ethnopharmacol. 2002 Aug;81(3):403-6
Testing Vision In Periphery


- Second study tested the population further.

- Testing was double blind graduated dose of 0-20mg in the form of Marinol with placebo.

- Used portable device, the LKC Technologies Scotopic Sensitivity Tester-1 (SST-1) which has 1 Hz flicker target. Russo EB, J Ethnopharmacol. 2004 Jul;93(1):99-104

- See or not see dot of flickering light.
Found the tadpole could see better in extremely low light, when cannabinoid receptors were stimulated.

https://elifesciences.org/content/5/e15932
Tadpoles Swam To Light
Marijuana Prenatal Peripheral Motion

- Tested 145 children ages 4 and 5.
- Global motion perception improved with those having prenatal exposure to marijuana.
- Global motion perception decreased with alcohol.

However, an increase may be at the expense of other functions.

Generally, in the dark the central vision is suppressed and thus extreme periphery is improved.

Night vision, cones suppressed rods enhanced.

An example of impact on function is vision changes in dark theatre. Takes a few seconds to adapt when go outdoors.

During full daylight may work to be more “aware” of extreme periphery, learn to ignore central. Ball sports are examples.

The reverse are shooting sports and golf.

If marijuana exposed child is more sensitive to peripheral may be unable to suppress normally and thus may be inattentive in school or easily distracted.
CB2 is localized in cone and rod photoreceptors, horizontal cells, some amacrine cells, and bipolar and ganglion cells.

In dark a waves slower in mice genetically engineered not to have CB2, but in those absent CB1 there was no change.

Under photopic conditions, b-wave in CB2 absent mice required more light adaptation. No effects were observed in CB1 absent. This explains much longer glare recovery.

CB1 and CB2 receptors could have different roles in visual processing.
Mice exposed prenatally to marijuana have thinner retinas, with inner retina showing greatest reduction.
Based out of UC Berkeley

Did a series of human studies specific to marijuana.

Rare for then and now, they were double blind and placebo controlled.

Used NIH marijuana.

Extensive set of research on visual functions.

Am J Ophthalmol. 1977 Mar;83(3):350-4
Psychopharmacology (Berl). 1978 Jan 31;56(1):81-6
The time to recover normal retinal function after a bright light exposure is significantly longer with the consumption of cannabis.

Adams A: Psychopharmacology, 56, 81-86, 1978
Glare Recovery

- Doses for marijuana were 8 or 15 mg.
- The impairment with marijuana was dose related.
- Dysfunction lasted about two hours.
Adams et al; Marijuana Eye-tracking

- Found dysfunction with alcohol.
- No dysfunction with marijuana or placebo.
- Tested central 7.5 degrees.
- Gradually went from .5 to 3 Hz in 40 seconds.
Reduced Function With Marijuana in Dynamic Acuity

- No dysfunction when acuity testing was static.
- Reductions occurred with 12% contrast and with 49% contrast using dynamic acuity, motion contrast target.
- Dysfunction in dynamic acuity occurred with two different doses of marijuana, 8 mg and 15 mg.
Marijuana Impairs Retinal Ganglion Cell (RGC) Function

Chronic, but abstinent use
Reported Fall 2016 in the Journal of the American Medical Association

Schwitzer T: JAMA Ophthalmol. 2017 Jan 1; 135(1):54-60
Cannabis Acute Use Changes Retinal Response
Chronic Abstinent Users
Changes In Retinal Response

From: Association Between Regular Cannabis Use and Ganglion Cell Dysfunction


Figure Legend:
Dot Plot of Pattern Electroretinography N95 Implicit Time for Cannabis Users and Controls
For controls: n = 24; median implicit time, 88.4 milliseconds (95% CI, 85.0-91.1). For cannabis users: n = 28; median implicit time: 98.6 milliseconds (95% CI, 93.4-99.5). Median of the differences between the 2 groups: 8.4 milliseconds (95% CI, 4.9-11.5; P < .001, Mann-Whitney test). The black horizontal lines indicate medians.
Early Onset Chronic Use Abstinent Contrast Function

- Early onset use defined as those having started use of marijuana/cannabis prior to age sixteen.
- Dysfunction in contrast sensitivity at low spatial frequencies in both static and dynamic 8 Hz.  
  Eur Neuropsychopharmacol. 2017 Dec;27(12):1289-1297

- Low Frequency Left
- High Frequency Right
Reduced Motion Perception In Chronic Abstinent

- Stimulus contrast was under 16% for a moving target.
- Chronic users deficit even when abstinent.
- Using ERG there was reduced response to coherent motion, incoherent motion, and static.

Mikulskaya E1,2, Martin F1

Skosnik PD1, Krishnan GP
Retinal Cell Specific

- There is delayed ganglion and bipolar cell responses in cannabis users.

- There is a delay in the transmission of visual information from the retina to the brain.

This retinal dysfunction likely an effect of cannabis use on retinal synaptic transmission.

https://www.flickr.com/photos/nihgov/38267283871

J Psychiatr Res. 2018 Aug;103:75-82
IMMAD Midperipheral Test of RGC Function

Test midperiphery 40 degrees.

Table top uses sixteen ten degree targets and a single central five degree target.
FDT Is Table Top Version
Used To Demonstrate Efficacy

The stripes appear in various locations, with each presentation having less less contrast.

If a person is impaired due to marijuana, they can not see the lower contrast targets.
Test one eye at a time.

Chronic users have more unreliable tests, even when abstinent.
White is normal. The darker the grey within the squares, the worse the vision. The tests middle and right were with casual (not chronic) users having consumed marijuana twenty minutes earlier.
IMMAD In Casual User Shows Tunneling Vision

Visual Function Absent

Normal Vision
Portland, Oregon  April 13, 2018
Squad car hit after other vehicle ran red light.
Driver in other vehicle impaired by marijuana.
Officer suffered injuries.
A driver having tested positive for marijuana alone, no other drugs or alcohol is six times more likely to kill someone other than themselves compared to a driver positive for alcohol alone.

Marijuana positive drivers more likely to kill a pedestrian, bicyclists, passenger or other driver.
Aggregate Averaged Data Both Eyes
While the study did not identify a direct relationship, found an increase in pedestrian deaths in those states with legal adult use of marijuana.

https://www.ghsa.org/resources/spotlight-pedestrians18

Photos
Ronaldo Oliveira
The primate lateral geniculate nucleus has cannabinoid receptors throughout.

The functional layers are stained to show CB1 receptors

Yellow, Red and Blue all CB1

Javadi P: Neuroscience. 2015 Mar 12;288:135-44
Cannabis Excitation/Inhibition CB1

- LGN has two populations of CB1 cells
  - 28% are excited
  - 72% are inhibited

3/4 of cells NOT Functional?

Cannabinoids: THC and CBD

Red indicates more activity and blue less, yellow is similar. Placebo, THC, CBD were compared to normal controls.
Temporal target, instead of alternating stripes used checkerboard.
Early Onset Use in Chronic Users Brain Activation

- There is greater connectivity between the front of brain and the primary visual area.
- The magnitude of this connectivity was positively associated with age of onset and lifetime use.
- Changes may have a compensatory role in mitigating cannabis-related impairments in cognitive control or perceptual processes.

Harding IH, Solowij N, Neuropsychopharmacology. 2012 Jul;37(8):1923-33
Similarly, decreased activation was observed in the dorsolateral prefrontal cortex, which co-activated with orbitofrontal and occipital areas and linked with attention-related processes.

Early Onset before age 15

- fMRI reductions in visual association area with early onset use.

- Early sign of Alzheimer’s are reduction function in visual association area using fMRI.

Tervo-Clemmens B, Simmonds D
Biol Psychiatry Cogn Neurosci Neuroimaging
Cannabis, Cognition and Driving Issues

Lane deviation is a frequent error with cannabis.

Alzheimer’s disease impairs driving.

Lane deviation is a prominent error with Alzheimer’s disease.
Cannabis Lack of Awareness of Impairment

- Ten experienced licensed private pilots trained on a flight stimulator landing task
- Each smoked a cannabis cigarette (19 mg)
- 24 hours later performance on the flight task showed trends toward impairment in all variables, some tasks showed significant impairment

**Despite the deficits, the pilots reported no awareness of impaired performance at 24 hours**

24 Hours Later
Dysfunction To Land A Plane

Mean distance off centre on landing (feet)

<table>
<thead>
<tr>
<th>Hours after smoking 19 mg THC</th>
<th>Distance (feet)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>30</td>
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<tr>
<td>4</td>
<td>30</td>
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More Research Needed
CBD has been shown to spike the pressure of the eye

- In human studies  

- And animal studies  
Thank you
IMMAD, LLC
deniseavalenti@gmail.com