

Identification of Δ^9 -tetrahydrocannabinol (THC) impairment using resting-state neuroimaging

Michael Pascale, Nisan Ozana, Kevin Potter, Brian Kendzior, Gladys N. Pachas, A. Eden Evins, Jodi M. Gilman

Center for Addiction Medicine, Department of Psychiatry, Massachusetts General Hospital; Harvard Medical School



Abstract

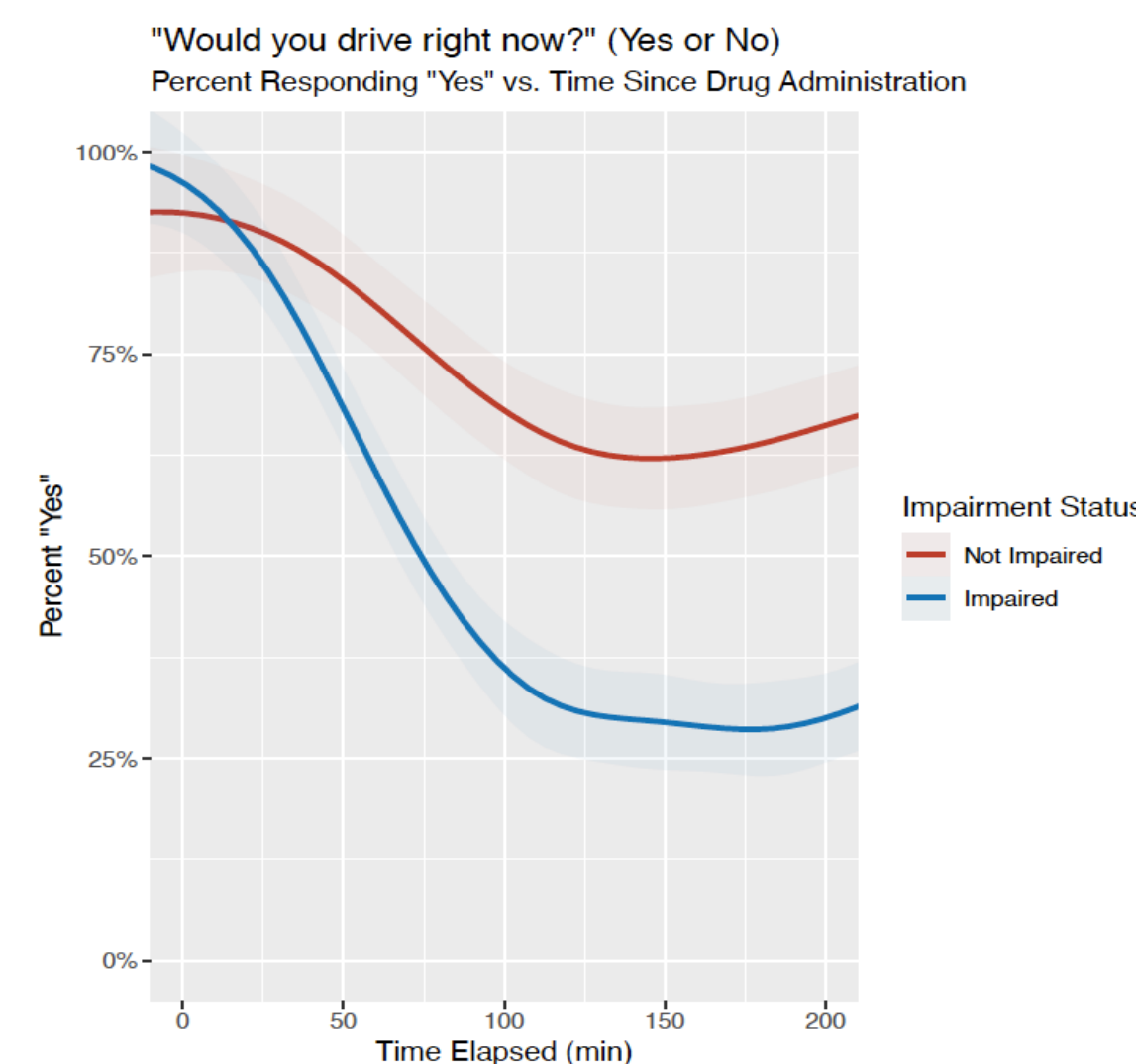
There are no evidence-based methods to detect cannabis impairment, relevant to road and workplace safety. Field sobriety tests are prone to bias. We evaluated whether prefrontal cortical resting-state connectivity (RSC), assessed with portable functional near infrared spectroscopy (fNIRS), could classify individuals with THC impairment. RSC pre and post placebo or THC identified clusters of decreased connectivity in THC impaired participants that informed a machine learning impairment classifier.

ClinicalTrials.gov Identifier: NCT03655717

Methods

- 169 participants with regular cannabis use were given a single dose of up to 80mg of dronabinol (an FDA-approved synthetic THC ingredient in MARINOL® Capsules) or identical placebo.
- Participants completed the Drug Effects Questionnaire (DEQ), a 100mm visual analogue scale, pre-dose and every 20-25 minutes post-dose to assess the extent to which participants (1) felt any THC effect(s), and (2) felt high.
- Heart rate and blood pressure measurements were collected at baseline and at 25-minute intervals after dronabinol administration.
- Participants underwent two fNIRS sessions; one before dronabinol administration ("pre-THC"), and the other at approximately two hours after dronabinol administration ("post-THC"), which is the median peak of pharmacokinetic effects for dronabinol.
- During each session, 6 minutes of resting-state functional data were collected using a continuous-wave NIRS device, in which 8 sources and 7 detectors were placed on the forehead, resulting in 20 channels covering PFC regions.
- Impairment was operationalized as convergent classification by consensus clinical ratings and an algorithm based on post-dose tachycardia and self-rated "high". This was compared with results of extended field sobriety tests, which were performed by certified Drug Recognition Expert (DRE) police officers after THC or placebo.

More than 25% of clearly impaired subjects continued to say that they would drive, suggesting either that they were not aware of their impairment or that the dangers given their impairment were not great.



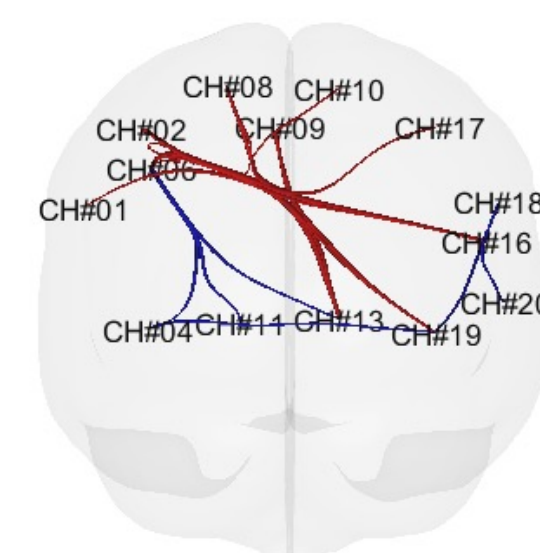
Results

Participant Characteristics

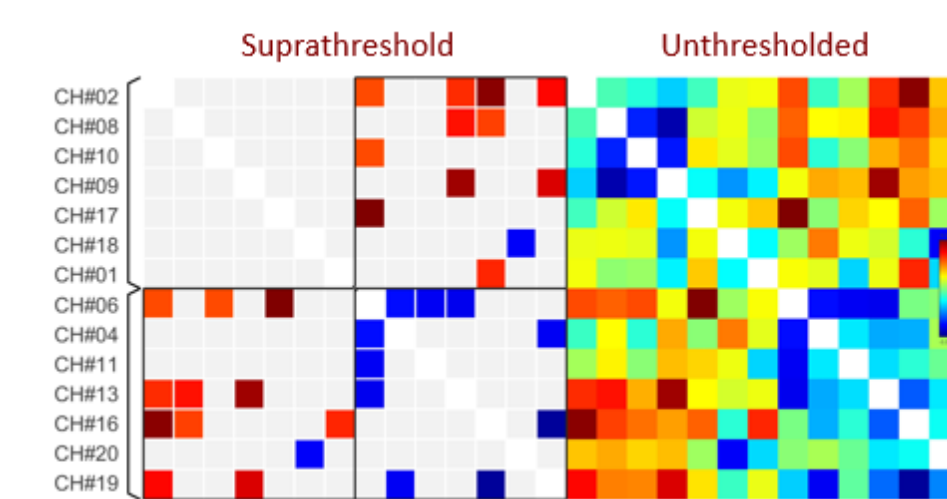
Variables	Overall	Impaired post active study drug (THC)	Not clearly impaired post active study drug (THC)	Discordant/ No valid scans
Sample size	169	80	57	32
Demographics				
Age	25.2 (6.4)	24.4 (5.3)	26.3 (7.5)	25.4 (6.6)
Sex: % Male (n)	50.9% (86)	57.5% (46)	47.4% (27)	40.6% (13)
Race				
% White (n)	67.5% (114)	68.8% (55)	70.2% (40)	59.4% (19)
% Black (n)	11.2% (19)	5% (4)	14% (8)	21.9% (7)
% Asian (n)	6.5% (11)	10% (8)	3.5% (2)	3.1% (1)
% Multi-racial (n)	7.7% (13)	10% (8)	5.3% (3)	6.2% (2)
% Other (n)	7.1% (12)	6.2% (5)	7% (4)	9.4% (3)
Ethnicity: % Hispanic (n)	20.1% (34)	25% (20)	17.5% (10)	12.5% (4)
Years of education completed	15.3 (2.1)	15.4 (2.2)	15.3 (2.1)	15 (1.8)
Cannabis use characteristics				
Age began regular use ¹	19 (3.9)	18.6 (3.6)	19.7 (4.6)	18.8 (3.6)
Weekly users: % Yes (n)	42% (71)	48.8% (39)	38.6% (22)	31.2% (10)
Daily users: % Yes (n)	56.2% (95)	51.2% (41)	56.1% (32)	68.8% (22)
Used multiple times per day: % Yes (n)	45% (76)	36.2% (29)	56.1% (32)	46.9% (15)
Urine THC-COOH (ng/mL)	221.8 (473.2)	98.1 (147.5)	456.2 (795.3)	163 (136.1)
CUDIT score	12 (5.3)	11.6 (5.2)	12.4 (5.2)	12.4 (5.7)
Psychiatric characteristics				
STAI - State (Baseline)	31.9 (6)	31.2 (5.1)	32.2 (6.2)	33 (7.7)
Lifetime depression				
% Diagnosed (n)	17.2% (29)	12.5% (10)	17.5% (10)	28.1% (9)
Lifetime anxiety				
% Diagnosed (n)	18.9% (32)	15% (12)	22.8% (13)	21.9% (7)

Comparing resting-state connectivity of post-dose THC and post-dose placebo in impaired participants, we identified two clusters of decreased connectivity after THC. The groups are matched on placebo, indicating that we are measuring a state-level, not trait-level, effect.

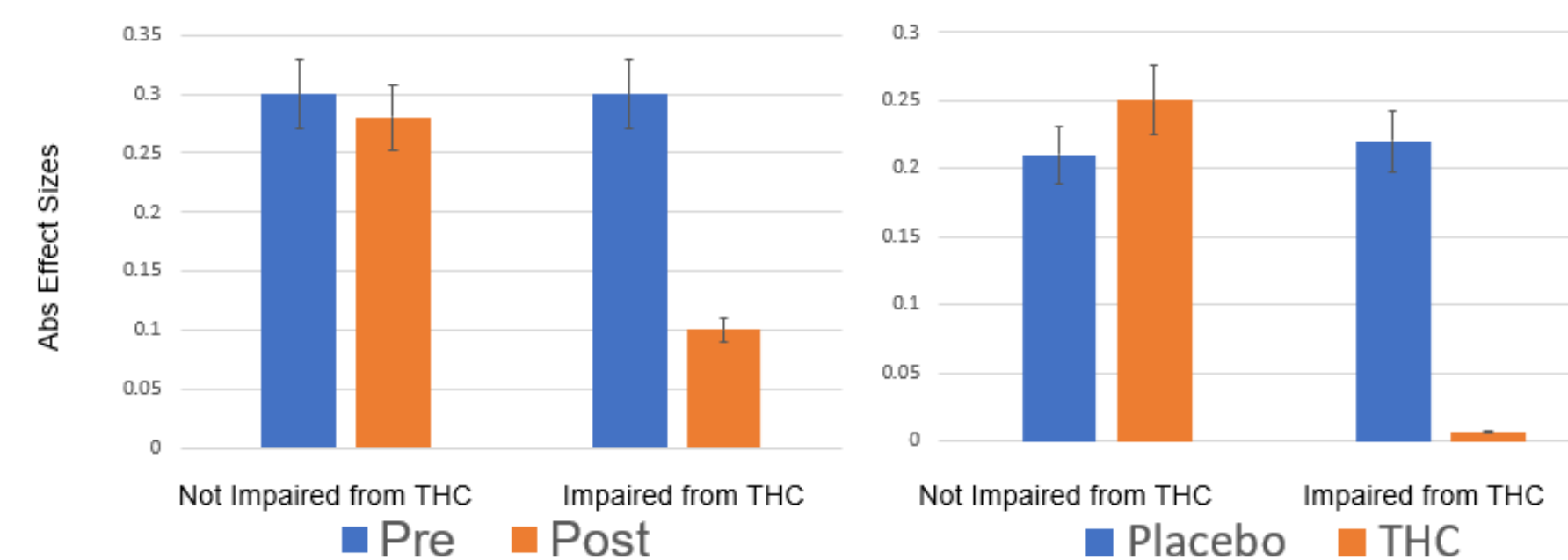
A. Schematic of the near-infrared spectroscopy (NIRS) probe array clusters



B. ROI-to-ROI connectivity

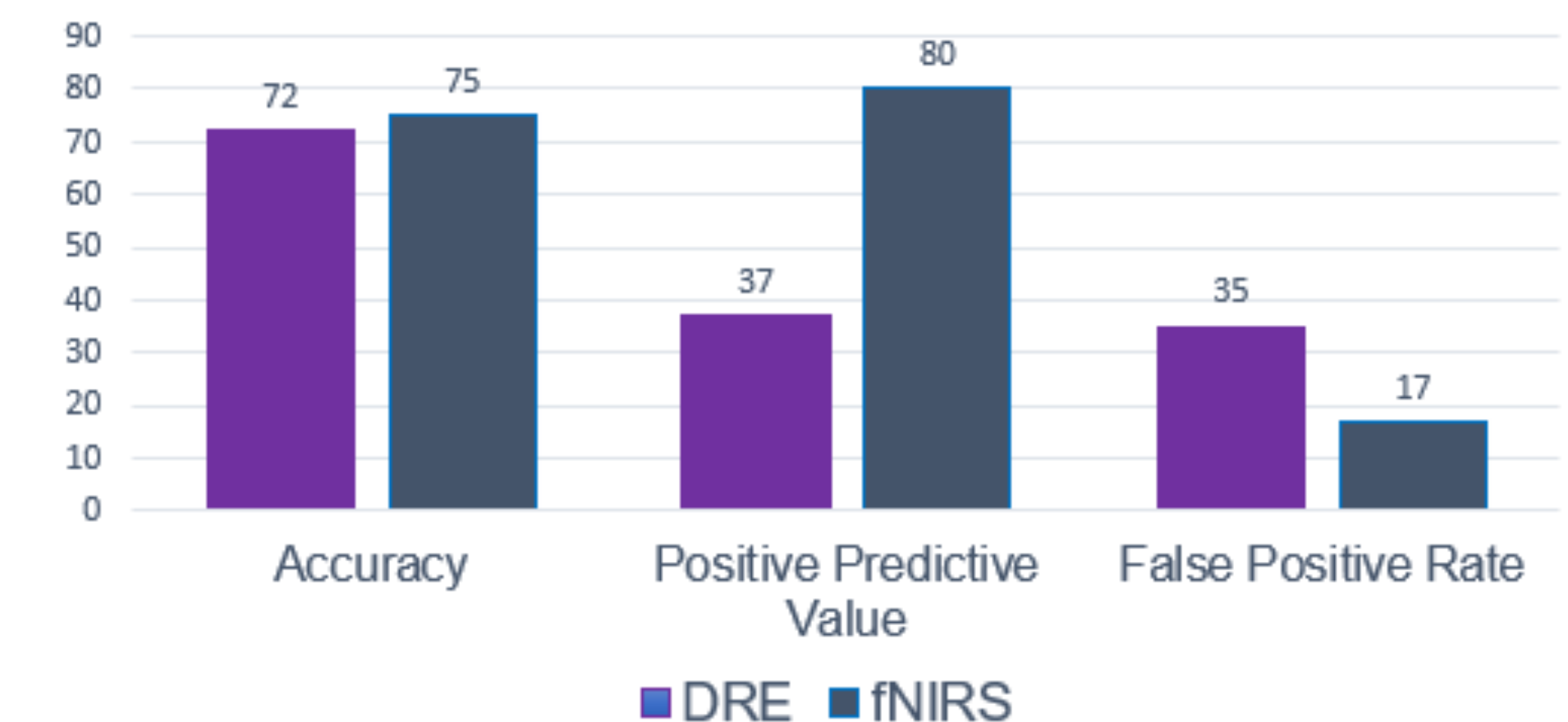


C. Resting State Connectivity of Pre-dose with respect to Post-dose THC and Pre-dose THC with respect to Post-dose Placebo in Impaired Participants



Results

Using only resting-state fNIRS data, a recurrent neural network (RNN) machine learning model predicted individual impairment with greater accuracy and lower FPR than Field Sobriety Tests.



This method exceeded expanded field sobriety examinations conducted by Drug Recognition Experts (67.8% accuracy, 35.4% PPV, and 35.4% FPR).

Conclusions

- There is a growing public health need for an objective, reliable, unbiased method to detect impairment due to THC.
- This is not achievable solely with blood or body fluid THC or metabolite concentrations.
- Impairment due to THC intoxication was associated with reduced PFC connectivity suggesting the PFC response can be applied to determine who is impaired.
- The PFC response alone classified participants as impaired or exposed but not clearly impaired with high PPV and accuracy.
- Future work is warranted to determine if these observations are specific to impairment with THC or are more general signatures of impairment.

For more information

Contact Jodi Gilman (jgilman1@mgh.harvard.edu)