CROSSROADS
TREATMENT CENTER

OVERVIEW OF CROSSROADS TREATMENT CENTER, CURRENT RESEARCH & UCSD FMRI STUDY

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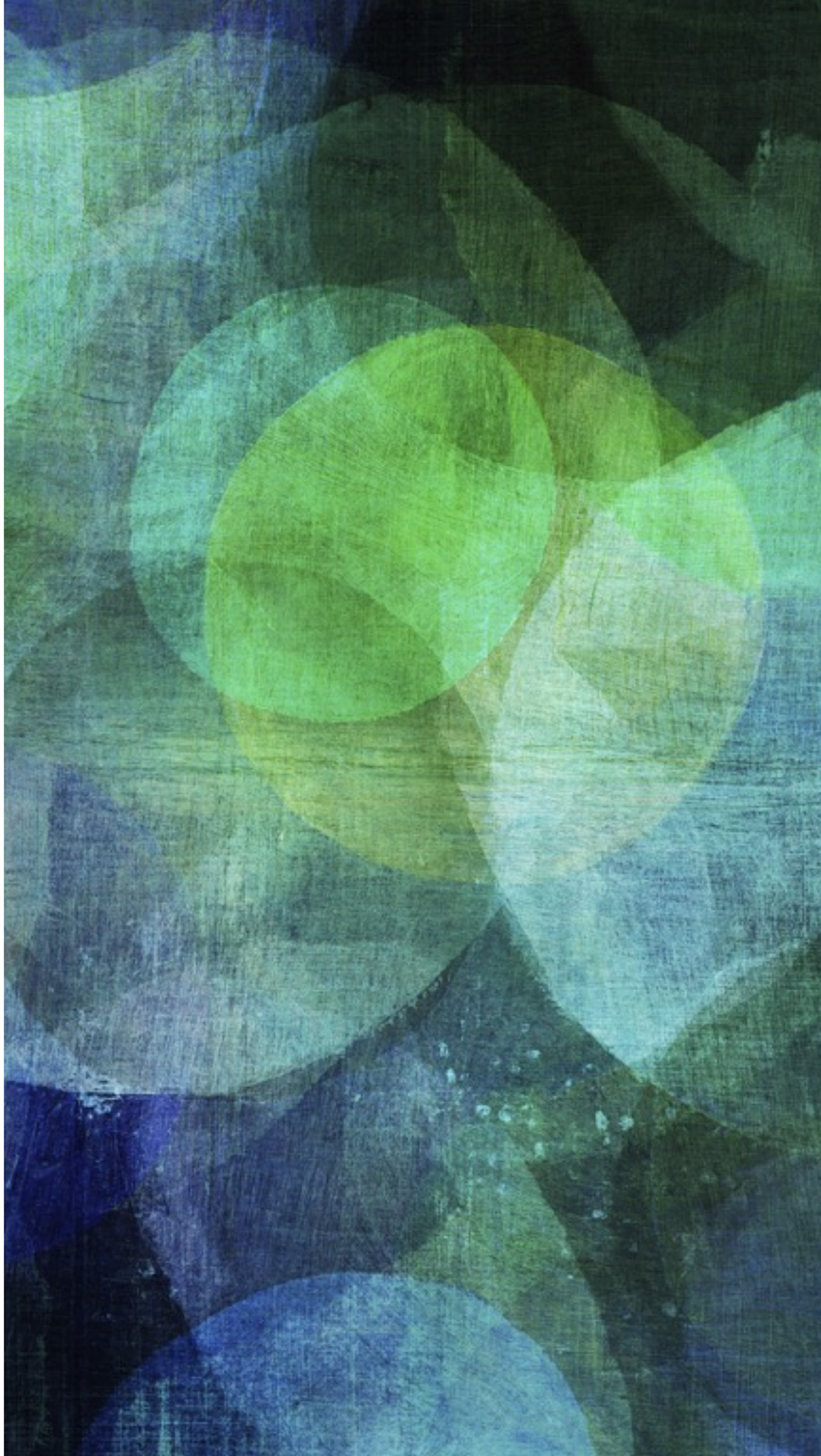


OUTLINE

Background

Ibogaine & 5-MeO-DMT Overview

Overview of Crossroads Program

Outcome Findings

SPECT Results

Areas for future direction

Bryson & Tapert fMRI draft design

POLITICAL / RESEARCH BACKGROUND

- Increase in Opioid Epidemic
  - Rx opioid sales & overdose deaths up 400% last 10 years
  - Prevalence 2-3x greater in veterans
- Vermont & New York this year had bills under review to open Ibogaine clinics, did not pass in Vermont.
- Numerous Ibogaine clinics internationally
- Host of preclinical studies, several observational studies
- Mid-nineties NIDA funded/ FDA granted Deborah Mash Phase I study. Dose escalation studies halted at University Miami due to insufficient funds, death in one patient.
- Interest heightened w/ MAPS and Hefter interested in hosting
- Sao Paulo, state in Brazil and New Zealand have approved use of ibogaine in research and controlled clinical settings
- No prior neuroimaging studies due to Schedule I status

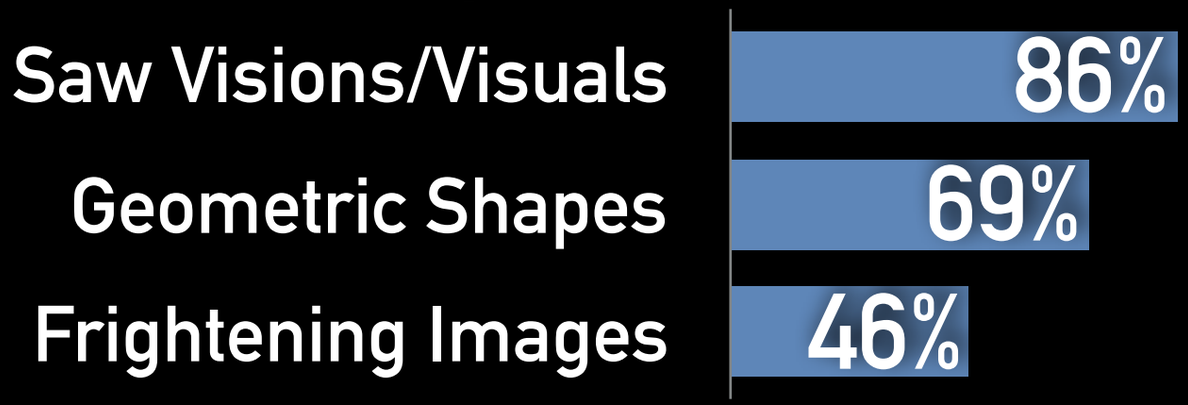
METHADONE VS IBOGAINE

● TRUE
◐ PARTIALLY TRUE
○ FALSE

	Methadone	Ibogaine
Targets multiple addictions	○	●
Full results in one dose/session	○	●
Alleviates anhedonia [1]	◐	●
Decreases craving	◐	●
Alleviates withdrawal	◐	●
All natural	○	●
Alleviates anxiety	○	●
Elevates Mood	○	●
No ongoing cost	○	●
No long term commitment	○	●
No potential for abuse [2]	○	●
Minimal life disruption	○	●
Covered by health insurance [3]	◐	○

DURING IBOGAINE

Visual Experience



Physical Experience

Psychospiritual Experience

% AGREED YES

SUMMARY OUTCOME STUDY

- Vast majority found Ibogaine effective (80%), better than other treatments (86%), and would have made same decision to take Ibogaine (86%).
- ~30% never returned to using, 50% reduced use if did relapse, remainder ineffective (~20%)
- In those > 1 year post treatment:

  74% of Rx opioid users and 38% of heroin users had not used any opioids in the past 6 months.
- Argues for need to make this treatment accessible
- Large percentage of those who returned to using, returned immediately which speaks to need for continuing care

SUMMARY OUTCOME STUDY

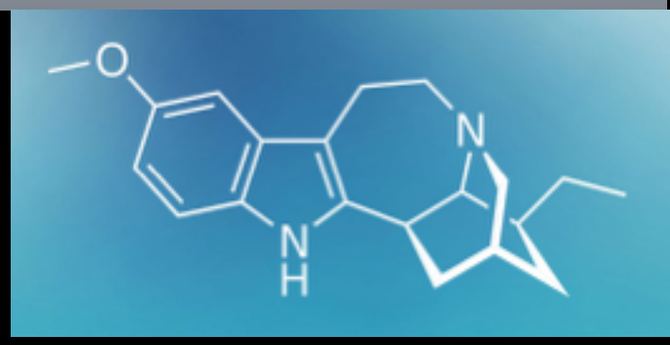
> 2/3 of sample experienced visions, gained self insight, had spiritual experience

30% said was one of the most, or the single most spiritually meaningful event in entire life

Duration of mood improvement and craving reduction vary widely:
1/3 sample - no benefit or <1 week; 1/3 sample 1-8 weeks
1/3 ≥ 3 months

Thus, lower expectations about experience during and argues for need to investigate physiological process reasons for the variability (genetics/metabolism/dosage factors)

IBOGAINE PHARMACOLOGY



Using 99.5% Ibogaine from Voacanga africana

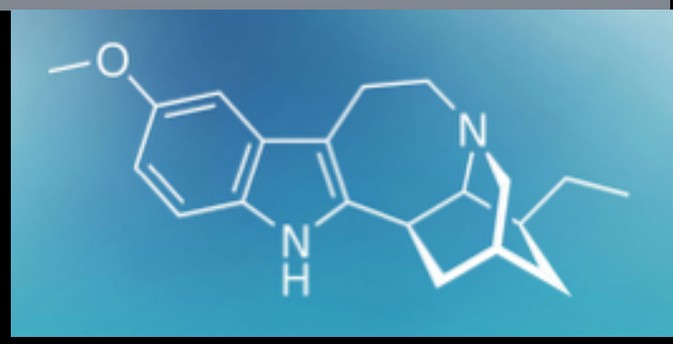
Attenuates withdrawal to opioids & effective for interrupting addiction to alcohol, stimulants, & has anti-depressant, anxiolytic effects, promise as PTSD treatment, has anti-viral and anti-fungal properties

Induces a waking dream state, REM-like followed by period of increased insight lasting 24-72 hours.

Highly lipophilic, half life 4-7 hours, 90% eliminate 24 hrs
Noribogaine (metabolite) half life 28-50 hours, “Ibo-glow” ~2-3 weeks

Side effects of nausea, ataxia, tinnitus, visual tracers

IBOGAINE PHARMACOLOGY



Broad spectrum effect

Dr. Ken Alper - “We don’t know.” Ibogaine is a case study in pharm

- NMDA antagonist
- Nicotinic acetylcholine antagonist - anticholinergic
- Affinity kappa /mu opioid, sigma2 agonist (toxicity), sodium channels
- Inhibits serotonin reuptake transporter
- 5HT2a and 5HT3 agonist
- Muscarinic acetylcholine agonist
- Increases GDNF in the VTA - regenerative properties
- Polymorphism in the CYP2D6 enzyme can influence blood concentrations of both ibogaine

5-MEO-DMT "GOD MOLECULE"

- Potent Tryptamine
- 4x stronger per weight than N,N DMT
- Present 10-15% weight in secretion of the Sonoran Desert Toad
- Vaporized and inhaled, experience last 15-60 minutes
- Present in Ayahuasca, Yopo snuffs used in Amazonian Shamanism
- 5HT1A, 2A Agonist, similar pathways as psilocybin, far more potent
- Not scheduled in U.S. until 2011
- Observe powerful cathartic emotional releases, transcendental and mystical experiences, yogic poses, orgasmic behavior
- Coding 500 testimonials and cataloging video of sessions

5-MEO-DMT PATIENT

“Oh My!!!! Best experience of my life. It really put the Love, joy, freedom, bliss, and lust for life in me that I haven't felt in 20 years. Icing on the cake for me after the ibogaine because the ibogaine "beat me up" and really put me in my place and showed me what i was doing wrong all these years. then the 5 MEO DMT put that love right back in me.”

“No words can describe how much positivity I have for this experience. Of everything that happened while I was there [in treatment], the 15 minute session I had with this has changed my life.”

5-MEO-DMT EXPERIENCE

States of Consciousness Questionnaire (n = 18)

100-items re: mystical experiences; >2/3 individuals

88% Experience of overflowing energy.
81% Feelings of peace and tranquility.
75% Loss of your usual sense of time.
75% Sense of awe or awesomeness.
75% Feelings of joy.
79% Experience of amazement.
73% Freedom from the limitation of your personal self and feeling a unity or bond with what was greater than your personal self.
69% Feeling of emotional closeness with your guide or assistant guide.
69% Feeling that you experienced something profoundly sacred and holy
68% Sense that the experience cannot be described adequately in words.
68% Feeling that consciousness during the session was more real than your normal awareness of everyday reality.
65% Feelings that you experienced eternity or infinity.
65% Loss of your usual sense of space.

Rating scale 1 to 5.
slight to extreme

% rated strong or extreme ≥ 65 %

CROSSROADS OVERVIEW

CLINICAL OFFERINGS

1 week Ibogaine Detox for Addiction

Pre-treatment EKG, CMP, Drug testing
Ibogaine flood dosages 15-20 mg/kg
5-MeO-DMT from Bufo 50mg Vaporized
Post flood boosters PRN
Recovery Coaching + Aftercare w/ Practical Recovery in SD

3 days psychospiritual program

Ibogaine 10-13 mg/kg + 5-MeO-DMT Bufo

5-MeO-DMT only program starting in two months, 1 day in TJ

CROSSROADS OVERVIEW

- Crossroads was tapped as potential clinic trials site
  - Crossroads supported w/ connections at MAPS & donors from Heffter
- Most developed research data collection of any clinic
  - Past year collected observational data on 100 patients
  - Have baseline addiction assessment on >100 patients
  - Pilot data on two vets w/ PTSD on SPECT imaging
  - Starting Veteran Program
  - Have plans to build out hospital to be psychedelic research center

CROSSROADS
TREATMENT CENTER

6 beds, building out clinic
Across street from Angeles Hospital in Tijuana
Live Cardiac Monitoring
IV line in all patients
1-2 physicians, 1-2 nurses present at all times
Emergency Cardiac Equipment, Defibrillator

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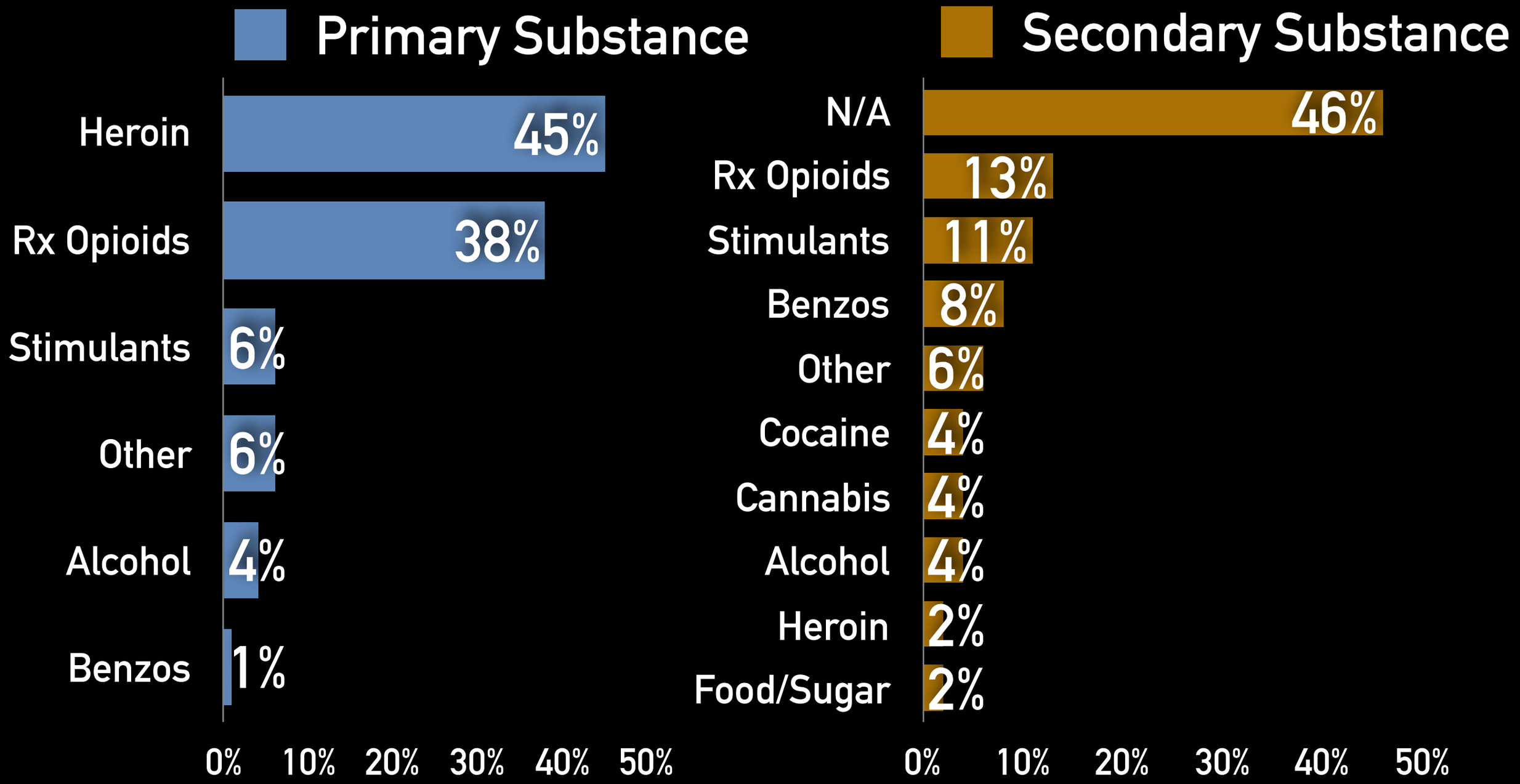
SUBSTANCE USE DEMOGRAPHICS



SUMMARY OF SPECT PROTOCOL

TWO VETERANS SCANNED 2 days PRE, and one vet 3 days post, second 5 days post. Both received Ibo + 5-MeO

AMEN CLINIC SPECT:

All SPECT scans were performed using a high resolution Picker (Philips) Prism XP 3000 triple- headed gamma camera

Approximately 30 minutes after the injection with Technetium, subjects were scanned.

Data was acquired in 128x128 matrices, yielding 120 images per scan with each image separated by three degrees spanning 360 degrees.

62 ROI's from AAL atlas in SPM, assessed for cerebral blood flow, compared to age-matched normative samples.

SUBJECT 1 – MR. P

<u>Clinical background:</u>

31 year old male mixed ethnicity Air Force veteran

Alcohol use disorder, moderate, 2 liters of hard cider per night (4-5% alcohol) for past year

PTSD (childhood physical/emotional abuse and military vet-on-vet) for 5+ years duration

included nightmares, dissociative fits of rage, social isolation, PTSD interpersonal in nature - easily triggered to anger, 100% service connected at the VA.

compulsive sexual behavior to regulate dysphoria

felt compulsive with work, neglecting nutrition

Dx ADD as child, likely due to abuse grew out of symptoms

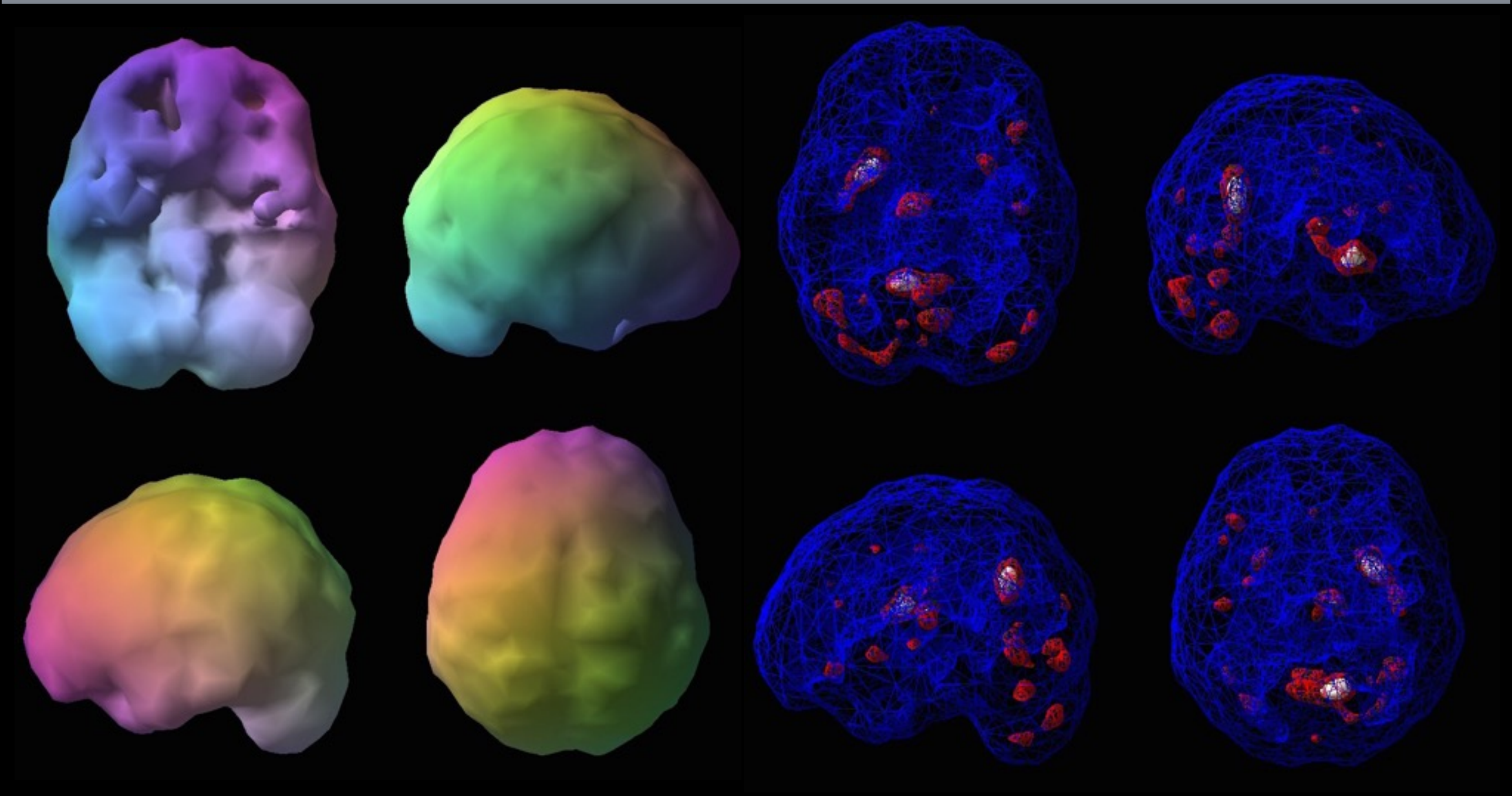
History of excessive fights and binge drinking in college.

No major medical issues

BDI = 18 Mild range, PCL = 30, 33 cutoff clusters D/E mood/arousal

Sought Crossroads to quit drinking and for PTSD/ isolation

MR. P – BEFORE IBO



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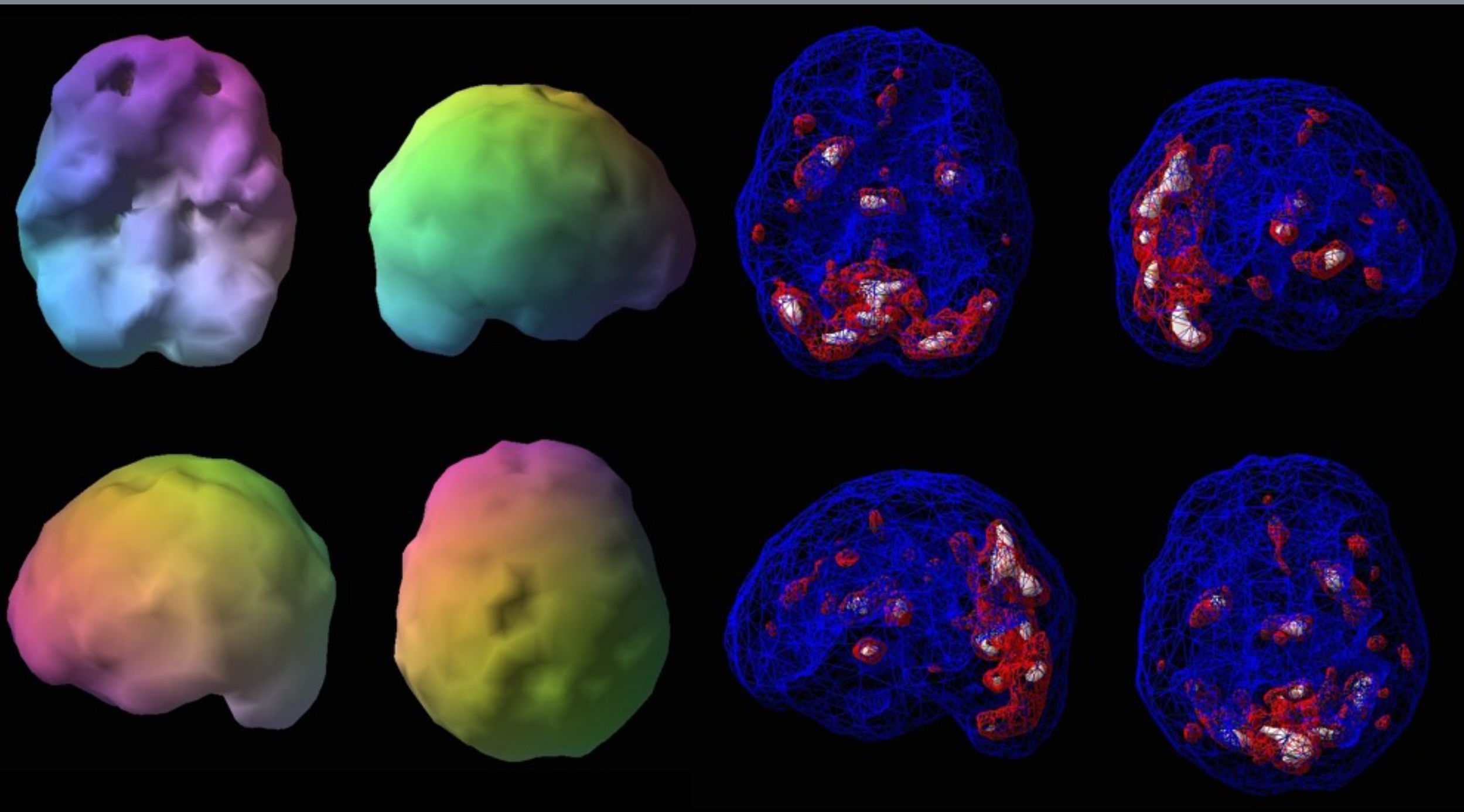
MR. P – POST IBO



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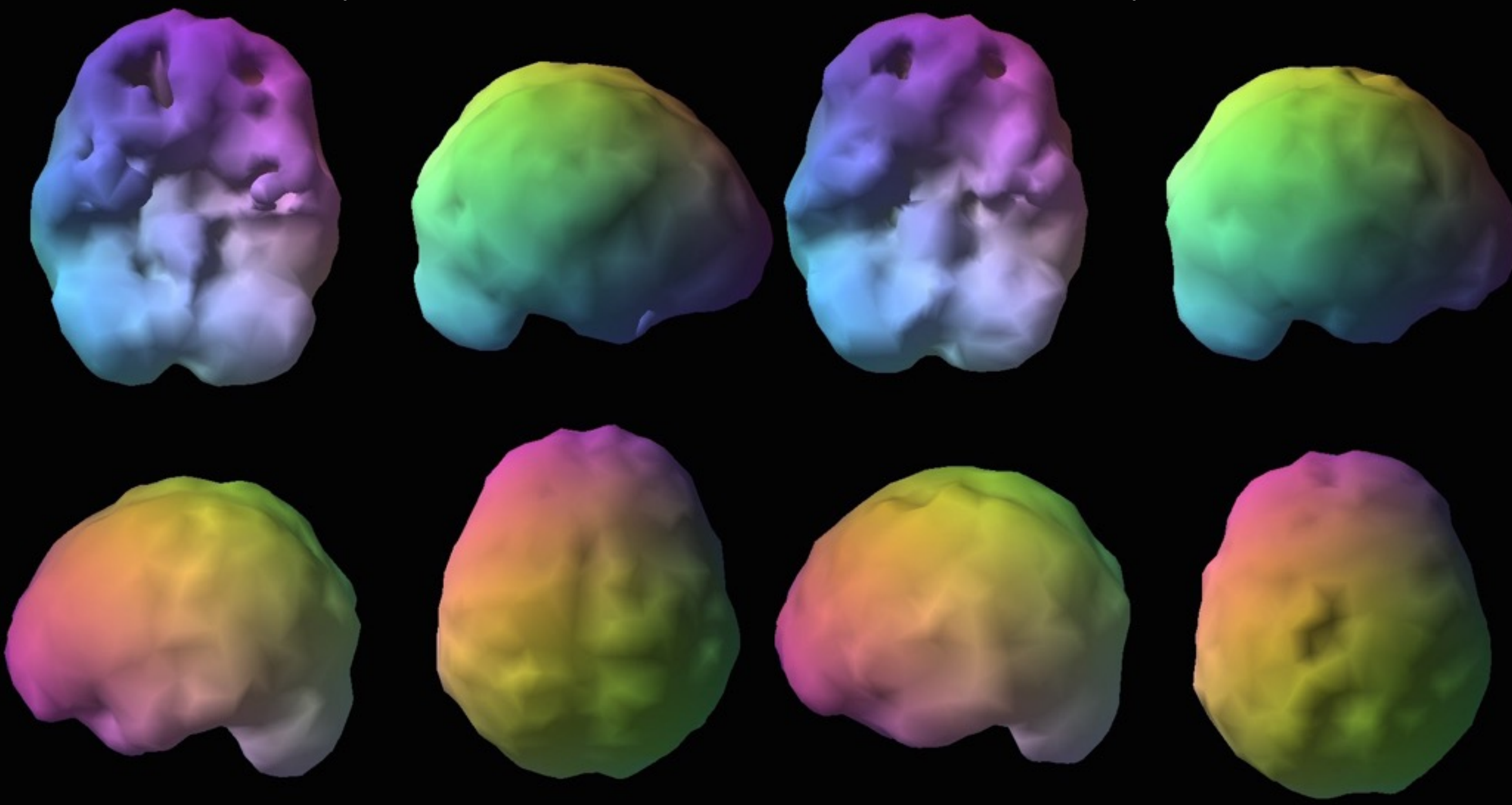
SUBJECT 1 – MR. P

Before

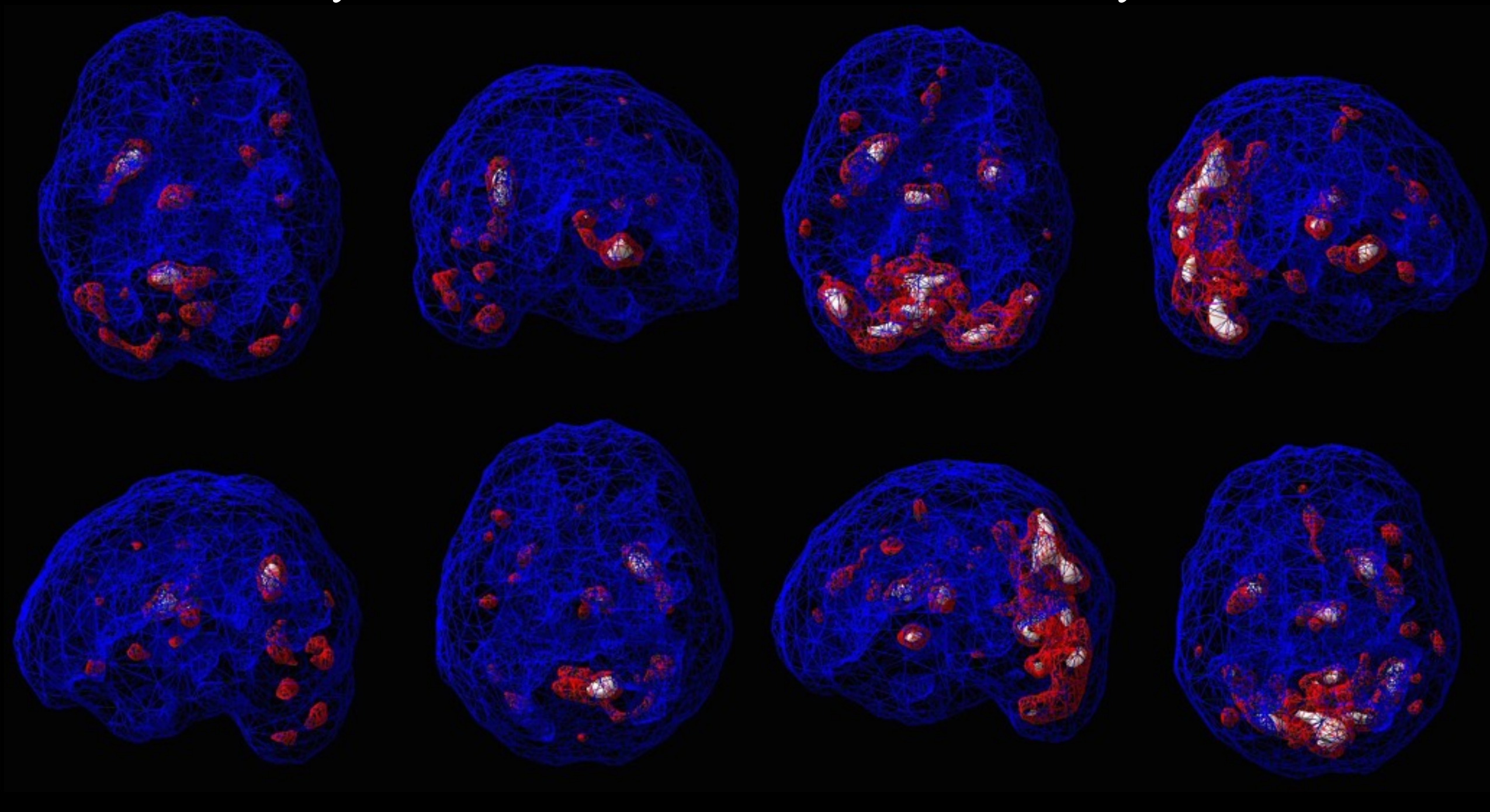
After



SUBJECT 1 – MR. P

Before

After



SUBJECT 1 – MR. K

51 year old Caucasian Male, US Army Vet, West Point grad, attorney, served Panama during Operation Just Cause

History of complex PTSD, subclinical now with residual mild anxiety /excessive worry, subclinical attentional symptoms “addicted to going to fast” and “prone to becoming easily bored.”

Utilized meditation, yoga and plant medicines ayahuasca dozens of times and over 50+ healing journeys with psilocybin. Was overweight “lost lbs of stomach fat from aya”

No prior psychiatric treatment

Extensive trauma history: numerous car accidents, childhood sexual abuse, near drowning incident, near death experiences as Black Hawk fighter pilot,

Prior history of PTSD with nightmares, extreme rage, depression.

Hx of 4 mTBI’s with loss of consciousness 5-10 minutes, 8 concussions as soccer player

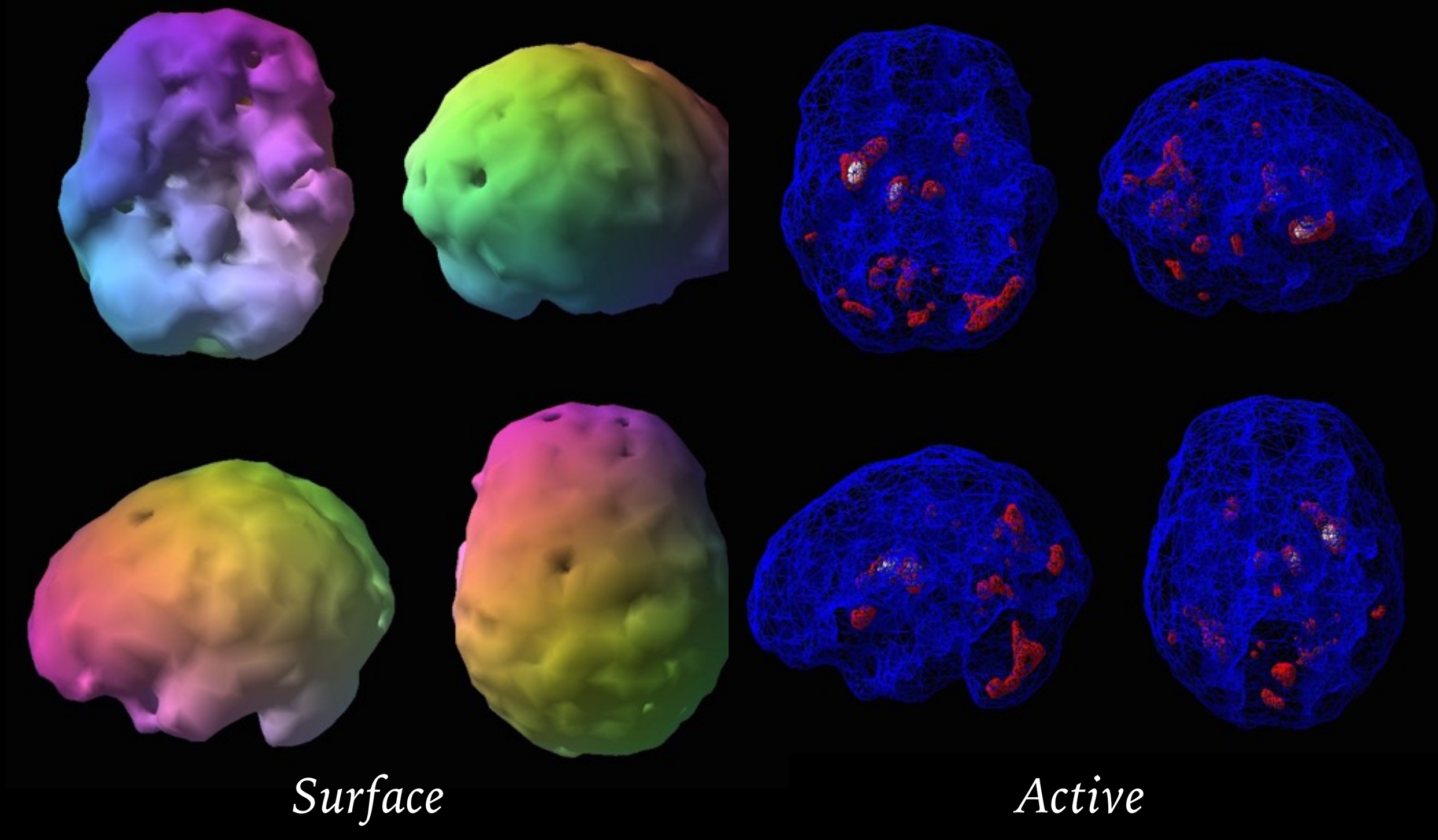
Daily marijuana smoker

Medical history of HTN treated with Lisinopril, hypogonadism

Seeking Crossroads Treatment for trauma resolution, pilot test for other vets

BDI = 3, PCL = 2

MR. K – BEFORE IBO



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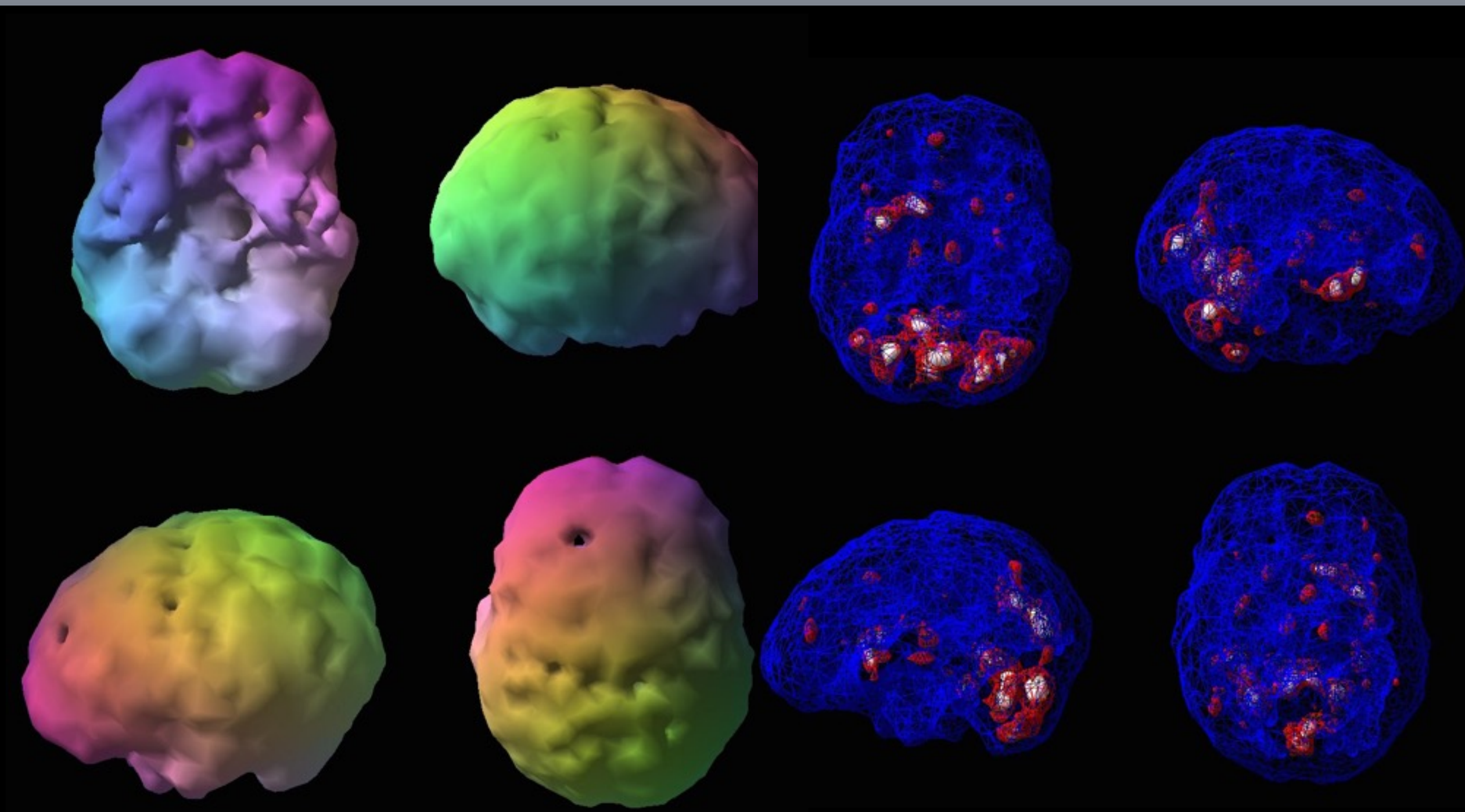
MR. K – AFTER IBO



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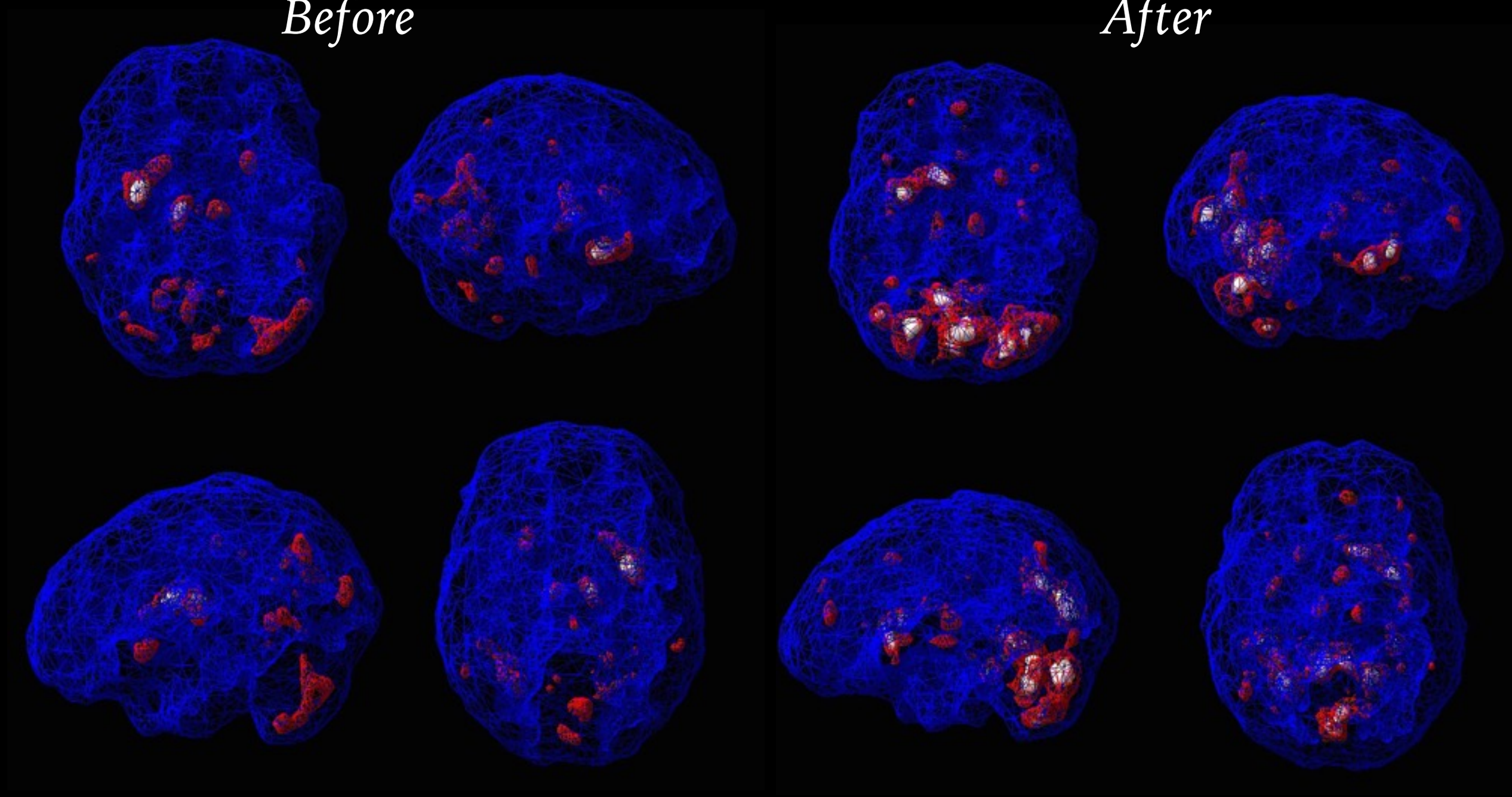
MR. K – AFTER IBO

Before

After



SUMMARY OF SPECT PROTOCOL

ROI's with Time 2 - Time 1 consistent differences averaged together for Subject 1 & 2

Increased	Value	Decreased	Value
Active Cerebellum Medial	2	Parietal Lobe Medial	-1
Basal Ganglia - Right	2	Longitudinal Fissure Anterior	-0.75
Basal Ganglia - Left Putamen	2		
Active Cerebellum Left	1.75		
Active Cerebellum Right	1.75		
Occipital Lobe Right	1.25		
Occipital Lobe Left	1.25		
Posterior Frontal Lateral	1		
Insular Cortex Right	1		
Posterior Frontal Lateral Left	0.75		
Posterior Cingulate Gyrus	0.75		

HYPOTHESES FROM SPECT PROTOCOL

Increase in Perfusion:

- Cerebellum - high level of glutamate tracts, reward/motivation/ cognitive control http://www.ncbi.nlm.nih.gov/pubmed/24851284
- Basal Ganglia (R>)- nucleus accumbens, - high density dopamine tracts, acetylcholine receptors - reward, learning attention.
- Cingulate - adenylylcyclase/ NDMA/glutamate dense. associated with drug cues, learning/memory, attention, depression, pain perception,
- Occipital Lobe - high density of cholinergic muscarinic receptors
- Insula (R>) - interoceptive awareness, anxiety, high density glutamate neurons
- Posterior Frontal Lobes ???

Reduced Perfusion:

- Longitudinal Fissure ???
- Diffuse Cortical effect - temporary cortical deactivation?

MOVING FORWARD

- Crossroads has IRB under review for prospective SPECT imaging before and after on vets with opioid dependence and PTSD. Considering obtaining 1-2 additional SPECT reports and doing case report.
- fMRI study
- Clinical Trials - UCSD w/ DEA approval or Through Angeles Hospital

UCSD Psychedelic Research Institute ???

CROSSROADS
TREATMENT CENTER

An fMRI Study of Ibogaine Treatment for Substance Dependence

4/21/16

Bryson Lochte

Goals

1. Understand neurobiological mechanisms underlying Ibogaine effect
2. Identify markers that predict treatment success
3. Identify cognitive and affective changes associated with treatment

Imaging Protocol

- Task fMRI:

Addiction-relevant Construct	Possible tasks	Regions or networks activated
Cognitive Control	go-no-go, flanker, Stroop, stop-signal, multi-source Interference task	Frontostriatal
Working Memory	N-back	Frontoparietal
Cue Reactivity	Drug-induced cue-reactivity	Ventral striatal
Emotional Regulation	Hariri faces, emotional n-back	Amygdala
Cognitive flexibility	Win-stay, Wisconsin	Executive network

- Resting state fMRI
- High-res MRI including cerebellum
- Spectroscopy?

Non-Scanner Data

Behavioral Tasks:

- Delayed discounting
- Probabilistic reward task
- Sustained attention
- Processing speed

Physiological monitoring:

- HRV

Questionnaires:

- Self report craving/ affective symptoms
- Use history
- Self-reported mood

Outcome data:

- Relapse

Potential Analysis

- Pre/ post assessments
- SUD vs. non-SUD receiving ibogaine treatment
- SUD receiving treatment vs. control treatment
  - Sham or wait list
- Dose based analysis