

Ibogaine Science:

How Ibogaine Works in the Brain to Treat Substance Use Disorder

Dr. Joseph Peter Barsuglia - Advisor to Beōnd + Crossroads Treatment Center, Mission Within, VETS, Sōhei, Journey Colab, Woven Science Ibogaine - Bwiti Ancient Indigenous Tech

"Iboga" derives from the word "boghaga" which means "to take care of"

Purification - ritual bathing and purgatives confess short comings

Spiritual experience to connect with spirit, nature, soul, ancestors

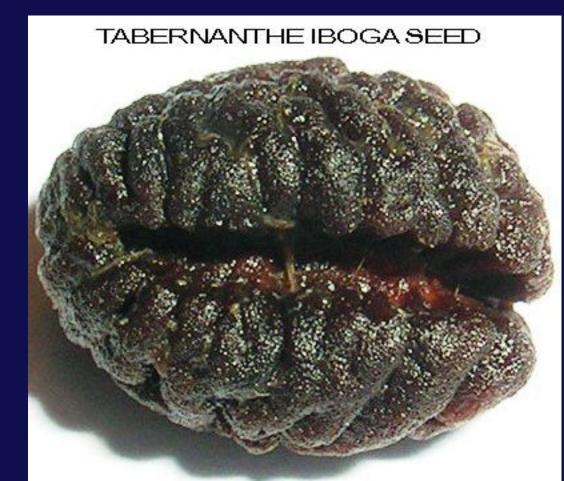
A death & rebirth

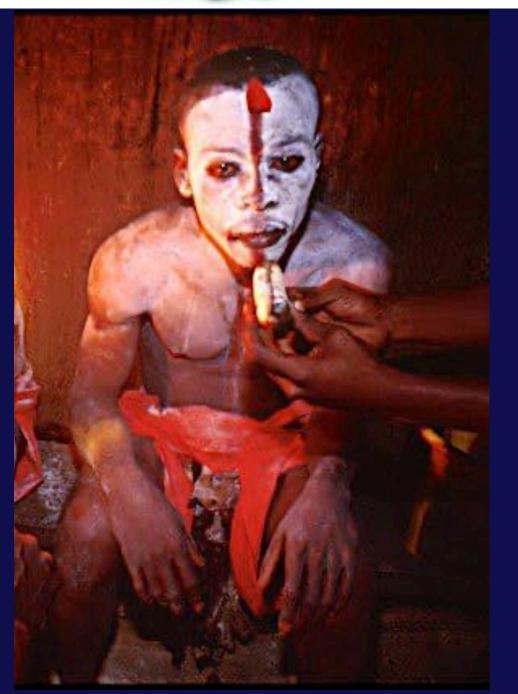
Initiatic doses - dawn of creation, and cosmic, collective, and personal memory

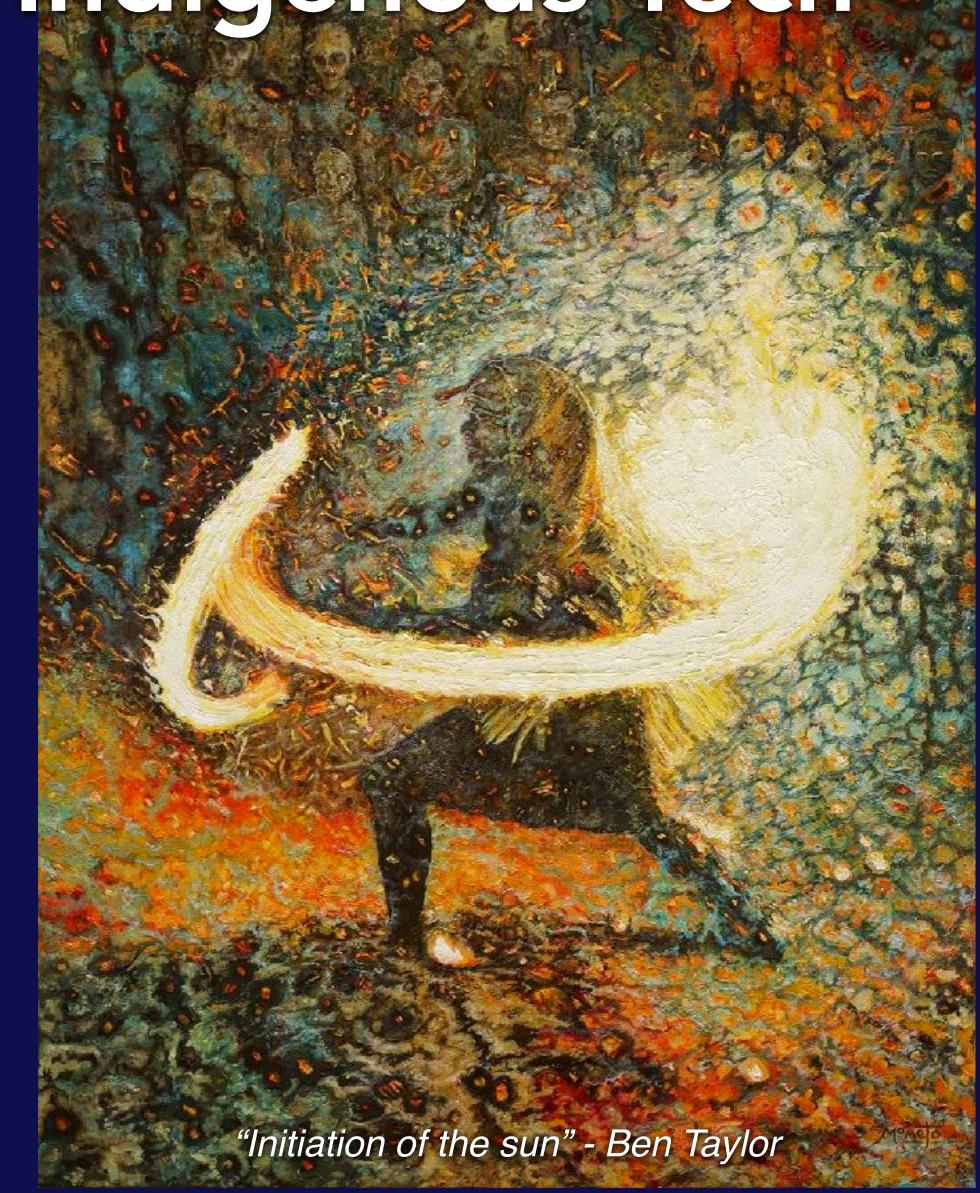
Sacrament understood as "God's spirit"

Dancing on iboga —> bridging spirit + body

Collective - uniting community to be One Heart







Core Diagnostic Facets of Substance Use Disorder

DEPENDENCE
CRAVING
TOLERANCE
WITHDRAWAL

IMPAIRED CONTROL





Cravings to use the substance



Wanting to cut down or stop but not managing to



Taking the substance in larger amounts or for longer than you're meant to



WINDRK FOR

Neglecting other parts of your life because of substance use



Continuing to use, even when it causes problems in relationships



Using substances even when it puts you in danger

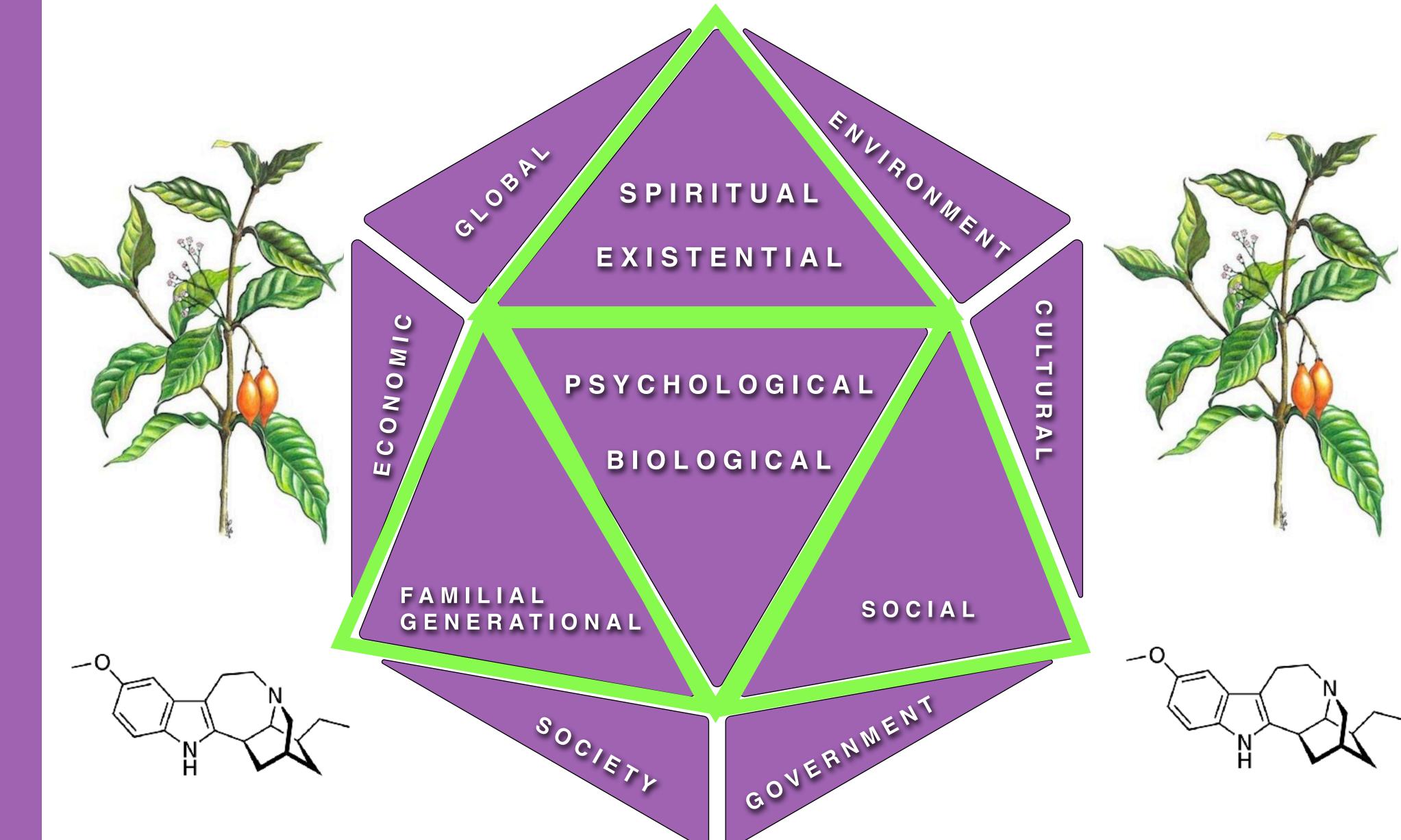
SOCIAL PROBLEMS

RISKY USE

verywell



Holistic View of Addiction





Anti-Addictive Effects of Ibogaine By Substance

Type of Drug People ages 12+ (millions)	
Alcohol	16 mil
Marijuana	12 mil
Pain relievers	9.7 mil
Hallucinogens	6.0 mil
Depressants	5.9 mil
Cocaine	5.5 mil
Rx Stimulants	4.9 mil
Inhalants	2.1 mil
Meth	2.0 mil
Heroin	.74 mil

IBOGAINE HAS ANTI-ADDICTIVE EFFECTS WITH:		
Alcohol		
Opioids / Heroin		
Cocaine		
Amphetamines		
Nicotine		
Sweet Preferences (Food)		



TRIUNE BRAIN THEORY

Executive State Prefrontal Lobes What can I learn from this? **Emotional State** Limbic System Am I loved? Survival State Brain Stem Am I safe?

Complex processes

 Perception, planning, attention, abstract thinking, language...

Limbic System

Cortex

150.000 years old

(Paleomammalian brain) 200-250 Million years old

Primitive survival functions

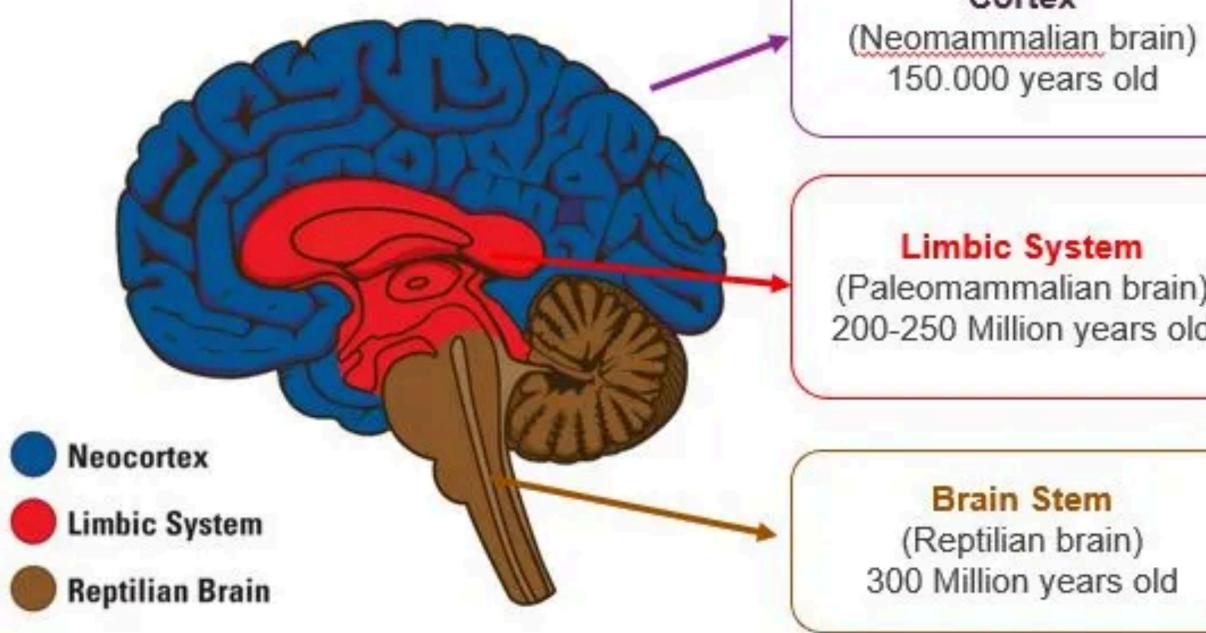
 Fulfilling our animal needs and emotions (feeding, reproduction, parenting...)

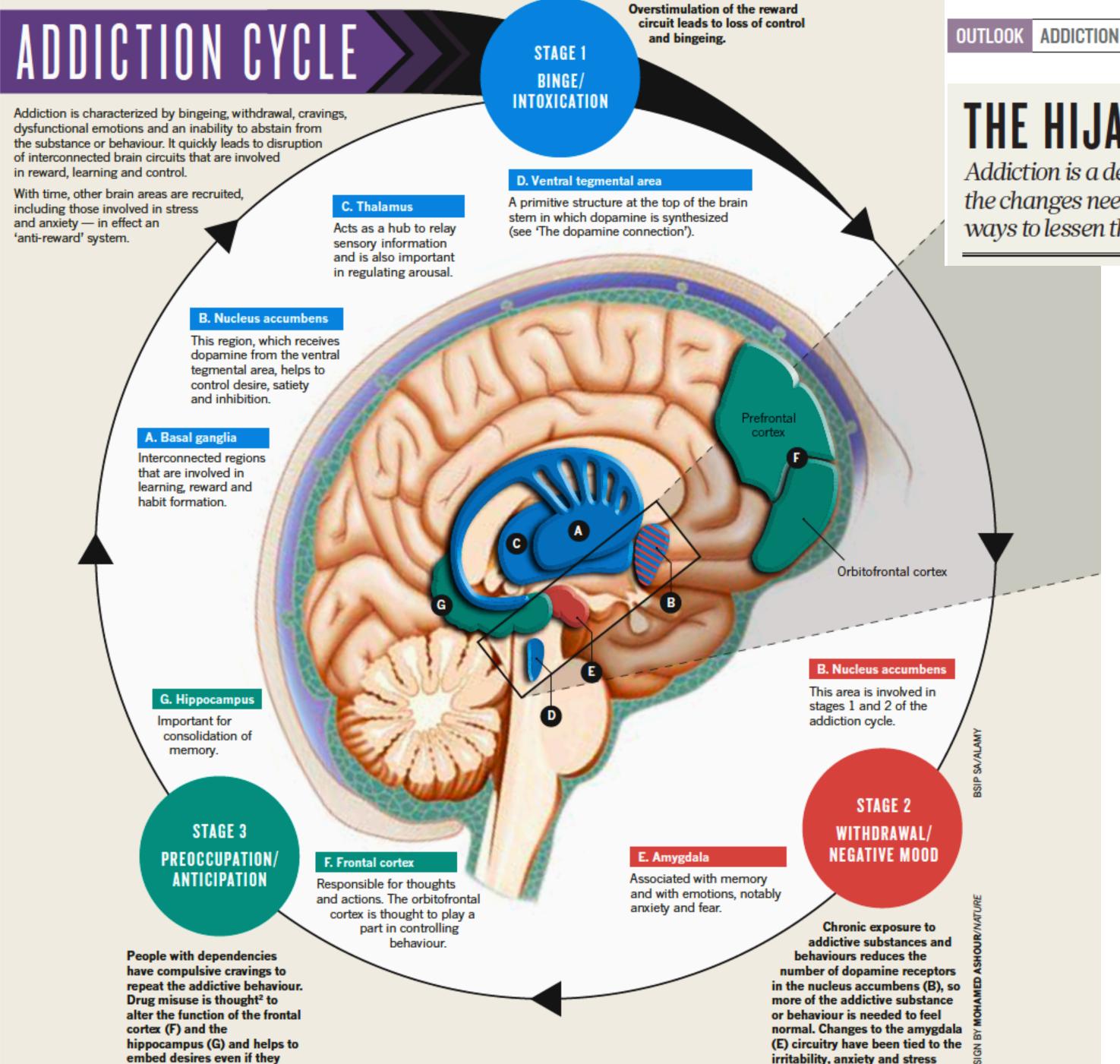
Brain Stem

(Reptilian brain) 300 Million years old

Maintaining body functions

- Routing information up and down
- Instinctive behaviours





have negative consequences.

associated with withdrawal1.

THE HIJACKED BRAIN

Addiction is a devastating disease that alters the brain's circuitry, notably in young adults. But the changes need not be permanent: improved understanding of them will help in developing ways to lessen the burden. By Margaret Munro. See a Nature Video at go.nature.com/e1gqkk.

- 'Addiction' from the Latin addicere Means 'to enslave'
- **Substance Craving**
- **Mathematical Conditioned Responses to Drug Cues**
- **M** Utilization of substances to avoid painful feelings
- **M** Compulsive behavior
- ☑ Substances use gets over learned as a survival pattern
- **M** Downregulation/reduction of dopamine receptors
- Market Reward- pleasure signaling need substance to feel normal



Psychopharmacological Pathways of Ibogaine & Anti-Addictive Effects

PRIMARY PHARMACOLOGICAL PATHWAYS	EFFECTS IN ADDICTION	
Mu and Kappa Opioid Receptors	 ✓ Ibogaine mitigates opioid withdrawal and craving through novel mechanism ✓ μ-Opioid receptor regulates pleasure/reward and reinforcing effects with drugs of abuse 	
N-methyl-D-aspartate (NMDA) Antagonist	 ✓ Reduces opioid + stimulant withdrawal and craving ✓ Unlearning of habits that persist even in the face of negative consequences - associated with drug cues ✓ Regulates Ventral Tegmental Area 	
Dopamine (DAT) and Serotonin Transporters (SERT)	 ✓ Mood boosting/regulating properties ✓ Maladaptive alterations in SERT = greater susceptibility to the rewarding properties of drugs of abuse ✓ Ibogaine's effect on psychological dependence (craving) attributed to long-acting effects on DAT and SERT 	
Nicotinic Acetylcholine Antagonist (nAChR α3β4 and α2β4)	t ✓ Regulates signaling in mesolimbic addiction pathways mediate reinforced behavior ✓ High density in the Ventral Tegmental Area ✓ High density in sensory regions - Visual Cortex	
Sigma (σ) receptors (σ ₂ > σ ₁)	 ✓ Associated with drug sensitization + reward and reinforcement (i.e. alcohol and cocaine) ✓ Target of interest in ameliorating depression and anxiety ✓ Neuroprotective and cognitive enhancing 	
Substance P	✓ Neuropeptide, implicated in stress-resilience and pain tolerance, inhibits opioid tolerance $be\bar{o}nd$	



"The Magic Sauce" & Regenerative Properties of Ibogaine

Neurotrophic Factors are proteins that promote the growth, differentiation, synaptogenesis, and survival of neurons. They modulate maintenance, protection, repair and plasticity of the nervous tissue. The "Miracle-Gro" for the brain

Ibogaine boosts Neurotrophic Factors such as:

- 1. **GDNF (Glial Derived Neurotropic Factor)
- 2. BDNF (Brain Derived Neurotrophic Factor)
- 3. NGF (Nerve Growth Factors)

Explains the long-lasting effects of ibogaine:

- Reverse adaptations to chronic exposure to drugs of abuse in the reward system
- Suppresses and inhibits drug seeking behavior

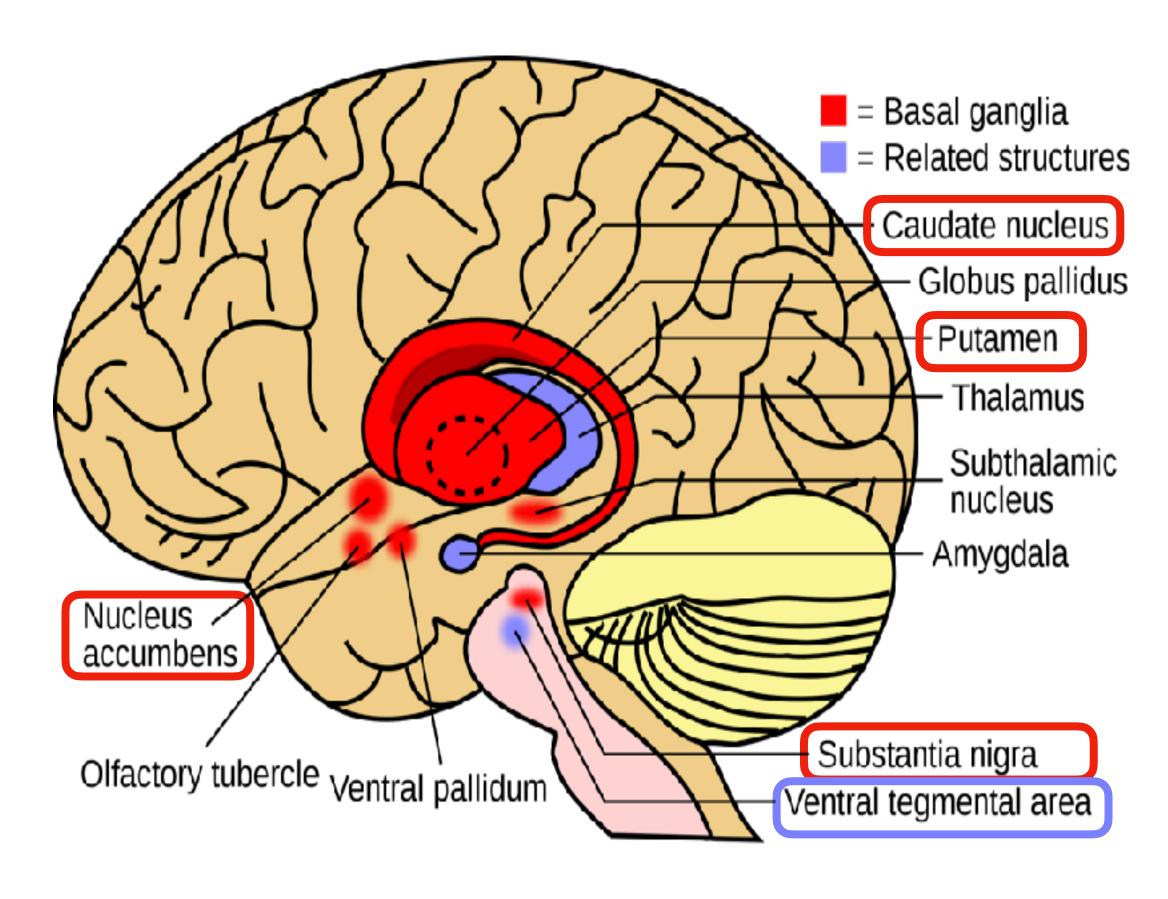
Ventral Tegmental Area & Nucleus Accumbens:

Primary sites where most addictive drugs act.

Alterations in dopamine and reward processing from repeated stimulation All drugs of abuse activate mesolimbic neurons in the Ventral Tegmental Area

Substantia Nigra

Involved in addiction cues and relapse





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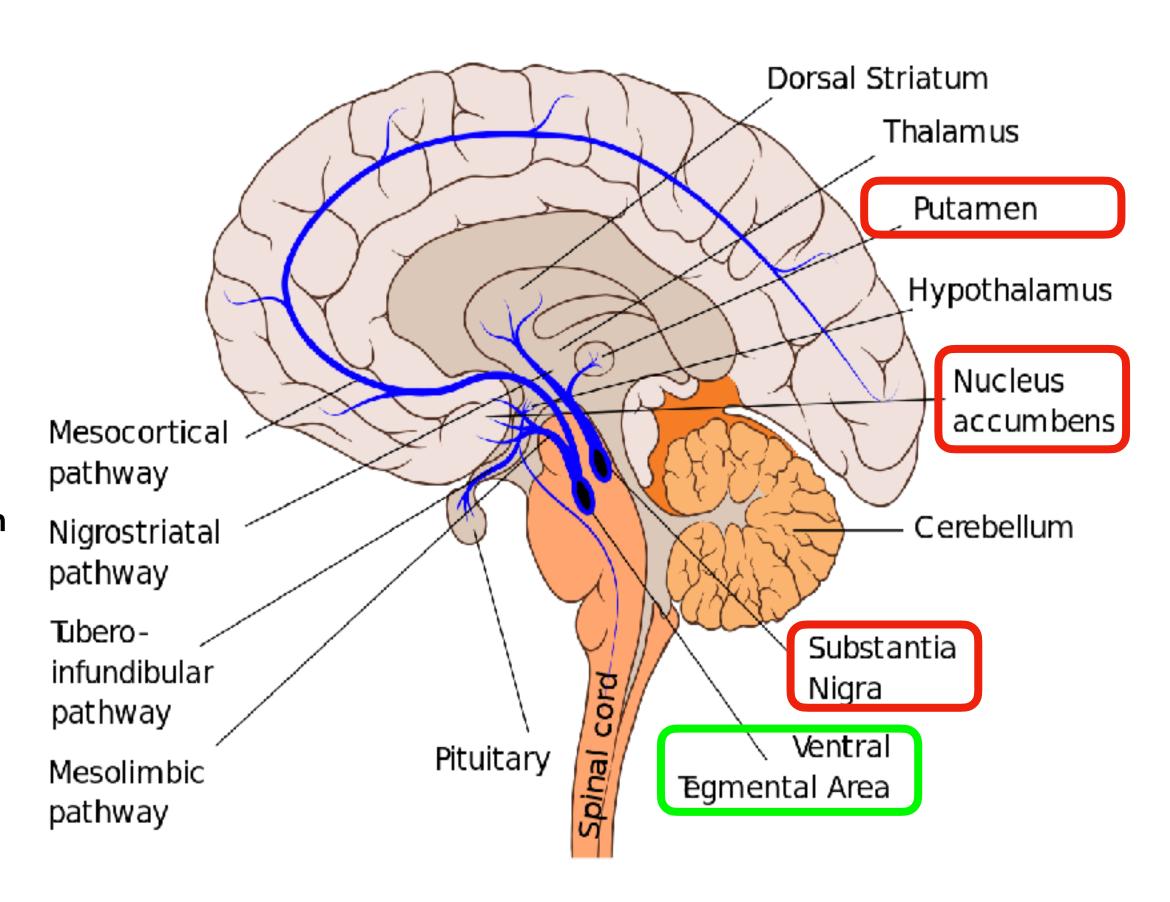
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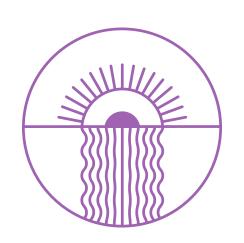
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<u>Substantia Nigra</u> Involved in addiction cues and relapse





"Suddenly, I realized that I was not in heroin withdrawal," Howard Lotsof later said of his own ibogaine experience. Nor did he crave it.

"Where previously I had viewed heroin as a drug which gave me comfort, I now viewed heroin as a drug which emulated death. The very next thought into my mind was, I prefer life to death."

TIME Magazine - Inside Ibogaine, One of the Most Promising and Perilous Psychedelics for Addiction





Journal of Psychoactive Drugs



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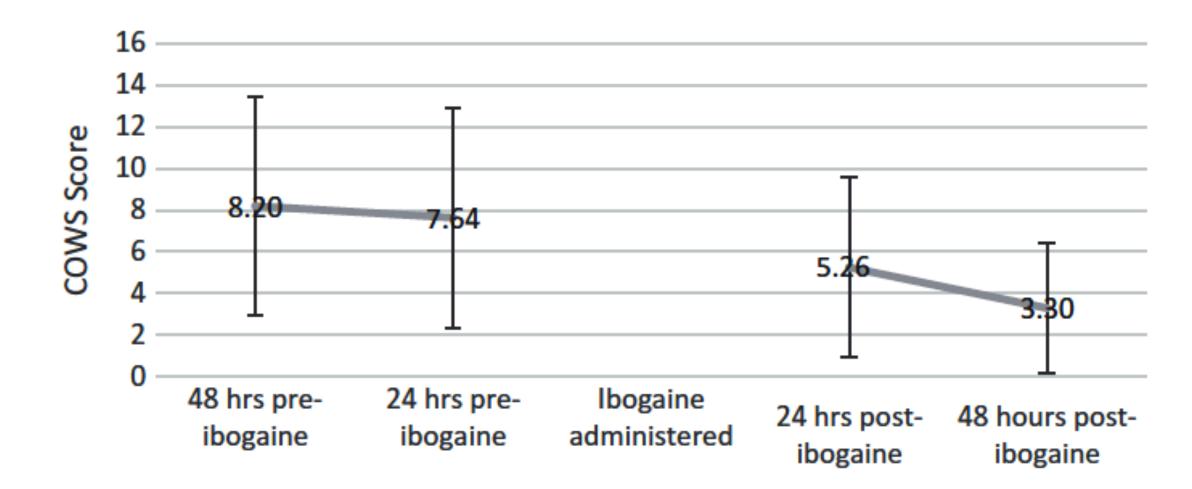
Changes in Withdrawal and Craving Scores in Participants Undergoing Opioid Detoxification Utilizing Ibogaine

Benjamin J. Malcolm, Martin Polanco & Joseph P. Barsuglia

To cite this article: Benjamin J. Malcolm, Martin Polanco & Joseph P. Barsuglia (2018): Changes in Withdrawal and Craving Scores in Participants Undergoing Opioid Detoxification Utilizing Ibogaine, Journal of Psychoactive Drugs, DOI: 10.1080/02791072.2018.1447175

To link to this article: https://doi.org/10.1080/02791072.2018.1447175

A) COWS Scores over Time ± S.D. (n=50)



C) BSCS Scores over Time ± S.D. (n=48)

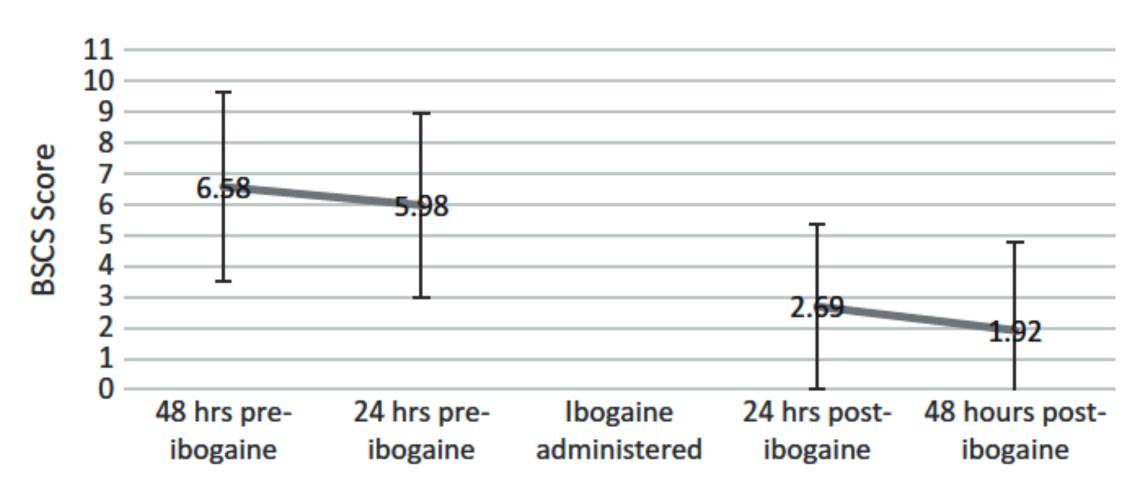


Figure 1. Opioid withdrawal and craving scores in subjects receiving ibogaine for opioid detoxification.

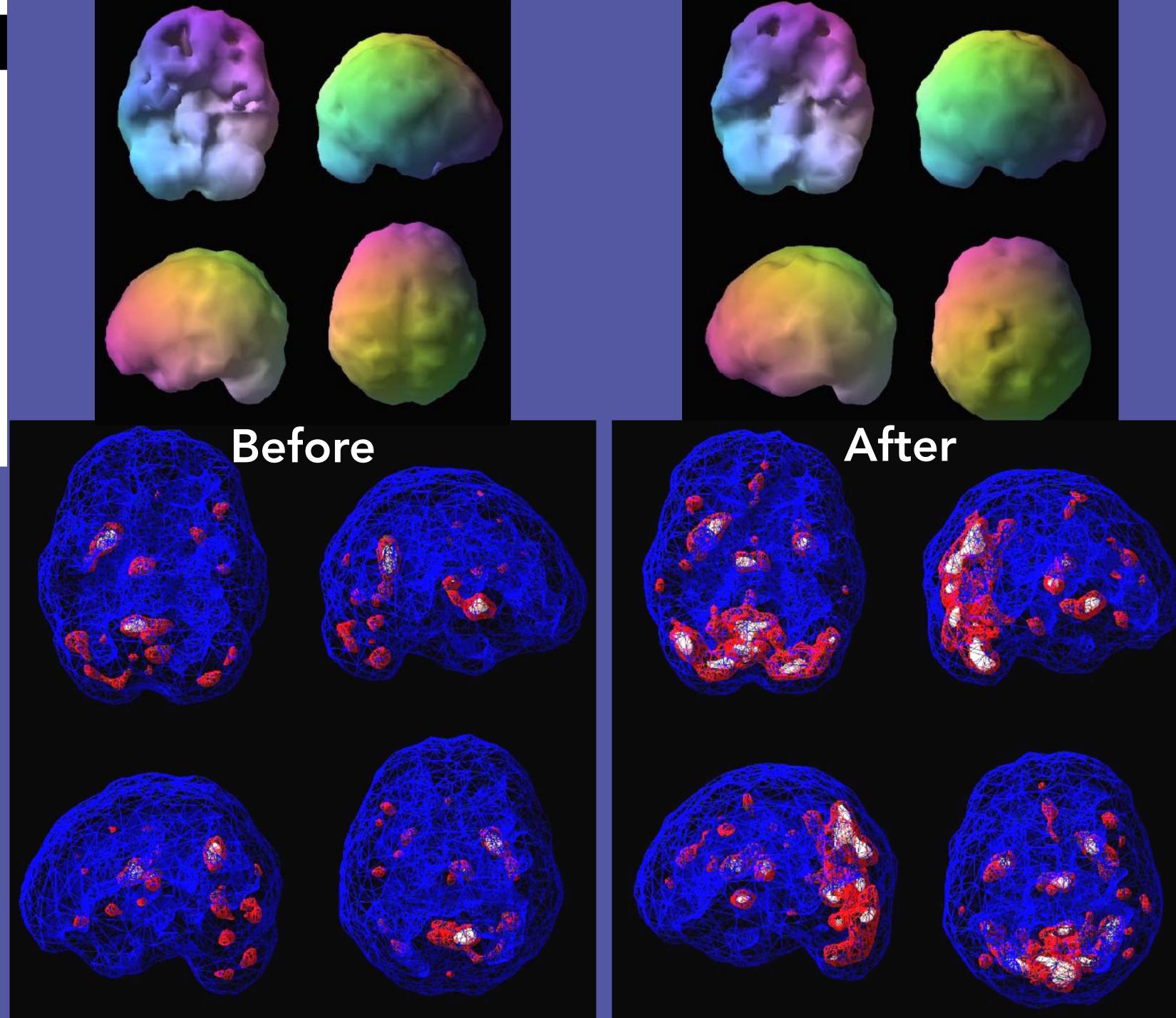
CHAPTER

A case report SPECT study and theoretical rationale for the sequential administration of ibogaine and 5-MeO-DMT in the treatment of alcohol use disorder

Joseph P. Barsuglia*,†,‡,§,1, Martin Polanco*,†, Robert Palmer¶, Benjamin J. Malcolm∥, Benjamin Kelmendi#, Tanya Calvey**

2 days Before 5 days Post Ibogaine

From Mission Within Veteran Program Crossroads Treatment Center - 2016



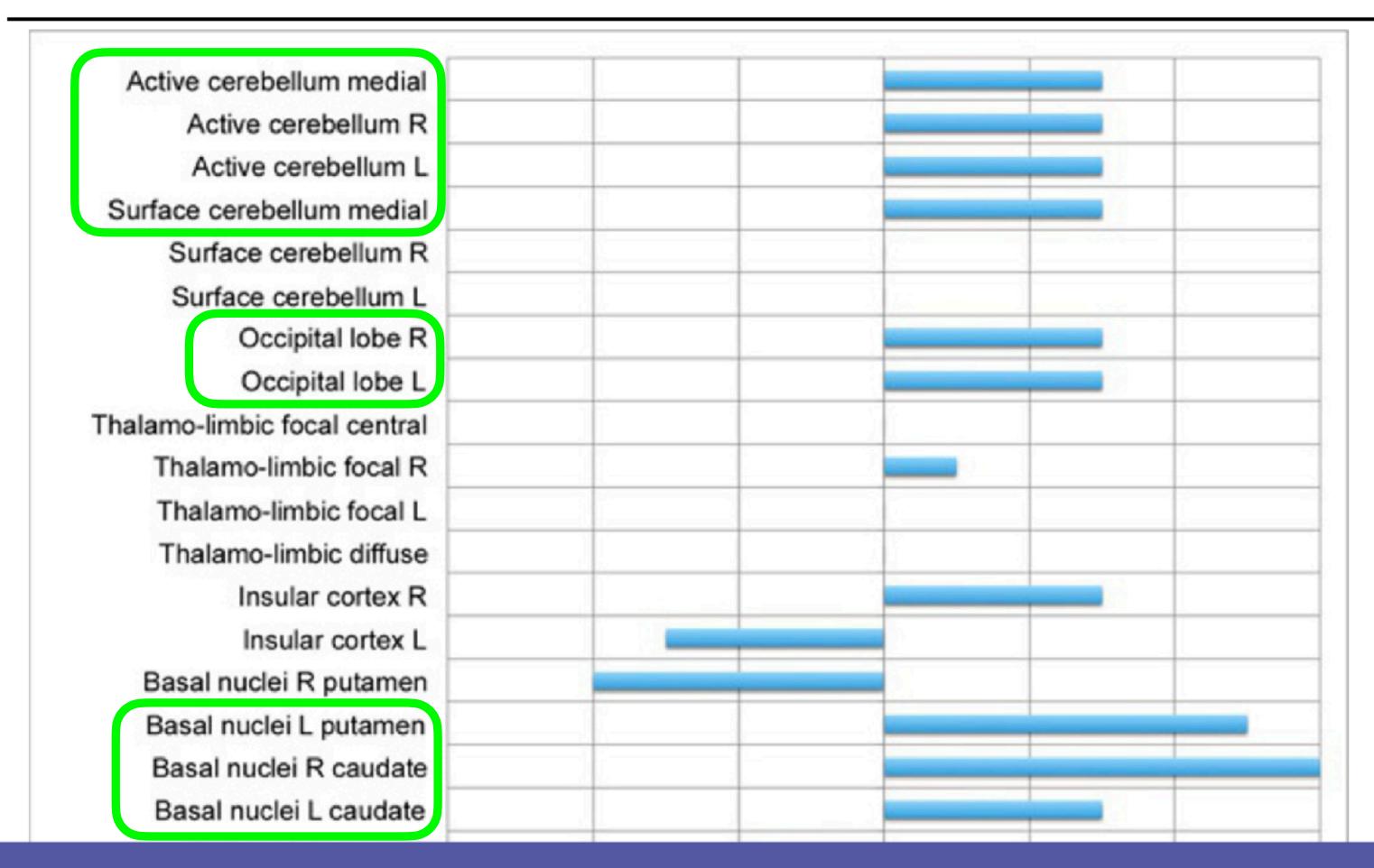
CHAPTER

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Table 2 Changes in Visual Ratings of Perfusion in Regions of Interest Between Baseline and Posttreatment





BASAL GANGLIA & FUNCTIONING IN ADDICTION

Implication of basal ganglia in addiction

Underlies responses to reward (and addiction) + habit formation

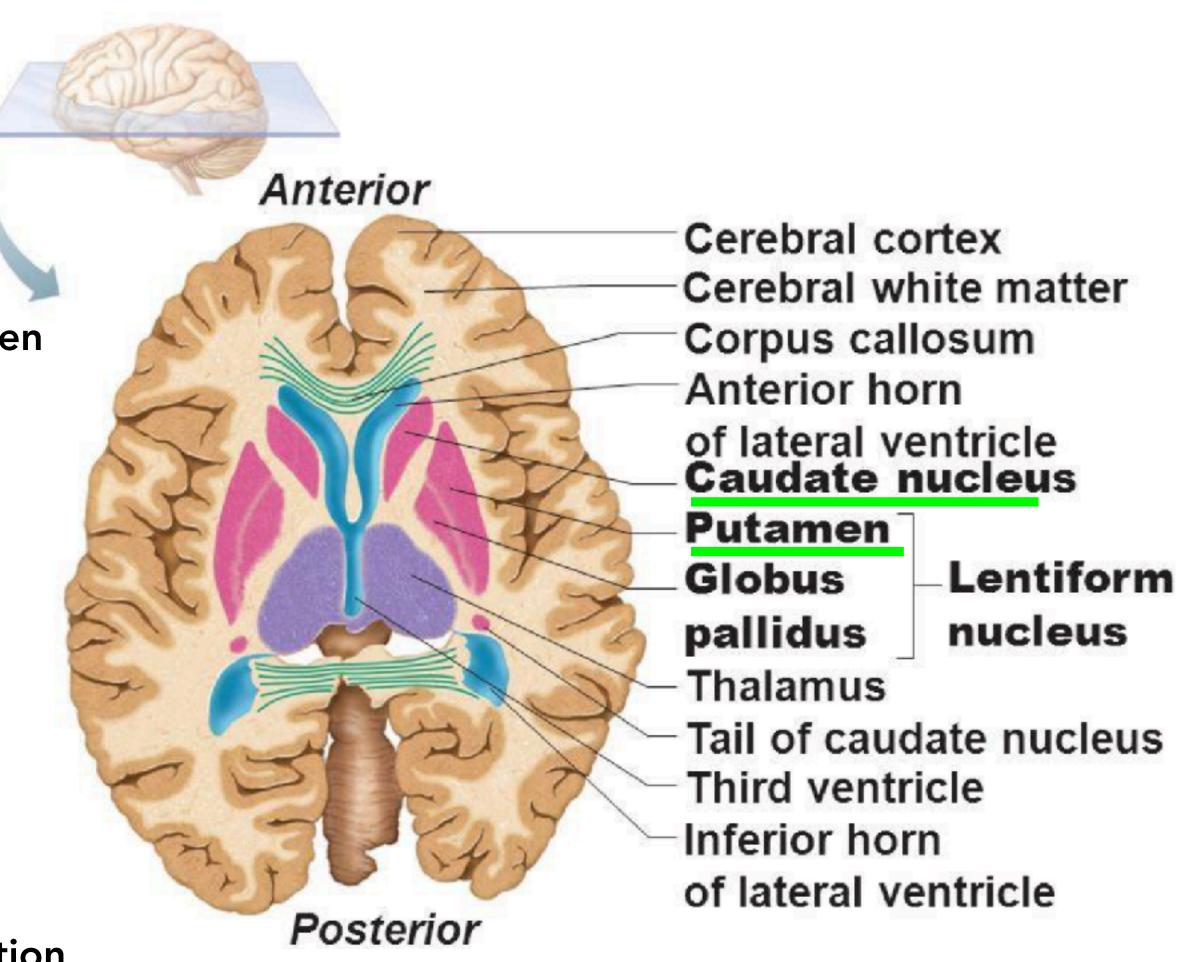
Ibogaine has documented dopaminergic effects the caudate and putamen

CAUDATE:

- Associated with reward, motivation, visual processing, risk analysis
- Craving linked to the mesolimbic pathway
- Goal-directed behavior and stimulus-driven habits

PUTAMEN:

- Learning and motor control, including language functions, reward, cognitive functioning, and addiction
- Associated with movement disorders and OCD
- Plays a critical role in the automatization of behavior and habit formation
- Habitual patterns reduced glutamate/NMDA turnover in putamen





CEREBELLUM & FUNCTIONING IN ADDICTION

Under-explored brain structures "reptilian brain"- classically associated with movement

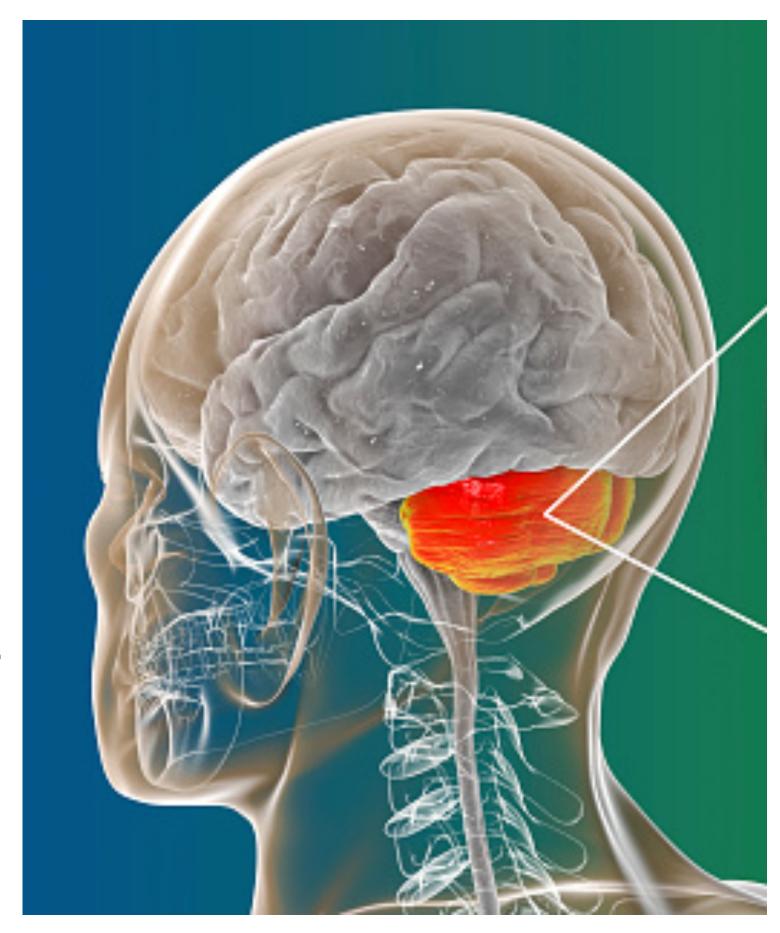
Recent investigations into cerebellar functioning + addiction identify region involved with:

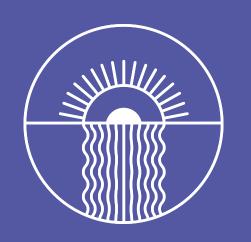
- Reward processing
- Motivational and cognitive control processing
- Pain perception
- Processing drug-induced cue-related memories & Pavlovian learning

Anti-addictive effects via loops through:

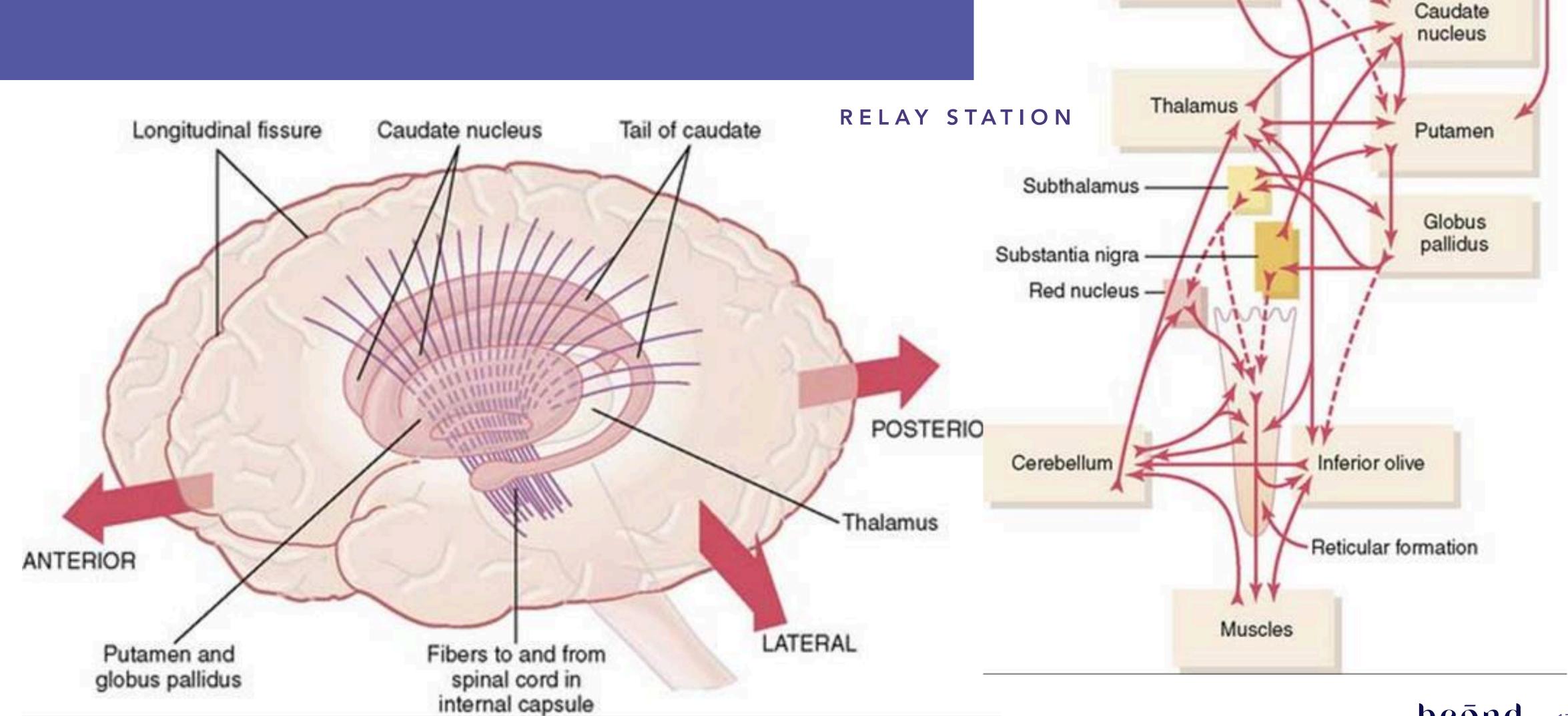
- Dopamine and Glutamate projections from cerebellum to the Ventral Tegmental Area (VTA) is responsible for persistence of drug-related conditioned memories and escalation behavior
- High density of opioid and sigma receptors

Hypotheses: Ibogaine may foster <u>neuroadaptive cellular changes</u> and <u>unlearning of conditioned drug responses</u> through cerebellar pathways





BASAL GANGLIA & CEREBELLAR TRACTS



Premotor and

supplemental motor

association areas

Motor cortex

How does Ibogaine work in the mind?





Psychological Facets of Ibogaine Experience

Visionary Content

Ancestors - faces, spirits
Panoramic Planetary Landscapes - Often African
Processing violence / destruction
Traveling through Outer-space / Cosmic Landscapes
Cinematic film reel / TV set / Screen

Psychotherapeutic Effects

Autobiographical / Trauma processing - Reliving life
Self/Meta-Observation
Confrontation / Awareness of defenses - denial/avoidance
Ego death / dying / rebirth - embryo to death to new life
Emotional Catharsis
Relational processing - empathy, forgiveness, love
Existential / Spiritual awakenings
Letting Go / Feeling Transformed

Cognitive / Perceptual Effects

Enhanced Vision / Acuity / Color Enhancement & Saturation Visual Tracers
Enhanced Auditory Acuity
Impaired Verbal Fluency / Reduced Attention Span

Physical Effects

Detoxification / Purification
Purgation / Vomiting / Sweating
Dizziness / Nausea / Ataxia
Abnormal heartbeat / Increased heartbeat perception



Artist: Chor Boogie

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Report of ibogaine psychedelic/spiritual experience

Air-Force Veteran with alcohol abuse

"He reported experiencing close-eyed visions shortly after the third ibogaine dosage that began with images of floating through the universe and being surrounded by the stars.

He began to ask himself questions that were previously transcribed with the counselor pertaining to his alcohol use and past traumatic events. He noted when he would ask himself or "God" a question, he experienced being visually transported to a new realm. He described these realms similar to levels of a video game, and the symbols and images were not immediately associated with the contents of his questions.

However, after being "transported to several levels," he began to see the symbols were showing him the answers to his questions in symbolic form. For example, on one "level," he was visually taken to a scene of "pesky beings that were leeching energy from [his] body," which he later interpreted as, "the spirit of the yeast in the alcohol that was holding onto [him]." He reported that when he became nauseated the, "pesky beings" were telling him not to vomit. When he began to physically vomit, the beings were shouting "No!" and appeared to be leaving his body through the purging.

He described seeing, "a universal cosmic matrix that had a central column of electric light and spiritual beings merging into the light." The "pesky beings" were telling him not to enter the light, but he was given "a pair of rocket boots" by "the creator of the matrix" and merged into the light, which felt healing and empowering to his "true self."



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A Mixed-Method Analysis of Persisting Effects Associated with Positive Outcomes Following **Ibogaine Detoxification**

Alan K. Davis, Elise Renn, Austin-Marley Windham-Herman, Martin Polanco & Joseph P. Barsuglia

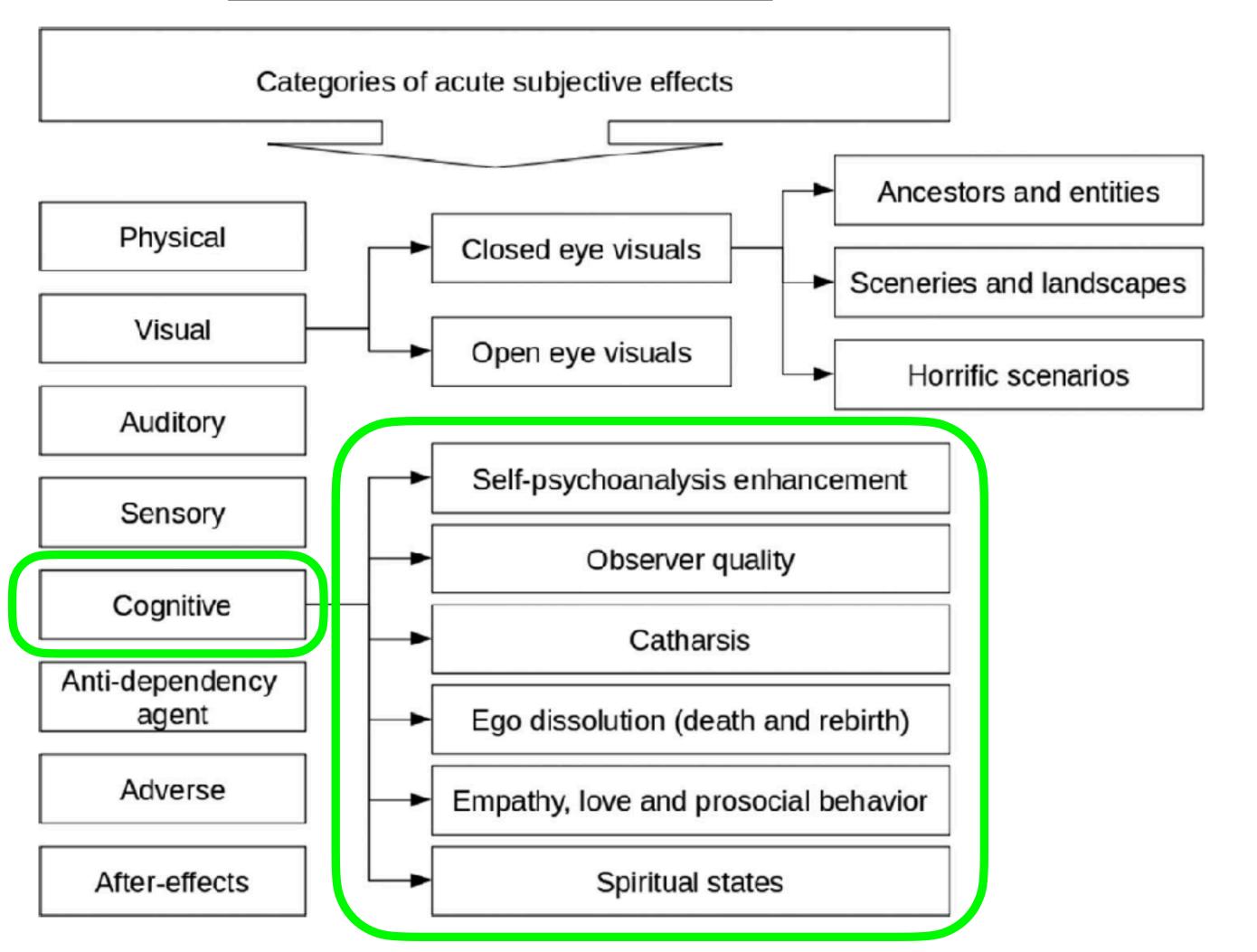
Out of 44-Items from Persisting Effects Questionnaire

Top Items Endorsed Between Treatment Responders from Non-Treatment Responders	
The sense of meaning in your life has increased	1.27†
Your ability to tolerate difficult or painful feelings has increased	1.22†
Your experience of sacredness in daily life has increased	1.18†
Your ability to be a more authentic person has increased	1.12†
Your feelings of love and openheartedness have increased	1.01†
Your experience of joy or bliss has increased	.96†
Your capacity for coping with stress has increased	.93†
Your gratitude or sense of gratefulness has increased	.91†
Your appreciation for life has increased	.90†
Your experience of inner peace (i.e., centeredness, serenity, calmness, contentment) has increased	.90†
Your feelings of unhealthy anger (e.g., bitterness, hostility, scorn) have decreased	.89†





The Ibogaine Experience: A Qualitative Study on the Acute Subjective Effects of Ibogaine



Cognitive Effects

The individuals experienced wakefulness for at least 24 hours.

Enhanced analytical capabilities and thought connectivity where abstract and fluid thoughts were making seemingly unrelated ideas intertwined, resulting in an abundance of new and insightful ideas.

Increase of creativity, producing enhanced problem-solving capabilities, child-like fascination, increased appreciation of things, and an overwhelming feeling of profoundness.

Immersion and memory enhancement, which enabled the individual to easily access stored memories and recall them.

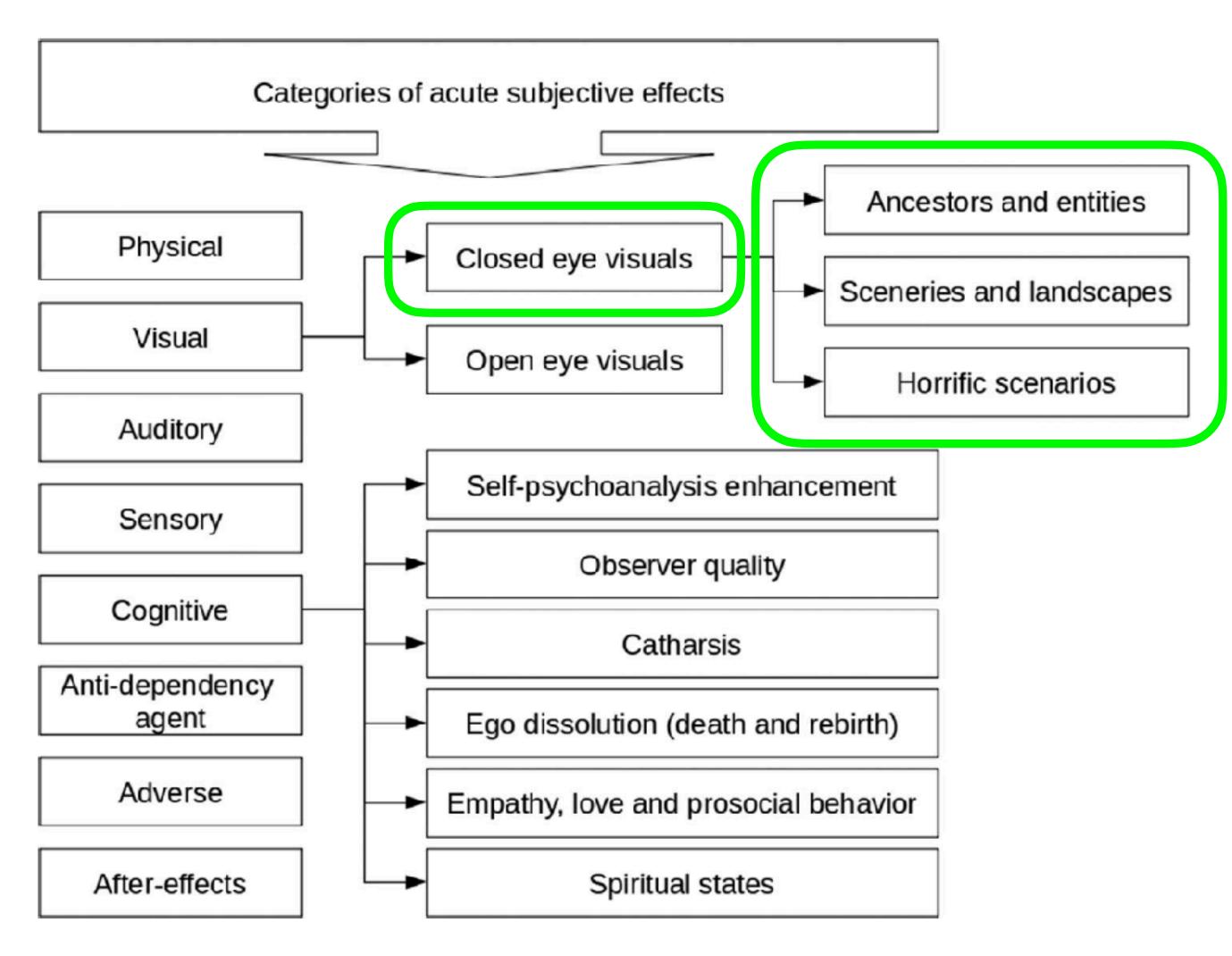
Deep understanding of everything (e.g., the organization or structure of the universe, consciousness, everyday life, causalities) due to enhanced conceptual thinking. The information was perceived both in its entirety and in overwhelming detail.

The individuals were very introspective, in a mindful, meditative-like state, with attention focused on the immediate experience. Some individuals experienced vomiting as part of "quieting the mind."

S

Closed Eye Visuals

The Ibogaine Experience: A Qualitative Study on the Acute Subjective Effects of Ibogaine



The visionary experience (as referred to by the study participants), dreaming while awake was experienced by many individuals and described as profound images or movies playing out in the head.

Most describe the images as being very intense, rapid, and containing a lot of information, even unnecessary information, which was, in some cases, perceived as confusing.

Ancestors & Entities

"I would see a young face that was very quickly morphing and aging in front of me. I would see this being go from young adulthood to old age. Actually they were just disembodied heads that I've recognized as ancestors. And then the heads started to look down as they disintegrated"

Sceneries & Landscapes

"It was a bit like the movie Baraka. Lots of different images of different cultures all around the world, beautiful cinematography. Kind of going from heaven to hell. Lots of beautiful images of pristine nature and then suddenly images of like really hectic city life and town and busy and pollution and industry, really contrasting. Essentially, what we are doing on the planet. Where we have come from and where we are headed and what we are doing now."

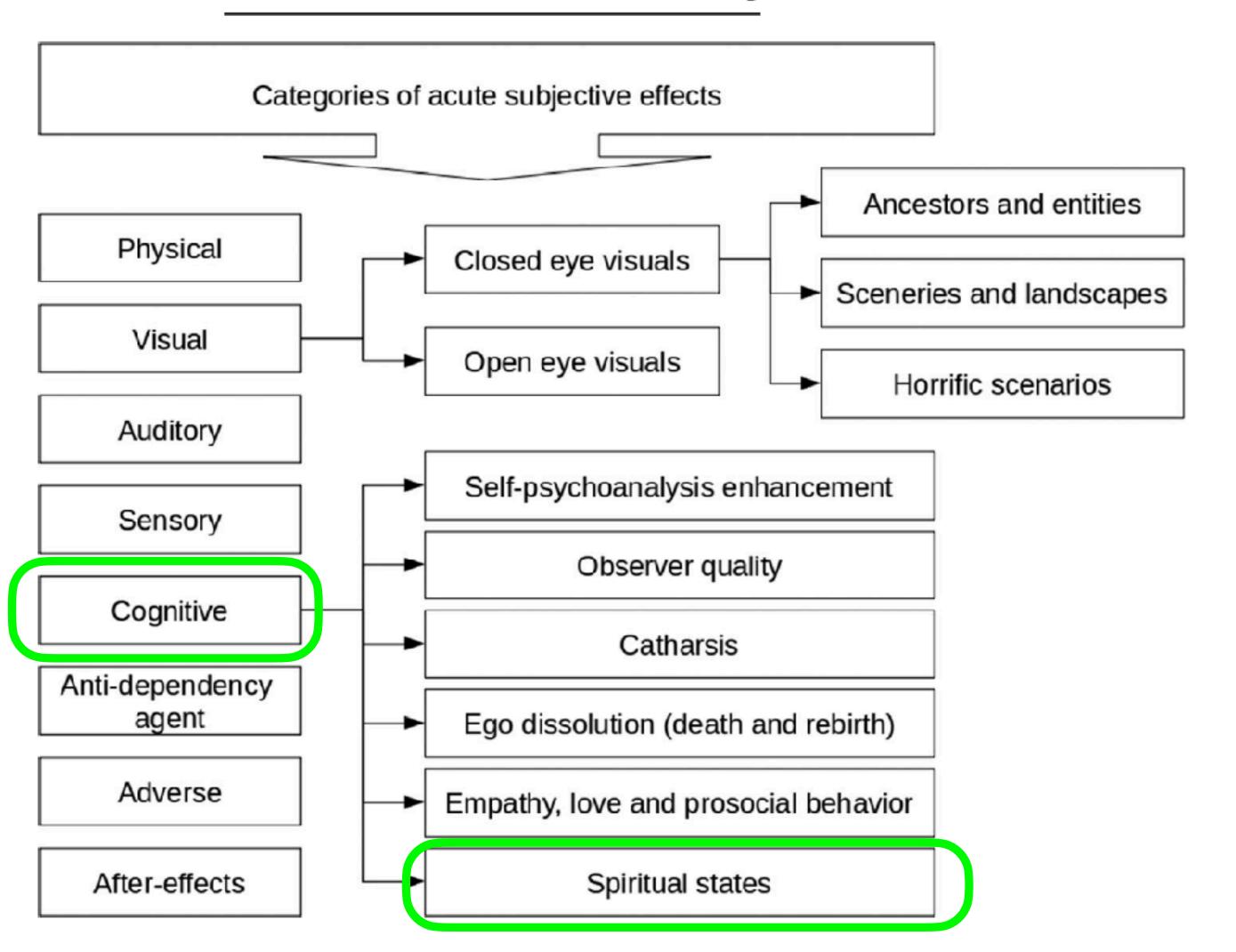
Horrific Scenarios

Common were feelings of impending doom and visions of apocalyptic scenes, or just darkness accompanied with a profound feeling of aloneness. The imagery was on occasion historical such as the mistreatment of women in the middle ages, or contemporary, like the controlling role of media and its influence on society. Sometimes futuristic scenarios of destruction on the planet were seen, such as scenes of wars, fires burning, and bloody images of dead animals and bodies.





The Ibogaine Experience: A Qualitative Study on the Acute Subjective Effects of Ibogaine



Spiritual Effects

Spiritually, a sense of unity or interconnectedness was experienced by most. While many gained an understanding of spiritual roots, the source of life or life's purpose, all agreed they had become better persons.

Most importantly, the experience brought a sense of hopefulness for the future, especially in cases of drug dependence. In some cases interdependent opposites were described such as light-dark; bad-good; life-death; disconnection-connection to people.

Subject 1:

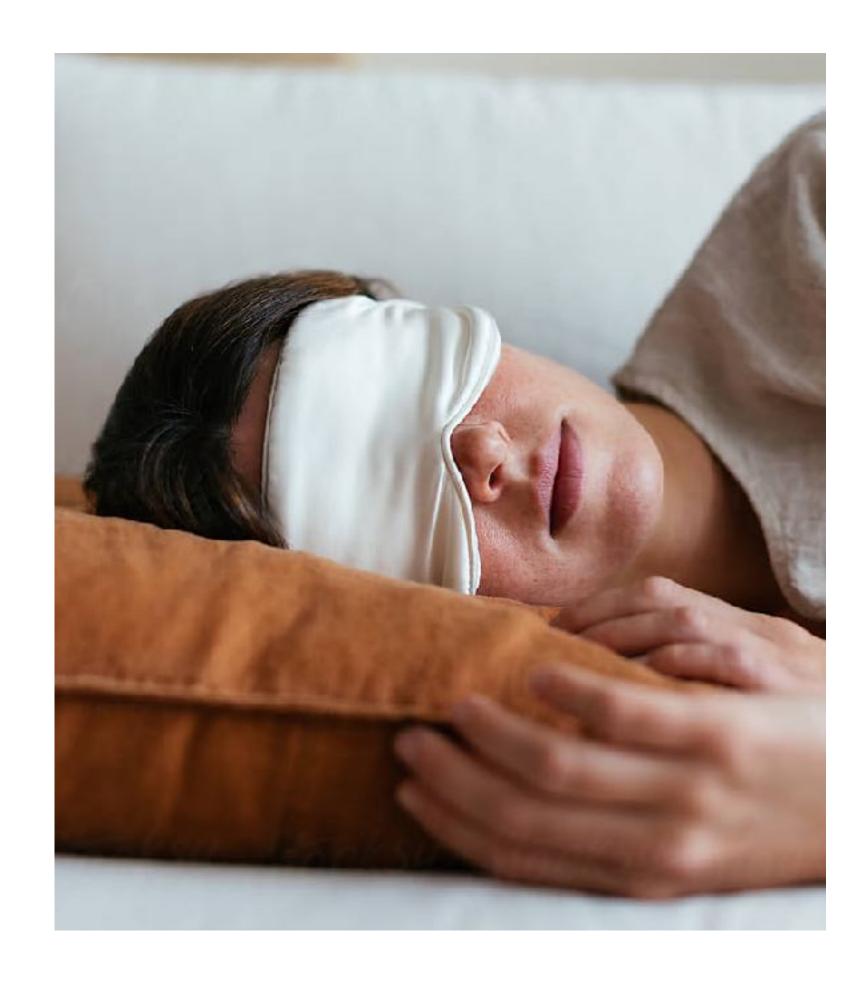
"Ibogaine reconnected me with my life's purpose. And I've discovered the fact that whenever I didn't had a life purpose, I've felt like I just wanted to die. Even if my life's purpose is not clear, it's present. I want to live and I want to love, and I want to connect and I want people to connect and love and create a better world."

Journal of Psychedelic Studies 1(2), pp. 74–83 (2017) DOI: 10.1556/2054.01.2017.007 First published online August 25, 2017

A phenomenological analysis of the subjective experience elicited by ibogaine in the context of a drug dependence treatment

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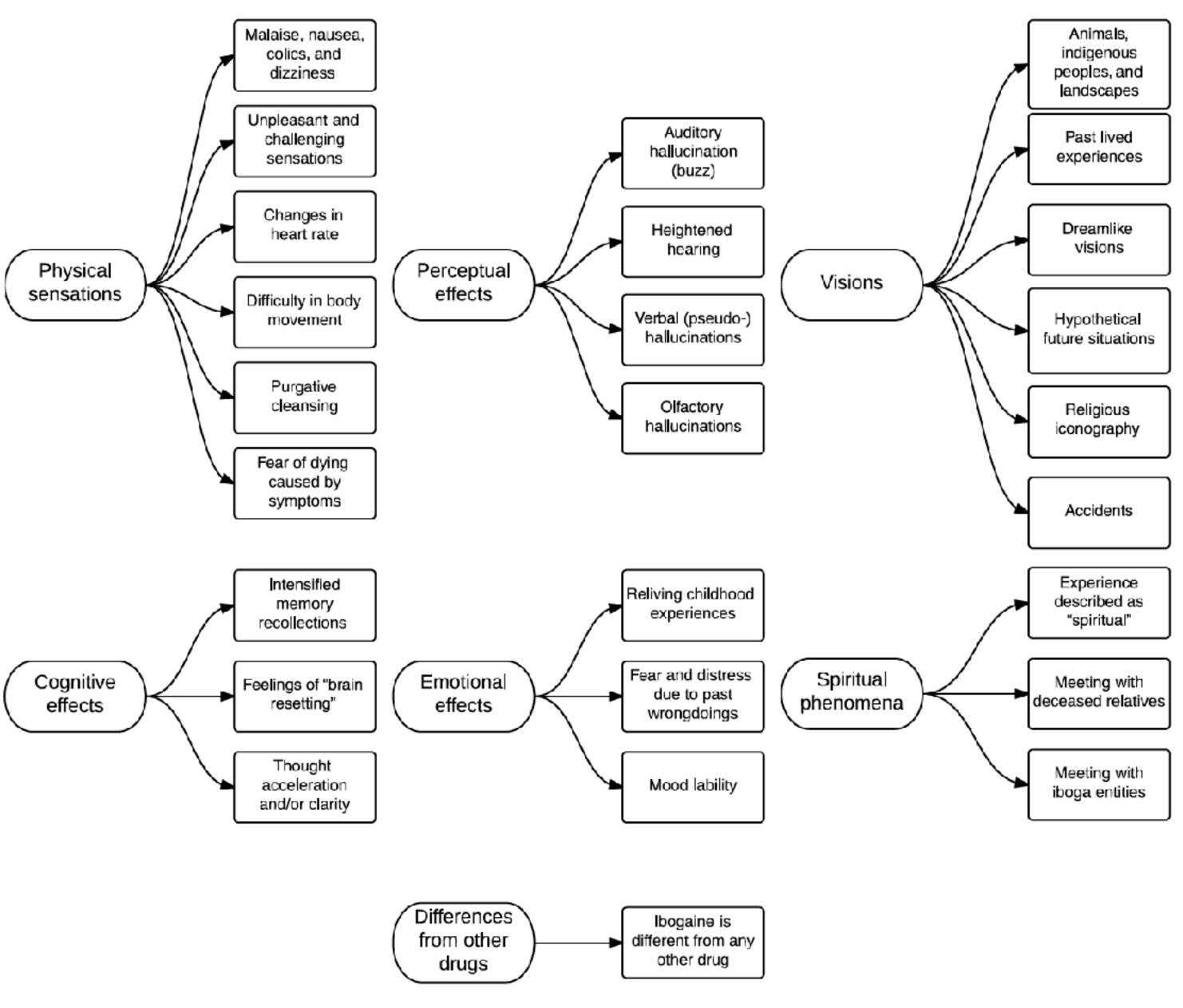


Figure 1. Themes and categories of the phenomenological description of the ibogaine experience reported by 22 patients that underwent combine ibogaine and cognitive behavior therapy in Brazil that emerged using interpretative phenomenological analysis

JOURNAL OF PSYCHOACTIVE DRUGS https://doi.org/10.1080/02791072.2019.1598603



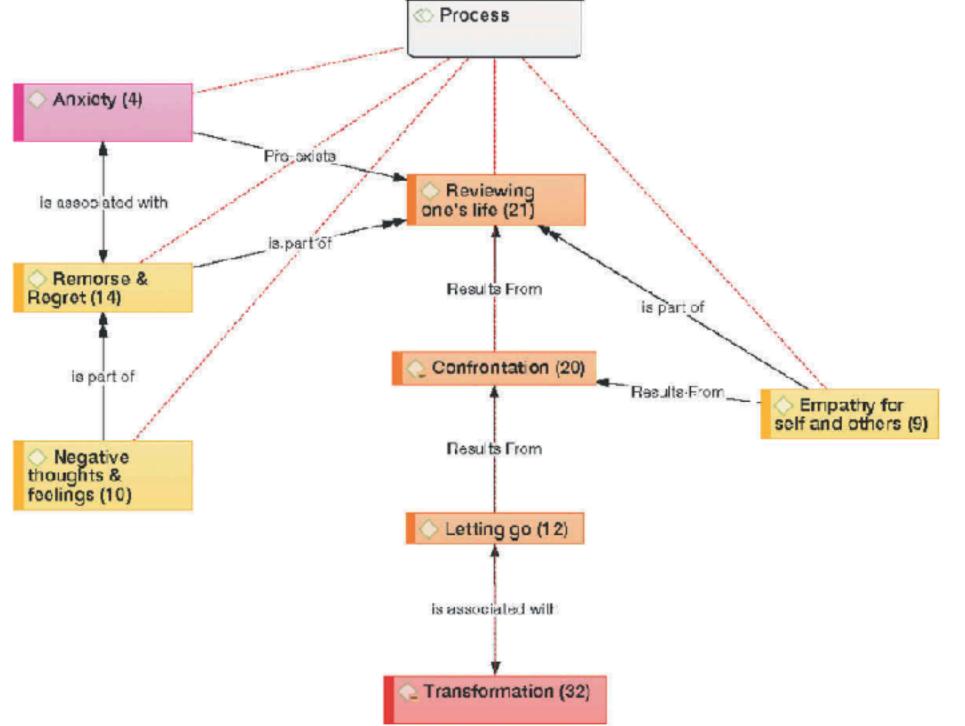
ARTICLE

Check for

Ibogaine and Subjective Experience: Transformative States and Psychopharmacotherapy in the Treatment of Opioid Use Disorder

Thomas K. Brown, PhDa, Geoff E. Noller, PhDb, and Julie O. Denenberg, MAc

^aAcademic Enrichment Programs, UC San Diego, La Jolla, CA, USA; ^bDepartment of General Practice and Rural Health, School of Me University of Otago, Aotearoa, New Zealand; ^cDepartment of Family Medicine and Public Health, UC San Diego, La Jolla, CA, USA



Higher-Order Construct	Grouped Themes (Number of Utterances, $n=x$)	Examples of Quotes
		<u>' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' </u>
Visions (n = African ima Colors (n = Spirit being	Auditory effects ($n = 15$)	"The first thing I began to notice was auditory—the sound like a water bottle caught in suction. A suction sound that turned into an insectoid buzzing sound." (S21, Mexico)
	Visions $(n = 21)$	"I remember one of the Bwiti slightly trembled and the Iboga spirit shook like a rattle." (S018 New Zealand)
	African images $(n = 9)$	"I also saw African things, wilderness, lions. Tribesmen. And this cycle was repetitive." (S23, Mexico)
	Colors $(n = 7)$	"Music was enhanced, and the sound was morphed into angelic sounds and colors." (S5, Mexico)
	Spirit being (n = 9)	"My first vision was of an African man who was very small in stature. He came and sat on m bed. I remember being really pleased to see him. I knew that he only had love for me and wa there to help." (S007, New Zealand)
	Planets, Earth, cosmic images $(n = 16)$	"We flew through the solar systems and came back to Earth." (\$21, Mexico) "The visions I remember most were Sci-Fi, like Star Wars." (\$005, New Zealand)
Perceptions	Physical experience of vision ($n = 15$)	"I felt my withdrawal symptoms begin to subdue. I felt a band of numbing ecstasy string across my body which took all the withdrawal away." (\$18, Mexico)
Negative references to impact of druct taking $(n = 7)$ References to family $(n = 15)$	Negative references to impact of drug	"I was mournful of the damage I'd done to my body and to my relationships with family an
		friends." (S28, Mexico) "There was some really horrible stuff, like my father saying: You stupid little bitch!" (S008, New Zealand)
		"I saw my family from young to older and how everything has been and how I affected them. (59, Mexico)
Cleansing/healing ($n = 8$) Sense of oneness with everything ($n = 8$)	"My brain was being repaired, rewired. When it passed over bits that needed damage control it would pop the damaged bit, like bubble wrap." (\$019, New Zealand)	
	Sense of oneness with everything $(n = 7)$	
Process	Anxiety $(n = 4)$	"On the day of my treatment, I remember sitting on the step outside my house, unable to sto shaking and trying not to back out of the plan that we had so carefully made." (\$007, New Zealand)
	Reviewing one's life $(n = 21)$	"I kept seeing clips—real memories, of high-school girlfriends and playing music with friend —but then also clips of the present day in an alternate reality where I hadn't squandered s much love or compassion that had been offered to me." (\$21, Mexico)
	Negative thoughts and feelings ($n = 10$)	"Many of these thoughts were reflections of my past, mainly my failures. When these feeling became intense I became very overwhelmed and upset at times." (\$15, Mexico)
	Empathy $(n = 9)$	"I was also able to begin to see how, because I felt so unlovable, I paid in one way or another for love. I was able to stop that and open myself up to real love for maybe the first time in madult life." (S2, Mexico)
	Confrontation $(n = 20)$	"In the various body motions crippled in pain I would feel the Iboga spirit meeting me in a wrestling combat." (S018, New Zealand)
	Letting go $(n = 12)$	"Around the time of my father's death, I had acquired from Dad a relentless and very negative voice in my head. During my journey, this voice left me. It was extraordinary! It was like a tape loop in my head broke and the tape spun off into space. It was so noticeable that
	Transformation $(n = 32)$	I could sense the space in my mind that was freed up by its departure." (S2, Mexico) "I awoke 3 days later in tears of joy KNOWING that I was never alone and never would be alone and that death is just a doorway to another reality." (S18, Mexico)



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