# EEG studies of the acute effects of 5-MeO- DMT.

WBAC, CDMX July 27-29, 2018

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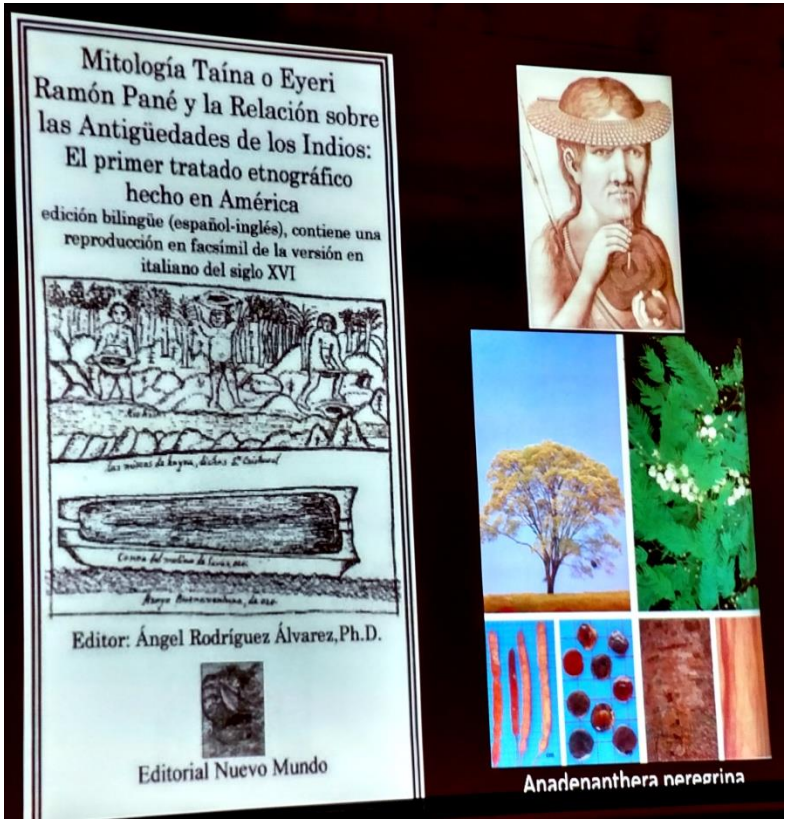
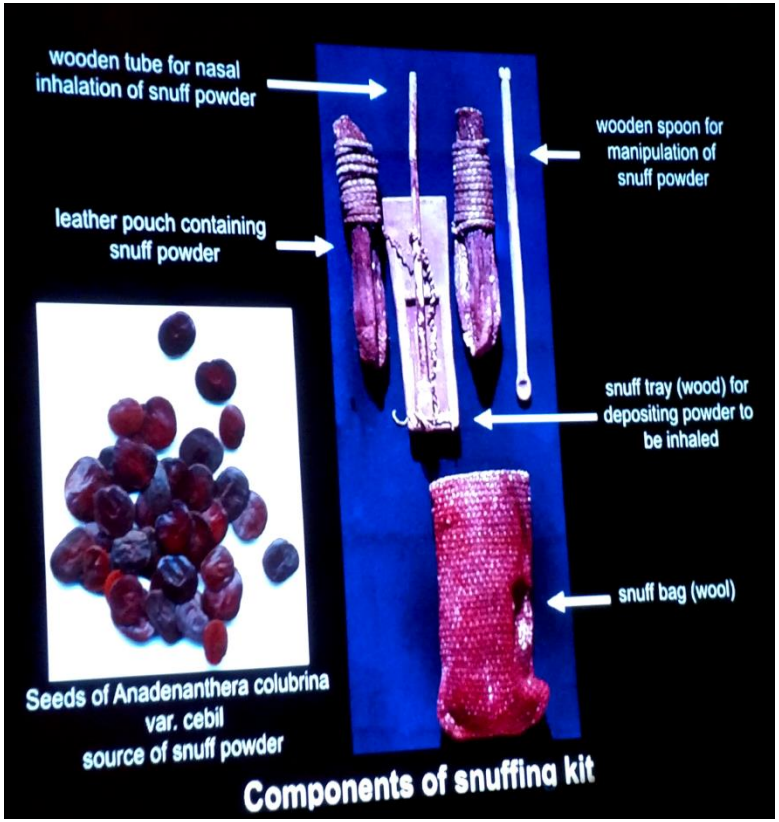
# New World use of 5-MeO-DMT plant preparations is ancient.




Left. 16th century Spanish Ethnographical treatise on A. peregrina insufflation by Native Americans. Courtesy L.E. Luna; right. Snuff kit containing A colubrina residue unearthed in grave site, Peru.

# Chemical analysis of 5-MeO containing plants

**1936, 5-MeO-DMT synthesis.** T. Hoshino and K. Shimodaira

**1953. First DMT trip report** (S. Szara (2007) **Neuropsychopharmacologia Hungarica, IX/4;201-205.)**

**1955**. (on the chemical constituents of the cohoba snuff used by indigenous South American tribes to induce states of religious ecstasy. Bufotenine and 5MeO-DMT in Cohoba snuff). Fish,Johnson and Horning. Piptadenia Alkaloids Indole bases of *P. peregrina,* Benth and related species**. J. Am. Chem. Soc. 77: 5892-5895.**

**1959 "Discovered" in S. America 3000+ yo Shamanic tradition. Schultes RE (1969) Virola as an orally administered hallucinogen. *Harvard Bot Mus Leaflets* 22:229–240**

**1959 Cohoba snuff, *Yopo*** *(A. peregrine);A. colubrine* (Peru), still in use today Orinoco basin tribes; Yanomani, Piaroa, S. America and Caribbean. Indole Alkaloids of *Acer saccharinum* **(the Silver Maple),** *Dictyoloma incanescens, Piptadenia colubrina, and Mimosa hostilis***.** Pachter, IJ et al. ***J. Org. Chem.*****,** 1959**, *24* (9), pp 1285–1287**

McKenna,D and Riba, J. New World Tryptamine Hallucinogens and the Neuroscience of Ayahuasca. ***Curr Topics Behav Neurosci*. 2015, 368**

Contemporary Yanomani tribe Yopo snuff session.

# 5-MeO-DMT (5-Methoxy)

1936. 5-MeO-DMT T. Hoshino and K. Shimodaira

Hoshino, Toshio & Kenya Shimodaira. 1936. "Über die Synthese des Bufotenin-Methyl-Äthers (5-Methoxy-N-Dimethyl-Tryptamin) und Bufotenins. Synthesen in der Indol-Gruppe. XV," Bulletin of the Chemical Society of Japan 11: 221-224.

1953. First DMT trip report (Szara)

1955. Bufotenine and 5MeO-DMT in Cohoba snuff (Fish, M.S. et al. Piptadenia Alkaloids Indole bases of P. Peregrina (L.) Benth. and Related Species. J. Am. Chem. Soc., 77:5892-5895.

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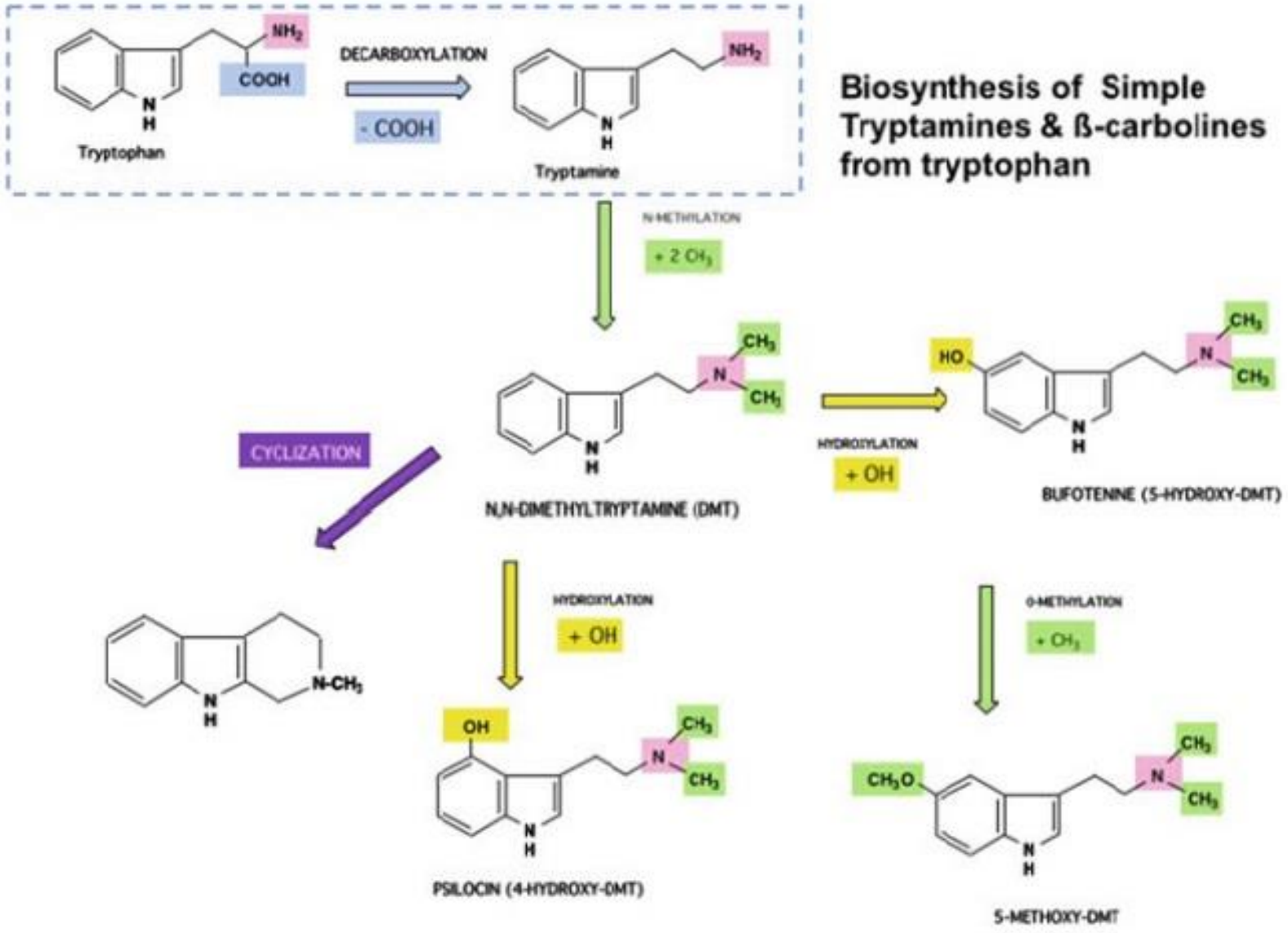
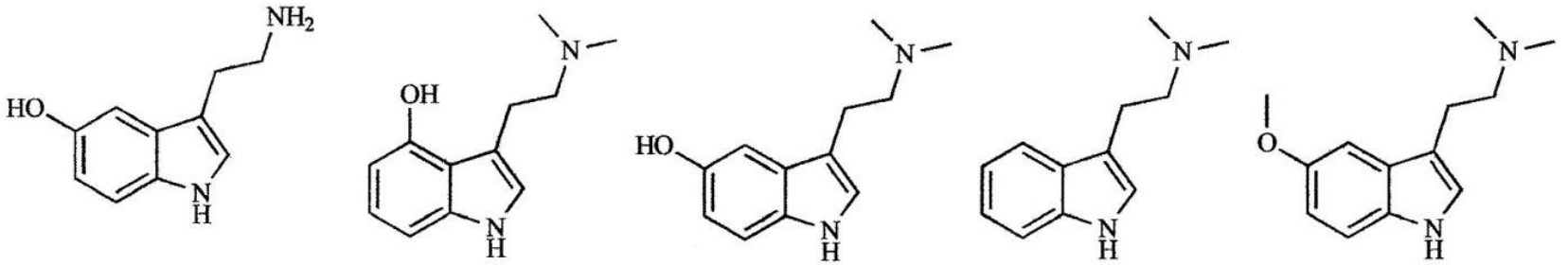



**Fig. 1** Biosynthesis of simple tryptamines and ß-carbolines from tryptophan

**Tryptamines**




LSD-25, Psilocin, DMT bind to 5-HT1A/2A/2C Serotonin receptor subtypes; the 5-HT2A is critical site. Review: The behavioral pharmacology of hallucinogens. W E. Fantegrossi a,*, K. S. Murnane , C. J. Reissig et al. *Biochemical Pharmacology 7 5 (2 0 0 8) 1 7– 3 32*

## DMT biogenesis: new research

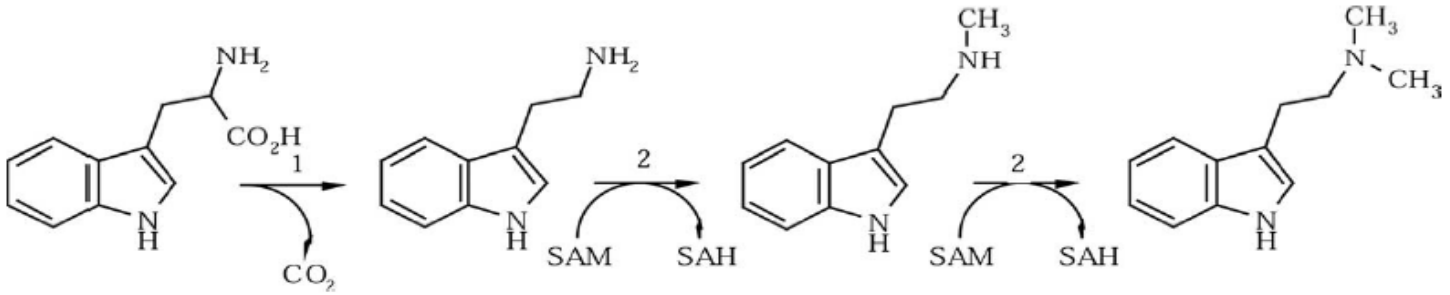
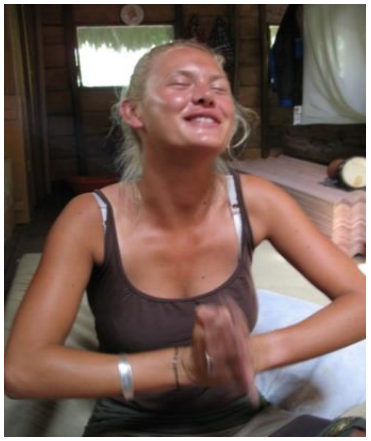
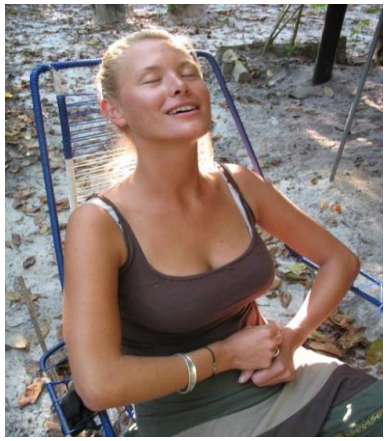



**Figure 1** Biosynthesis of DMT from the amino acid tryptophan: (1) aromatic amino acid decarboxylase (AADC) catalyzes the formation of tryptamine from tryptophan; (2) indolethylamine-*N*-methyltransferase (INMT) transfers a methyl group from SAM (S-adenosylmethionine) to tryptamine, yielding *N*-methyltryptamine (NMT). A repeat of this reaction (2) with NMT as the substrate transfers another methyl group and yields DMT and two equivalents of SAH (S-adenosylhomocysteine).

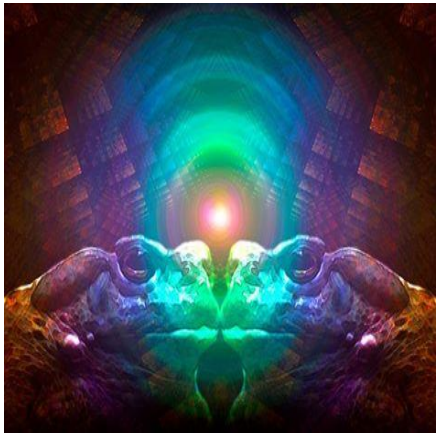
- The purpose of these studies was to explore the EEG acute effects of smoked (vaporized) N,N-Dimethyltryptamine (Mimosa DMT, 25 mg), and 5-MeO-DMT on a group of participants with their full consent. Bufo 5-MeO was tested (30 mg) and synthetic 5-MeO (10 mg).
- These experiments were carried out over the past years in Peru and Mexico.
- DMT is an endogenous molecule present in our brain and peripheral tissues. It is posited to act as a neuromodulator, but it's exact physiological role remains poorly understood.
- Smoked inhalation of DMT produces a very extraordinary reversible alteration of consciousness lasting 10-30 min. The magnitude of the EEG effects correlated with the intensity of the subjective experience.
- A subjective report of the DMT-induced experience was also video recorded. This study therefore, is a neurophenomenological approach to studying consciousness under the effects of a powerful psychedelic.

# 5-MeO-DMT early QEEG explorations.



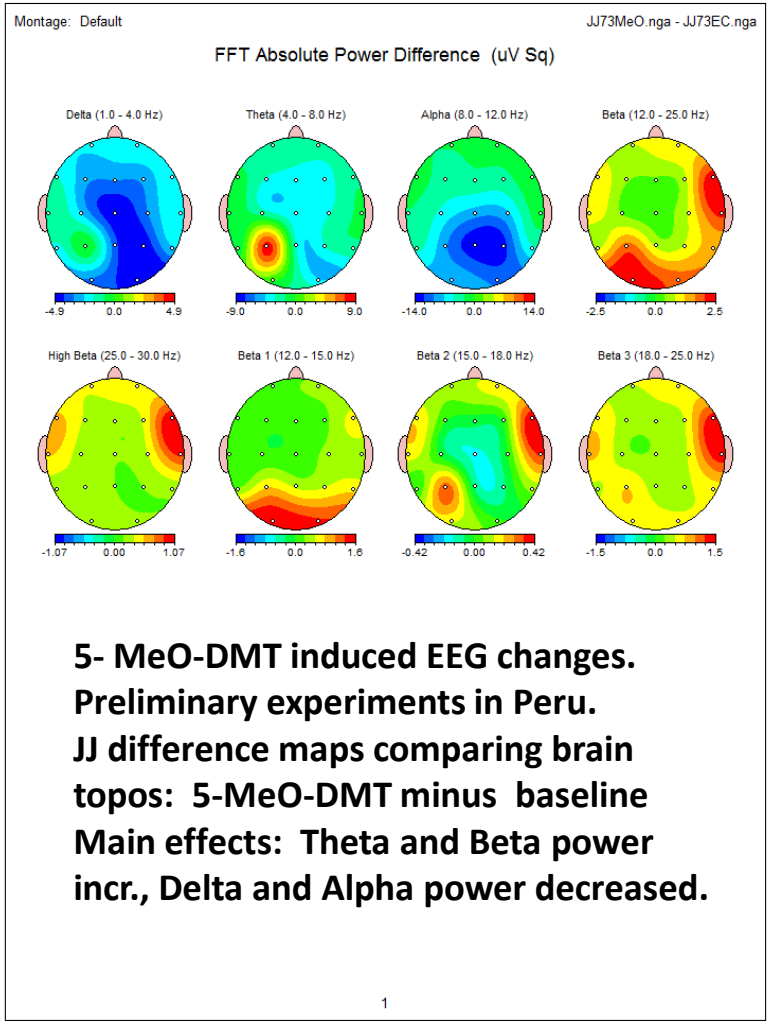


Iquitos, Peru, 2006

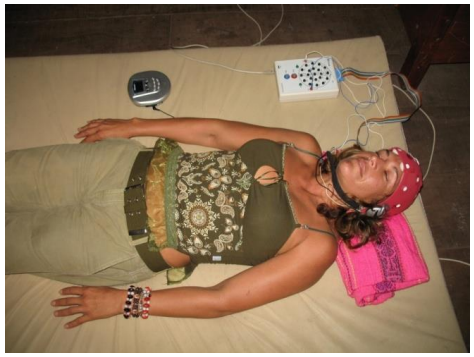

Bufo 5-MeO-DMT EEG sessions in Mexico with TI

# Iquitos, Amazon, Peru

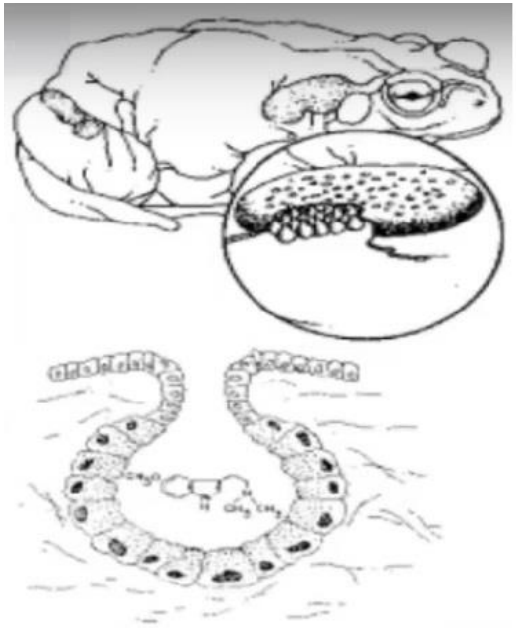


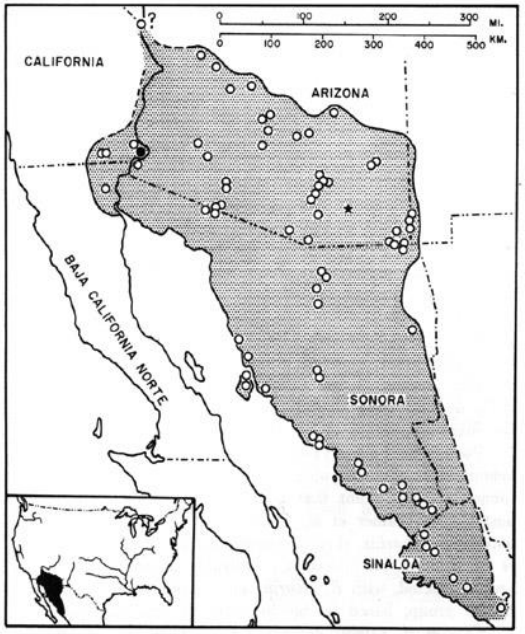

**5- MeO-DMT induced EEG changes.**
**Preliminary experiments in Peru.**
**JJ difference maps comparing brain topos: 5-MeO-DMT minus baseline**
**Main effects: Theta and Beta power incr., Delta and Alpha power decreased.**

1



# *Bufo alvarius*, Sonoran Desert Toad





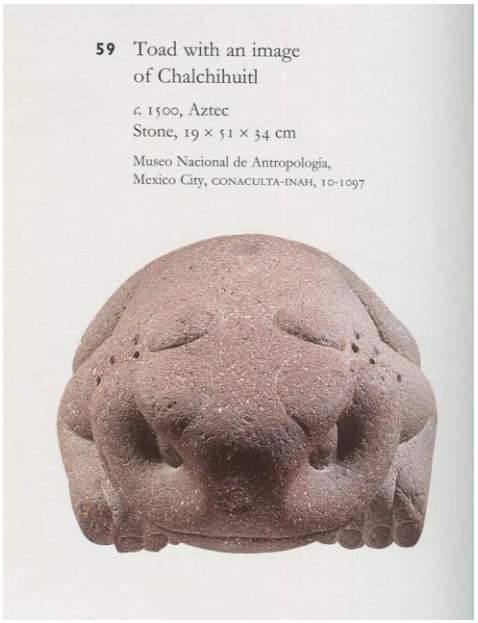

MAP. The solid circle marks the type-locality; open circles indicate other records. The star marks a fossil locality.

Detail of parotid gland

There are more than 260 species of Bufo (e.g. *Bufo marinus,* high toxicity*),* but only Bufo alvarius is known to contain 5-MeO-DMT in it's glands.

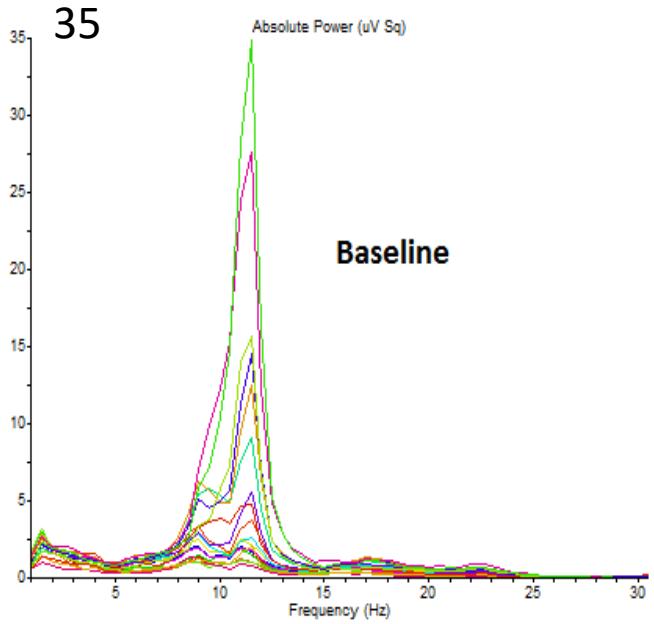
Venom glands are potent source of 5-MeO-DMT. HPLC and NMR analysis of my EEG test sample revealed it was 95%  5-MeO-DMT.

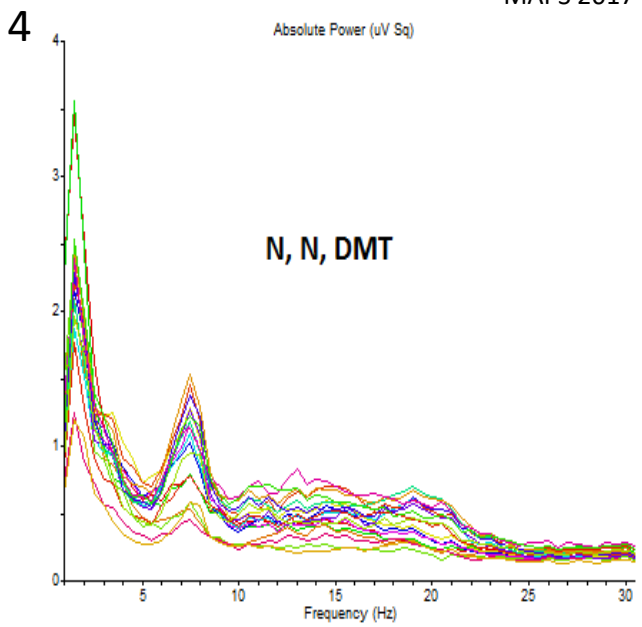
# *Bufo alvarius* in ancient Mesoamerica

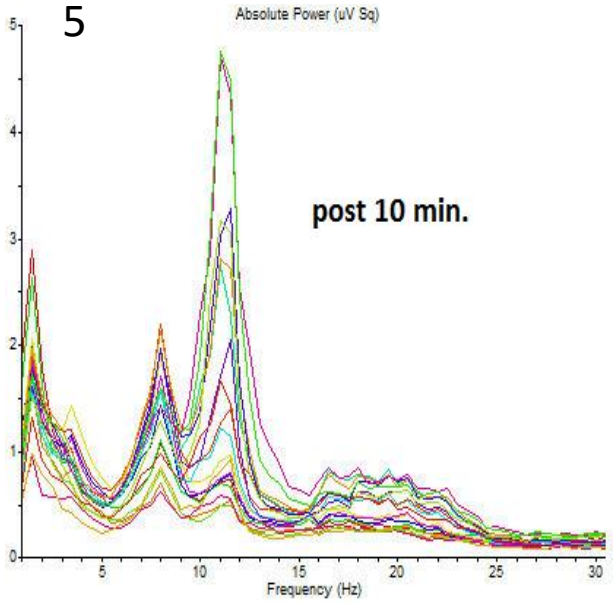



Ritual use of *Bufo* secretion (smoked inhalation, insufflation), dates back thousands years in Mesoamerica. Bufo skeleton remains found throughout archaeological sites and extensive pictorial and sculpture representations..

Davis W and Weil AT **Identity of a New World Psychoactive Toad.** Ancient Mesoamerica vol. 3, Issue 01: 51-59, 1992.
Weil AT, Davis W ***Bufo alvarius*: a potent hallucinogen of animal origin.** *J. Ethnopharmacology.* vol 41: 1-8, 1994.

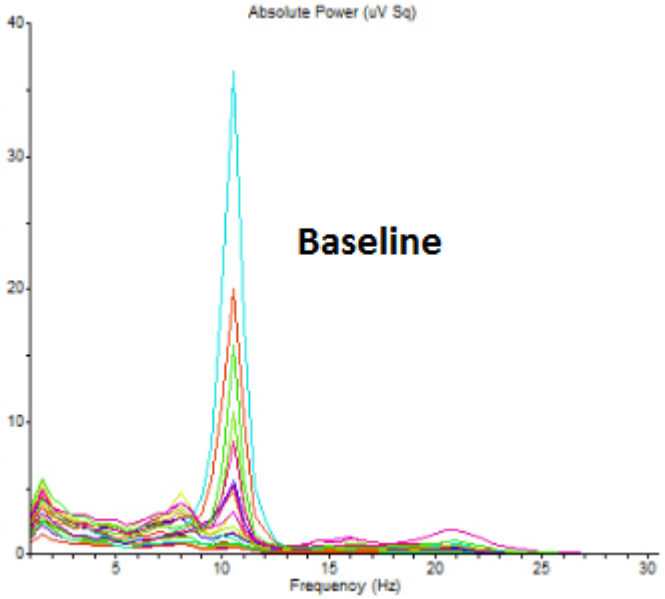


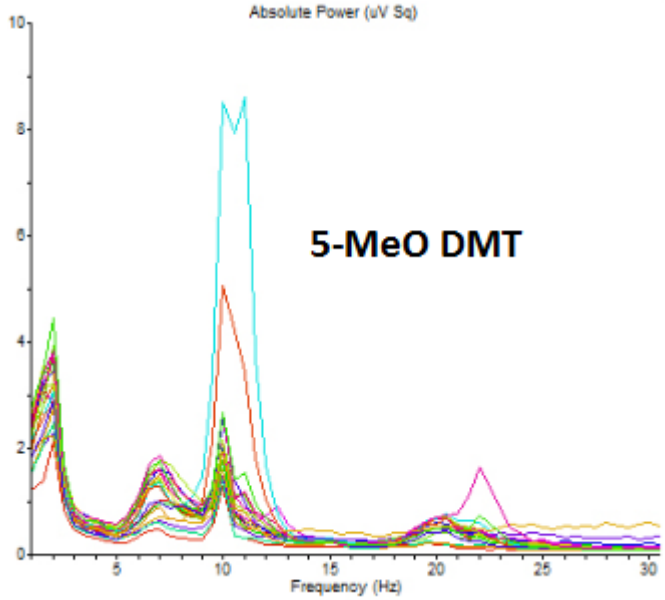




FFT power-frequency spectra shows marked **N,N-DMT-induced suppression of Alpha power (96% decrease)** and the appearance of new slower peak at ca. 8 Hz. Dominant peak (ca. 11 Hz) shows partial recovery at 10 min. post. Note diff. power scale y-axis. **Acosta-Urquidi J , 2015**

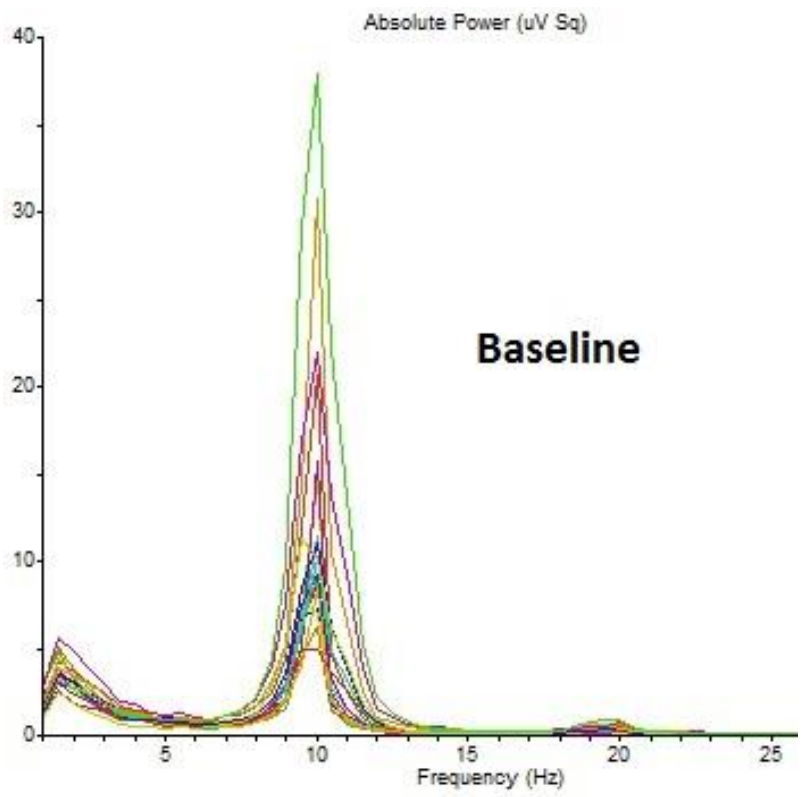
Current source density (CSD) analysis revealed **areas of significant CSD decreases in the alpha band of the EEG** following two consecutive doses of 0.75 mg DMT/kg ayahuasca. Riba, J. et al. 2004 *Neuropsychobiology* 50:89–101.

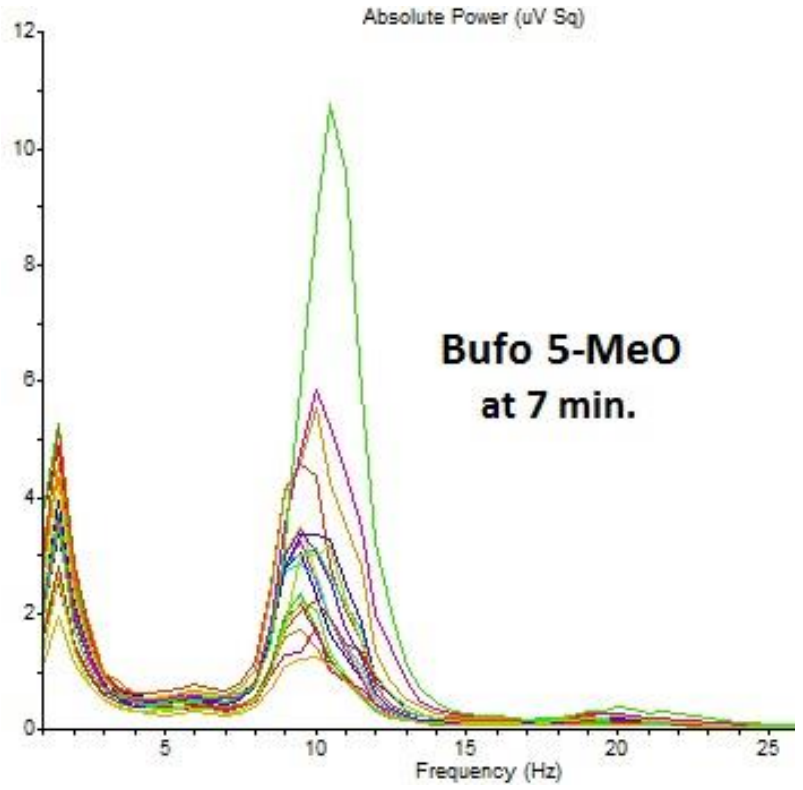



**QEEG 5-MeO DMT sessions Iquitos, Peru 2009**



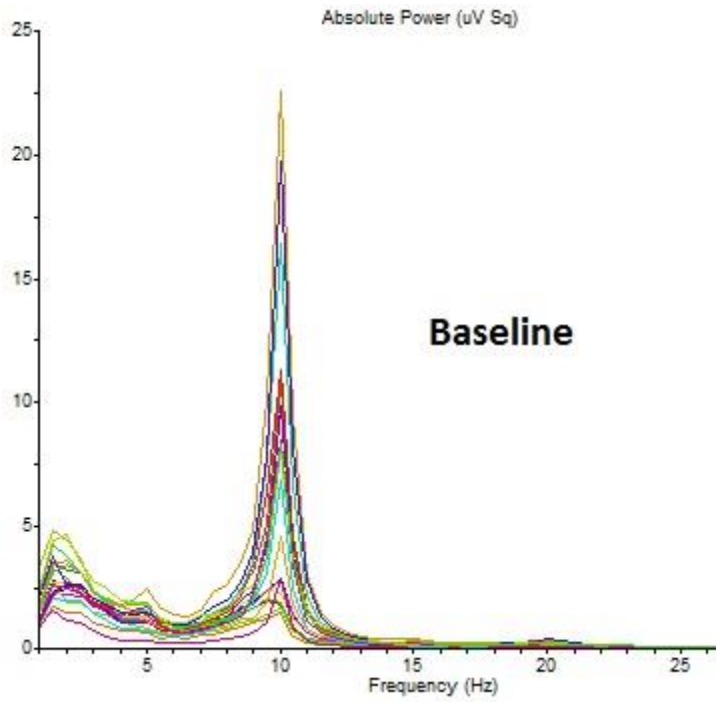

Comparison of FFT power spectra shows 5-MeO-DMT induced robust suppression of Alpha peak. Note scale difference uV2.

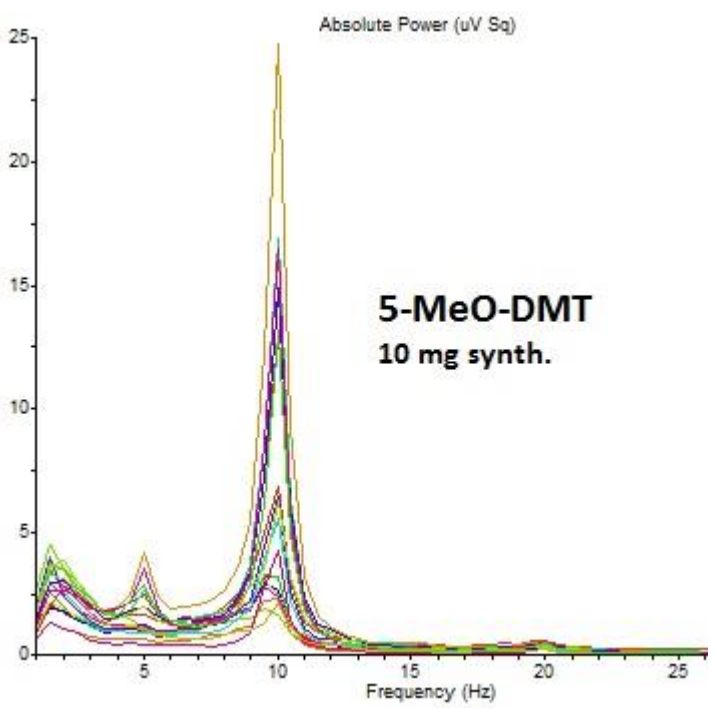



Bufo 5-MeO-DMT induced suppression of Alpha power(70% decrease)

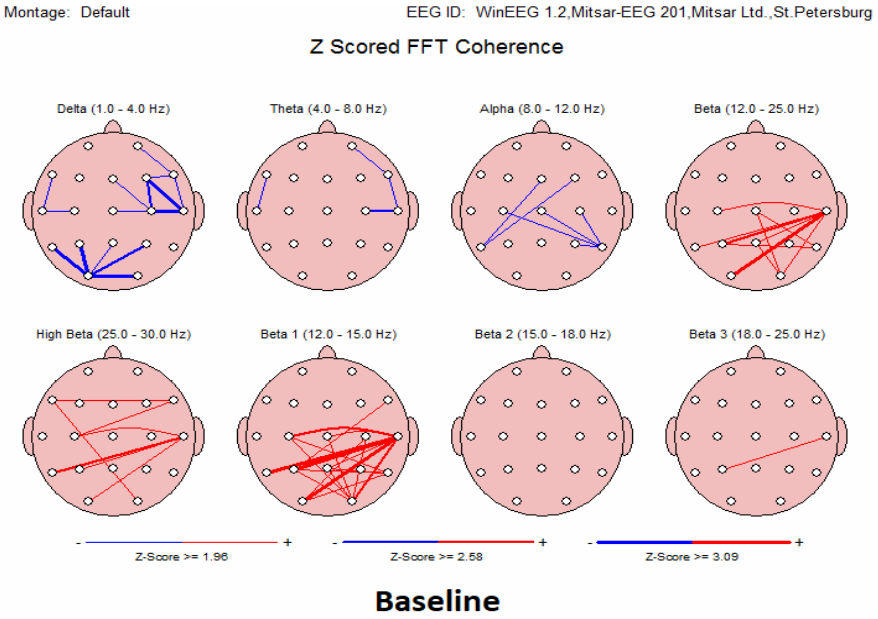
# Synthetic 5-MeO-DMT



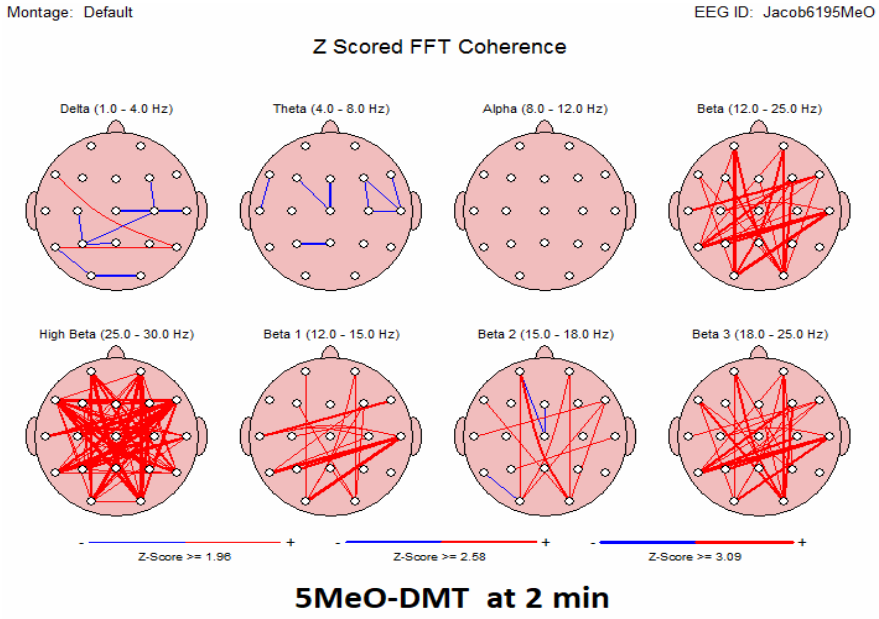




Comparison FFT spectra reveals new Theta peak ca. 5 Hz induced by 5-MeO-DMT synth, 10 mg inhalation.

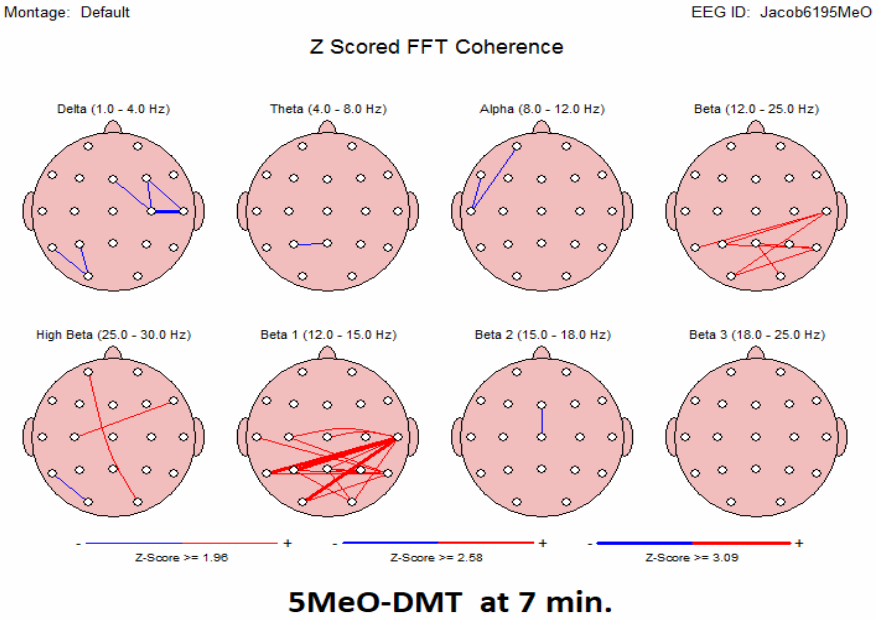
# Bufo 5-MeO-DMT induced Hypercoherence




**Baseline**




**5MeO-DMT at 2 min**

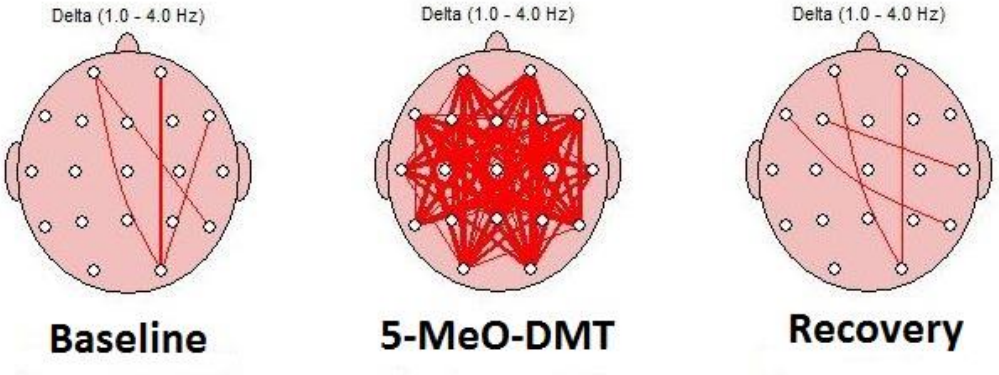



**5MeO-DMT at 7 min.**

Hypercoherence in Beta bands reversed toward Baseline at 7 min. post 5MeO inhalation.

Bufo 5-MeO increased coherence

# 5-MeO-DMT increased Coherence

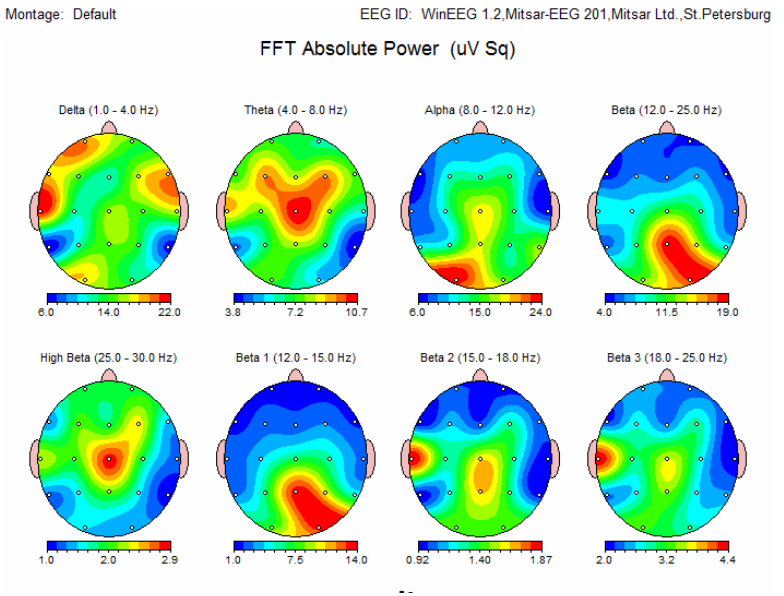


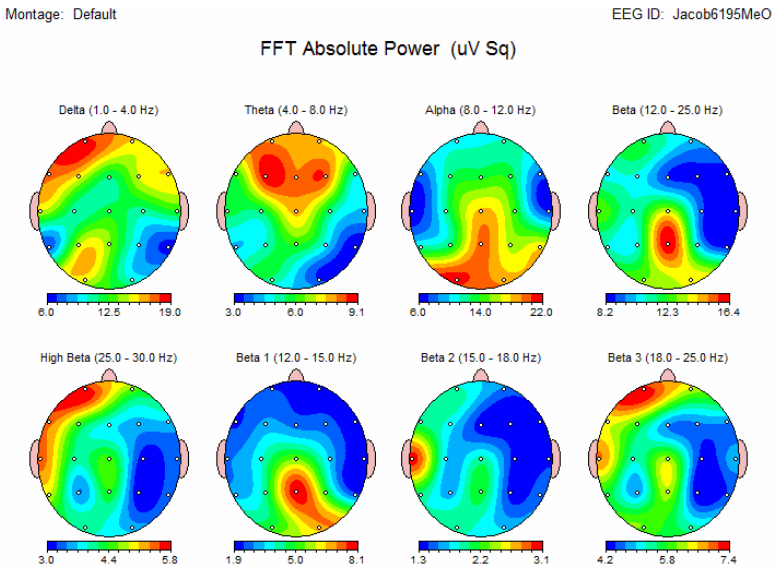

**Delta**

**High Beta**

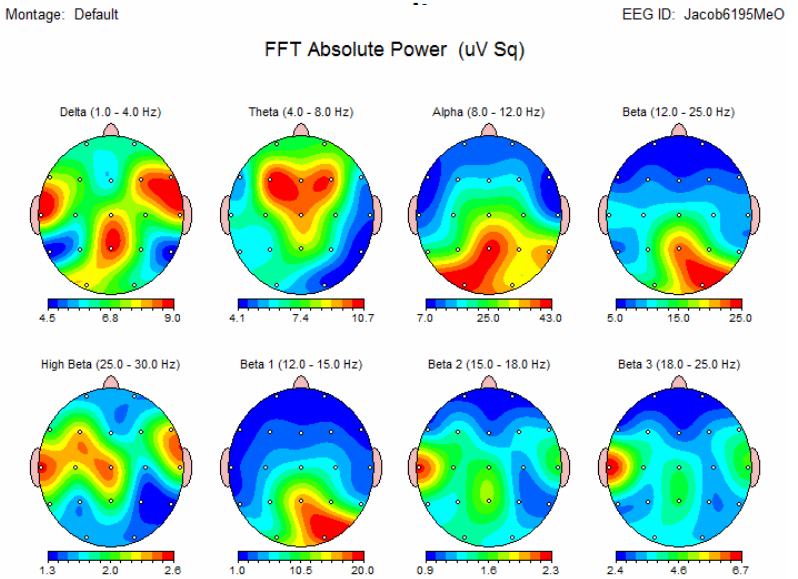
**5-MeO-DMT induced reversible increase in Coherence.**
**Examples of Delta (1-4 Hz, top) and High Beta (25-30 Hz, bottom) hypercoherence and recovery at 15-20 min. post, recorded in two different subjects.**
**Acosta-Urquidi,J (2015) *Cosmos and History* 11(2).**

# Synthetic 5MeO-DMT




**5MeO-DMT 10 mg at 2 min.**

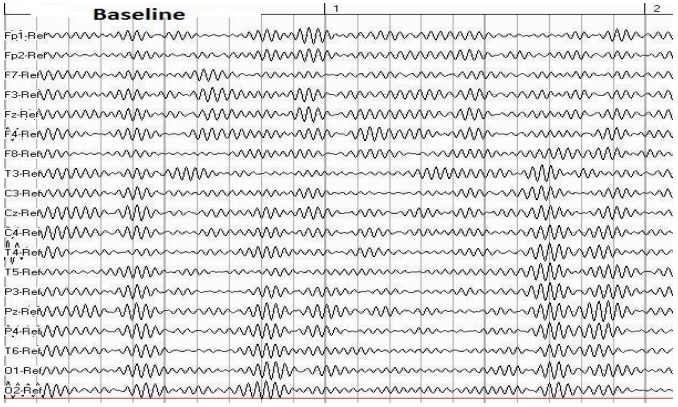



**5MeO-DMT at 7 min.**

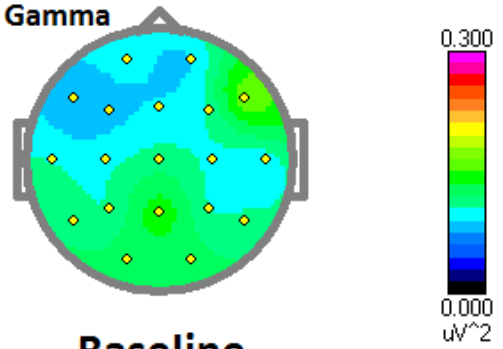
Absolute power uV2 max. values

| | Baseline | 5MeO 2 min | 5MeO 7 min |
|---|---|---|---|
| D | 22 | 19 | **9.0 *** |
| T | 10.7 | 9.1 | 10.7 |
| A | 24 | 22 | **43 *** |
| B1 | 14 | **8.1 *** | **20 *** |
| B2 | 1.9 | **3.1 *** | 2.3 |
| B3 | 4.4 | **7.4 *** | **6.7*** |
| HiB | 2.9 | **5.8 *** | 2.6 |

# 5-MeO-DMT induced Gamma power increase

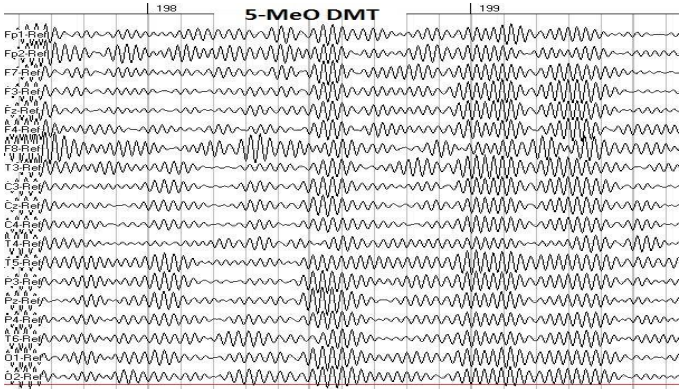



**Baseline**

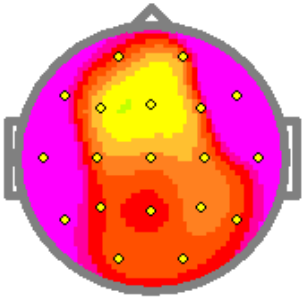



**Baseline**

**Increased Gamma (38-40 Hz) power during 5-MeO-DMT acute effects**




**5-MeO-DMT**



**5-MeO**

Topographic maps show robust increase in Gamma power (38-40 Hz) during Bufo 5-MeO-DMT (40 mg) inhalation.

**TABLE. Summary of N,N-DMT effects on absolute power comparisons (mean +- SEM) for all EEG frequency bands.**

| Frequency band (Hz) | Baseline | N,N-DMT | % change | P value* |
|---|---|---|---|---|
| Delta (0.1-4) | 22.2 +-3.5 | 18.5 +-3.6 | 17 ↓ | N.S. (N=17) |
| Theta (4-8) | 17.97 +-3.54 | 10.06 +-1.05 | 44 ↓ | .018 (N=17) |
| Alpha (8-12) | 133.65 +-27.06 | 17.2 +-4.4 | 88 ↓ | .0012 (N=17) |
| Beta 1 (12-15) | 16.23 +-4.16 | 5.63 +-2.0 | 65 ↓ | .002 (N=17) |
| Beta 2 (15-18) | 5.3 +-0.7 | 2.73 +-0.4 | 49 ↓ | .0001 (N=16) |
| Beta 3 (18-25) | 2.63 +-0.5 | 2.21 +-0.3 | -------- | .013 (N=6) |
| Hi Beta (25-30) | 2.74 +-0.8 | 4.53 +-1.13 | 65 ↑ | .05 (N=10) |
| Gamma (38-40) | .061 +-.003 | 0.145 +-.011 | 138 ↑ | .0001 (N=20) |

***(correlated paired t-test)**

**5-MeO-DMT acute effects showed some overlap with N,N-DMT. In some cases a Theta peak was expressed and Alpha peak reduced. Overall Alpha power was suppressed ave. 72% (N=11). Gamma power increased ave. 106%; (mean +-SEM) baseline, .07+-.003 vs 5MeO, 0.144+-.015, P<.0001 (N=20).**

Acosta-Urquidi, J. 2017, EEG studies of the acute effects of the visionary tryptamine DMT. Advances in Psychology Research Vol.130, Nova Science Publishers

# Tryptamines and 5-HT Receptor interactions

Nichols, DE. Psychedelics. *Pharmacol. Review* 2016, 68(2),264-355, presents this scheme for tryptamine serotonin receptors:

Brain 5-HT2AR (a member of family of G-protein coupled receptors (GPCRs) are the key targets for psychedelics.

**N,N-DMT** target 5-HT2A, 5-HT2C and 5-HT1A.

Other studies implicate Sigma-1 receptors (Fontanilla,D. et al. *Science* 13;323(5916), 934-7., and downstream 2nd messenger cascade via mGluR2 activation. (Carbonaro et al. 2014. *Psychopharmacology* DOI 10.1007/s00213-014-3658-3.

**5-MeO-DMT** targets 5-HT1AR, 2A and 2C, 5-HT7

Jiang,X., et al. 2013 .Pharmacokinetic interactions between monoamine oxidase A inhibitor harmaline and 5-methoxy-N,N-dimethyltryptamine, and the impact of CYP2D6 status***. Drug Metabolism and Disposition 41:975–86***

# Bufo 5-MeO purpose

- Heal traumatic experiences
- Release energetic residue, blockages and resistance patterns
- Expand fully into one's true energetic state
- Perceive and experience the fundamental energetic unity of all things, life and consciousness
- Achieve personal clarity into one's true nature
- Liberation from all personal imaginary limitations and ego produced perceptions and fears

From Dr Gerry's presentation, London 2017

# Phenomenology of 5-MeO experience

*"Our normal waking consciousness, rational consciousness as we call it, is but one special type of consciousness, whilst all about it, parted from it by the filmiest of screens, there lie potential forms of consciousness entirely different. We may go through life without suspecting their existence; but apply the requisite stimulus, and at a touch they are there in all their completeness, definite types of mentality which probably somewhere have their field of application and adaptation. No account of the universe in its totality can be final which leaves these other forms of consciousness quite disregarded."* ***William James (1902), The Varieties of Religious Experience***

**Entheonaut descriptions of 5-MeO-DMT experience :**

**The God Molecule**, **Rocket trip into the void**, **Astral propellant, Spiritual tuneup, Death and rebirth**,**Spiritual rocket fuel for mapping the limits of consciousness**,**This is it**, **Meeting the Godhead**, **Pure love light consciousness**, **Profound life changing spiritual experience, Soul journey to the ultimate reality of love, Source of Intelligence, Experiencing soul consciousness, Union with the matrix**

# 5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT): Patterns of use, motives for consumption, and acute subjective effects

Alan K. Davis, PhD[1,2,3], Joseph P. Barsuglia, PhD[3], Rafael Lancelotta, BA[3,4], Robert Grant, MD[5], Elise Renn, BS[3]

[1]Dept. of Psychiatry, Behavioral Pharmacology Research Unit, Johns Hopkins University School of Medicine,
[2]Dept. of Psychiatry, University of Michigan, [3]Source Research Foundation, [4]University of Wyoming, [5]University of California San Francisco

## Introduction

- 5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT) is a natural psychoactive indolealkylamine substance found in several plants and in high concentrations in Bufo alvarius toad venom.
- 5-MeO-DMT is a potent, fast-acting, psychedelic substance. In animal models, 5-MeO-DMT acts as a non-selective 5-HT agonist, active at both the 5-HT1A and 5-HT2A receptors.
- Human self-experiments describe the subjective effects of synthetic 5-MeO-DMT as similar to other classic hallucinogens, including a distortion in time perception, and auditory and visionary distortions, with peak effects between 35-40 minutes after insufflation. Inhalation (e.g., smoking or vaporizing) is also a common means of consumption with initial onset of effects within 60 seconds and peak total duration of effect between 5 and 20 minutes.
- Motivations to use include spiritual, recreational, and psychotherapeutic experiences, but prevalence and use characteristics are unknown. Furthermore, a lack of empirical evidence limits understanding of the potential clinical applications of 5-MeO-DMT which are reported to be similar to other tryptamines (e.g., psilocybin).

## Primary Study Aim

- Examine the patterns of use, motivations for consumption, acute subjective effects, and potential consequences and psychotherapeutic effects of 5-MeO-DMT among an international sample of 5-MeO-DMT users.

## Method & Data Analysis

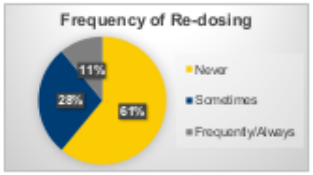
- Using internet-based advertisements we recruited English-speaking adults to complete an anonymous web-based survey.
- We conducted frequency counts and descriptive analyses of demographic characteristics, patterns of using 5-MeO-DMT, motivations for consumption, acute subjective effects, and biomedical/psychiatric harms/benefits variables.

## Sample Characteristics

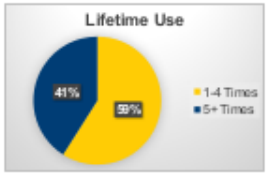
- The sample (**n=515**) was comprised of primarily middle-aged ($M_{age}$=35.4. SD=11.7), Male (79%), White/Caucasian (86%) individuals, less than half (42%) residing in the US.
- Type of 5-MeO-DMT used:

  Synthetic (n=284); Toad (n=148); Plant/Yopo (n=83).

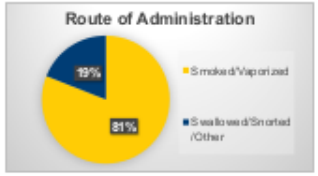
## Results

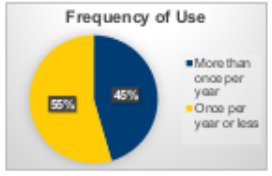


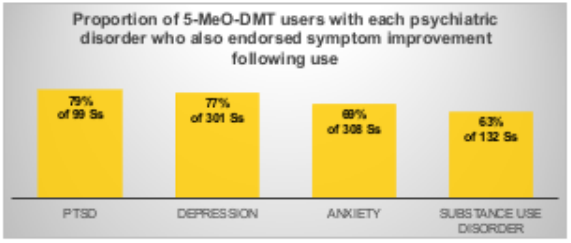


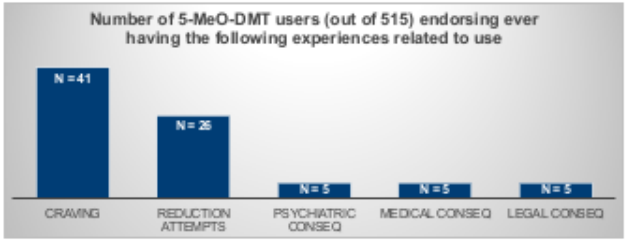


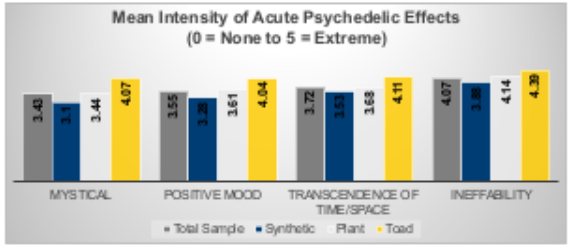


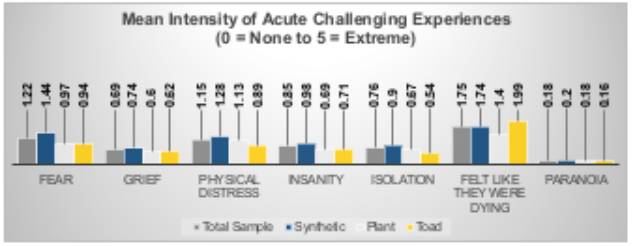



## Summary and Conclusions

- Similar to other psychedelic tryptamines, findings suggest that 5-MeO-DMT is used infrequently, predominantly for spiritual exploration, has low addiction liability, and might have psychotherapeutic effects.
- We recommend that future research examine the safety and pharmacokinetics of 5-MeO-DMT administration in humans using rigorous experimental designs.

## Funding and Contact Information

- AKD was initially supported by a postdoctoral training grant from NIAAA (AA007477) & is currently supported by a postdoctoral training grant from NIDA (DA07209). Source Research Foundation funded RL to provide administrative and research assistance on the study. The funding sources had no role in study design, data analysis, or interpretation.
- Contact email for AKD: **adavi157@jhmi.edu**

# Psychedelic Brain Science

- Psychedelics are valuable tools for the exploration of consciousness, objectively as neural correlates and subjectively.
- Psychedelics have been shown to suppress the part of the brain known as the default mode network (DMN), the neural network responsible for our autobiographical identity (sometimes called the ego). By dialing down the activity of the DMN, there occurs a large scale neural network reorganization. New networks and modes of thinking come into play, opening up our ability to experience life and reality in new ways.
- Disruption of the DMN,interrupting the hierarchical control systems and leading to a state of more global coherence and connectivity by interrupting more purposeful self- and ego-functioning and promoting a more global, multi-sensory state of awareness.

# The Spiritual Brain

- Our brain is designed with neural circuitry to perceive Music (the universality of music possibly even preceded language).
- Also, evidence suggests we have neural circuitry for experiencing Spirituality.

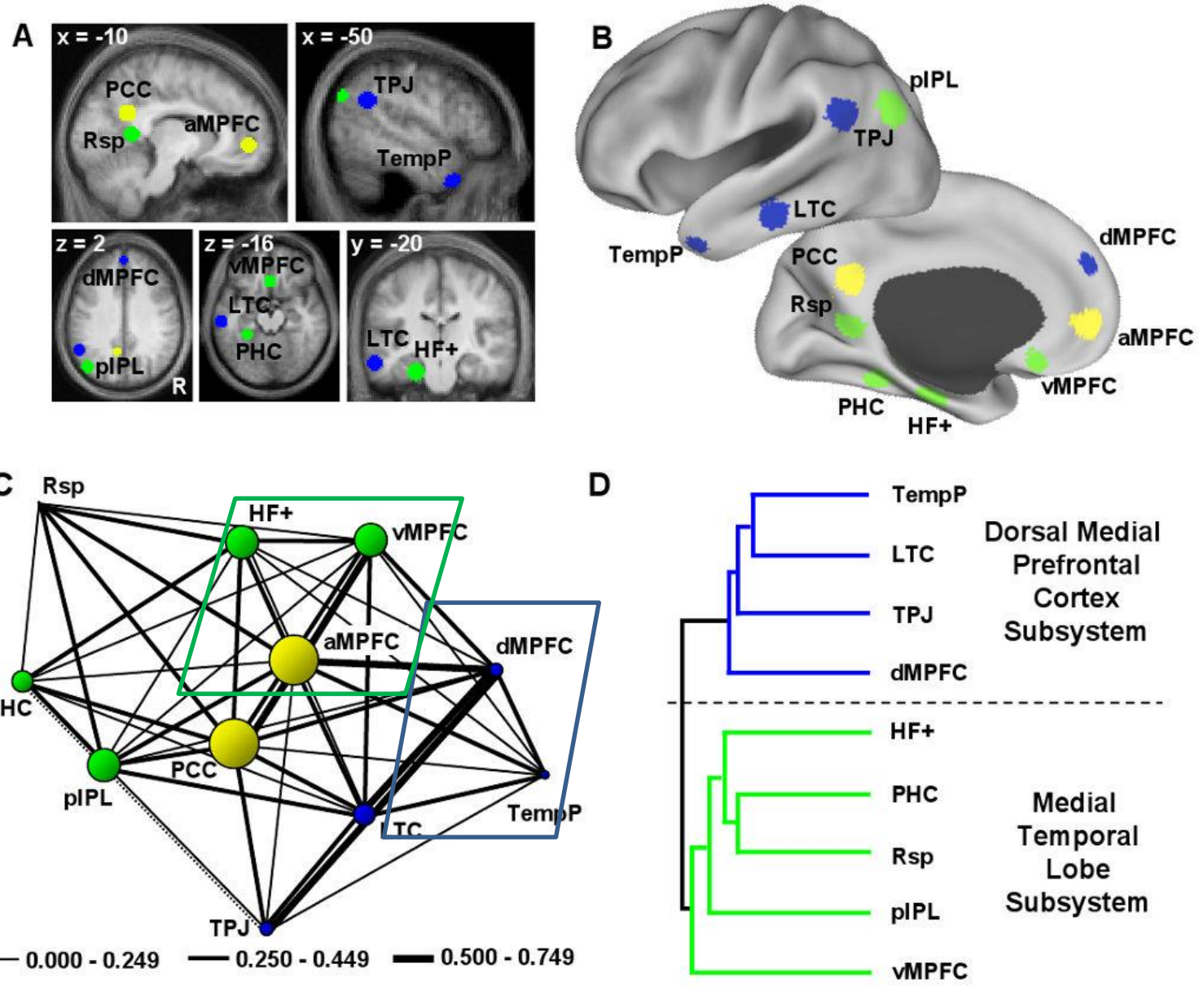
Paleoarchaelogical evidence suggests that the Human family all over the earth, from our early ancestors, have been making music. The Old and New World cultures also developed magico-religious rituals, inspired by the ingestion of psychoactive plant sacraments. 21st century Brain Science is discovering our brains are "wired" for music making and for experiencing transcendent spiritual states, posited to be the origins of religious activity.

**Where the Brain Processes Spiritual Experiences.**

*Summary: Researchers say the inferior parietal lobe, thalamus and caudate play key roles in processing spiritual experiences.* Miller, L. et al. 2018. Neural Correlates of Personalized Spiritual Experiences. *Cerebral Cortex;*1-8.

# Default Mode Network DMN

Andrews-Hannah, et al. *Neuron* (2010)



# DMN Default mode network

The DMN is a network of brain regions that are active when the individual is not focused on the outside world and the brain is at wakeful rest and not engaged in cognitive tasks with goal oriented actions. The activity of the DMN consists mainly of autobiographical ruminations. The DMN may correspond to task-negative introspection, or self-referential thought, and is characterized by dominant ego-consciousness. Its subsystems include part of the medial temporal lobe for memory, part of the medial prefrontal cortex for theory of mind, and the posterior cingulate cortex for integration,[5] along with the adjacent ventral precuneus [6] and the medial, lateral and inferior parietal cortex.

Recent Brain imaging studies (fMRI) have compared the effects of:

**Psilocybin** (D.Nutt, Carhart-Harris et al. PNAS 2012, 109(6): 2138-2143)

**Ayahuasca** ( Palhano-Fontes, F. et.al The Psychedelic State Induced by Ayahuasca Modulates the Activity and Connectivity of the Default Mode Network.. PLoS One 10(2), 2015).

**Meditation** (J. A. Brewer et al. PNAS 2011, 108 (50): 20254-20259)

and discovered that they all suppress the activity of the DMN and share some similar patterns.

**Conclusion:**

Shared neural networks are involved. This is presently an area of active research.

# Health benefits and therapeutic potential of DMT

## Inflammation and Immunomodulation

Psychedelics and immunomodulation: novel approaches and therapeutic opportunities. Attila Szabo *Frontiers in Immunology* July, 2015.

Psychedelic N,N-Dimethyltryptamine and **5-Methoxy N,N-Dimethyltryptamine** Modulate Innate and Adaptive Inflammatory Responses through the Sigma-1 Receptor of Human Monocyte-Derived Dendritic Cells. Attila Szabo et al. PLoS ONE, August 2014, Vol. 9: 8

## Neuroregulation/Neuroprotection

The Sigma-1 Receptor as a Pluripotent Modulator in Living Systems

Tsung-Ping Su et al. Trends Pharmacological Sciences 2016.

DMT stimulates neurotrophic factors (Gewirtz et al. 2002), and transcription factors (Frankel and Cunningham 2002; González-Maeso et al. 2007), associated with synaptic plasticity.

### Depression

Tanida Brown, et al. (2017): A Physician's Attempt to Self-Medicate Bipolar Depression with N,N Dimethyltryptamine (DMT), *Journal of Psychoactive Drugs*, DOI: 10.1080/02791072.2017.1344898

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